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Topical treatments for chronic plaque psoriasis (Review)

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[Intervention Review]

Topical treatments for chronic plaque psoriasis

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ABSTRACT

Background

Chronic plaque psoriasis is the most common type of psoriasis, and it is characterised by redness, thickness, and scaling. First-line management of chronic plaque psoriasis is with topical treatments, including vitamin D analogues, topical corticosteroids, tar-based preparations, dithranol, salicylic acid, and topical retinoids.

Objectives

To compare the effectiveness, tolerability, and safety of topical treatments for chronic plaque psoriasis, relative to placebo, and to similarly compare vitamin D analogues (used alone or in combination) with other topical treatments.

Search methods

We updated our searches of the following databases to February 2011: the Cochrane Skin Group Specialised Register, CENTRAL in *The Cochrane Library* (2011, Issue 2), MEDLINE (from 1948), EMBASE (from 1980), Science Citation Index (from 2008), Conference Proceedings Citation Index - Science (from 2008), BIOSIS (from 1993), Dissertation Abstracts via DialogClassic (all publication years), and Inside Conferences (all publication years).

We identified ongoing and unpublished studies from the UK Clinical Research Network Study Portfolio and the *meta*Register of Controlled Trials. We checked the bibliographies of published studies and reviews for further references to relevant trials, and we contacted trialists and companies for information about newly published studies.

A separate search for adverse effects was undertaken in February 2011 using MEDLINE and EMBASE (from 2005).

Final update searches for both RCTs and adverse effects were undertaken in August 2012. Although it has not been possible to incorporate RCTs and adverse effects studies identified through these final searches within this review, we will incorporate these into the next update.

Selection criteria

Randomised trials comparing active topical treatments against placebo or against vitamin D analogues (used alone or in combination) in people with chronic plaque psoriasis.

Data collection and analysis

One author extracted study data and assessed study quality. A second author checked these data. We routinely contacted trialists and companies for missing data. We also extracted data on withdrawals and on local and systemic adverse events. We defined long-term trials as those with a duration of at least 24 weeks.

Main results

This update added 48 trials and provided evidence on 7 new active treatments. In total, the review included 177 randomised controlled trials, with 34,808 participants, including 26 trials of scalp psoriasis and 6 trials of inverse psoriasis, facial psoriasis, or both. The number of included studies counted by Review Manager (RevMan) is higher than these figures (190) because we entered each study reporting a placebo and an active comparison into the 'Characteristics of included studies' table as 2 studies.

When used on the body, most vitamin D analogues were significantly more effective than placebo, with the standardised mean difference (SMD) ranging from -0.67 (95% CI -1.04 to -0.30; 1 study, 119 participants) for twice-daily becocalcidiol to SMD -1.66 (95% CI -2.66 to -0.67; 1 study, 11 participants) for once-daily paricalcitol. On a 6-point global improvement scale, these effects translate into 0.8 and 1.9 points, respectively. Most corticosteroids also performed better than placebo; potent corticosteroids (SMD -0.89; 95% CI -1.06 to -0.72; I^2 statistic = 65.1%; 14 studies, 2011 participants) had smaller benefits than very potent corticosteroids (SMD -1.56; 95% CI -1.87 to -1.26); I^2 statistic = 81.7%; 10 studies, 1264 participants). On a 6-point improvement scale, these benefits equate to 1.0 and 1.8 points, respectively. Dithranol, combined treatment with vitamin D/corticosteroid, and tazarotene all performed significantly better than placebo.

Head-to-head comparisons of vitamin D for psoriasis of the body against potent or very potent corticosteroids had mixed findings. For both body and scalp psoriasis, combined treatment with vitamin D and corticosteroid performed significantly better than vitamin D alone or corticosteroid alone. Vitamin D generally performed better than coal tar, but findings relative to dithranol were mixed. When applied to psoriasis of the scalp, vitamin D was significantly less effective than both potent corticosteroids and very potent corticosteroids. Indirect evidence from placebo-controlled trials supported these findings.

For both body and scalp psoriasis, potent corticosteroids were less likely than vitamin D to cause local adverse events, such as burning or irritation. Combined treatment with vitamin D/corticosteroid on either the body or the scalp was tolerated as well as potent corticosteroids, and significantly better than vitamin D alone. Only 25 trials assessed clinical cutaneous dermal atrophy; few cases were detected, but trials reported insufficient information to determine whether assessment methods were robust. Clinical measurements of dermal atrophy are insensitive and detect only the most severe cases. No comparison of topical agents found a significant difference in systemic adverse effects.

Authors' conclusions

Corticosteroids perform at least as well as vitamin D analogues, and they are associated with a lower incidence of local adverse events. However, for people with chronic plaque psoriasis receiving long-term treatment with corticosteroids, there remains a lack of evidence about the risk of skin dermal atrophy. Further research is required to inform long-term maintenance treatment and provide appropriate safety data.

PLAIN LANGUAGE SUMMARY

Skin treatments for chronic plaque psoriasis

Chronic plaque psoriasis is the most common type of psoriasis. Although any part of the body may be affected, the most commonly affected sites are the elbows, knees, and scalp. 'Topical' treatments (i.e. treatments applied to the skin) are usually tried first. These include vitamin D products, topical corticosteroids, tar-based preparations, dithranol, salicylic acid, and vitamin A products. As chronic plaque psoriasis is a long-term condition, it is important to find out which treatments work best and what adverse effects they have. This review describes average benefits of different treatments, while recognising that individuals will vary in their experience of each treatment.

The evidence was based on 177 studies, which, in total, included 34,808 people. Studies were typically about 7 weeks' long, but this ranged from 1 week to 52 weeks. Vitamin D products were found to work better than placebo (the base cream or ointment). Potent topical corticosteroids (strong, e.g. betamethasone dipropionate) and very potent (very strong, e.g. clobetasol propionate) topical corticosteroids were also effective.

Some studies compared vitamin D products directly with potent or very potent corticosteroids. These products had similar effects when applied to the body, but corticosteroids worked better than vitamin D for scalp psoriasis. Treatment that combined vitamin D with a corticosteroid was more effective than vitamin D alone and more effective than the topical corticosteroid alone. Vitamin D products generally performed better than coal tar, but studies found conflicting results when comparing vitamin D with dithranol.

Whether applied to the body or to the scalp, potent corticosteroids were less likely than vitamin D to cause 'local adverse events', such as skin irritation or burning, and people were therefore more likely to stop using vitamin D products. When studies examined whether topical treatments had effects within the body ('systemic adverse events'), we found no difference between placebo and any other treatment.

However, this may be because many trials did not properly assess systemic adverse events, rather than because there really was no difference.

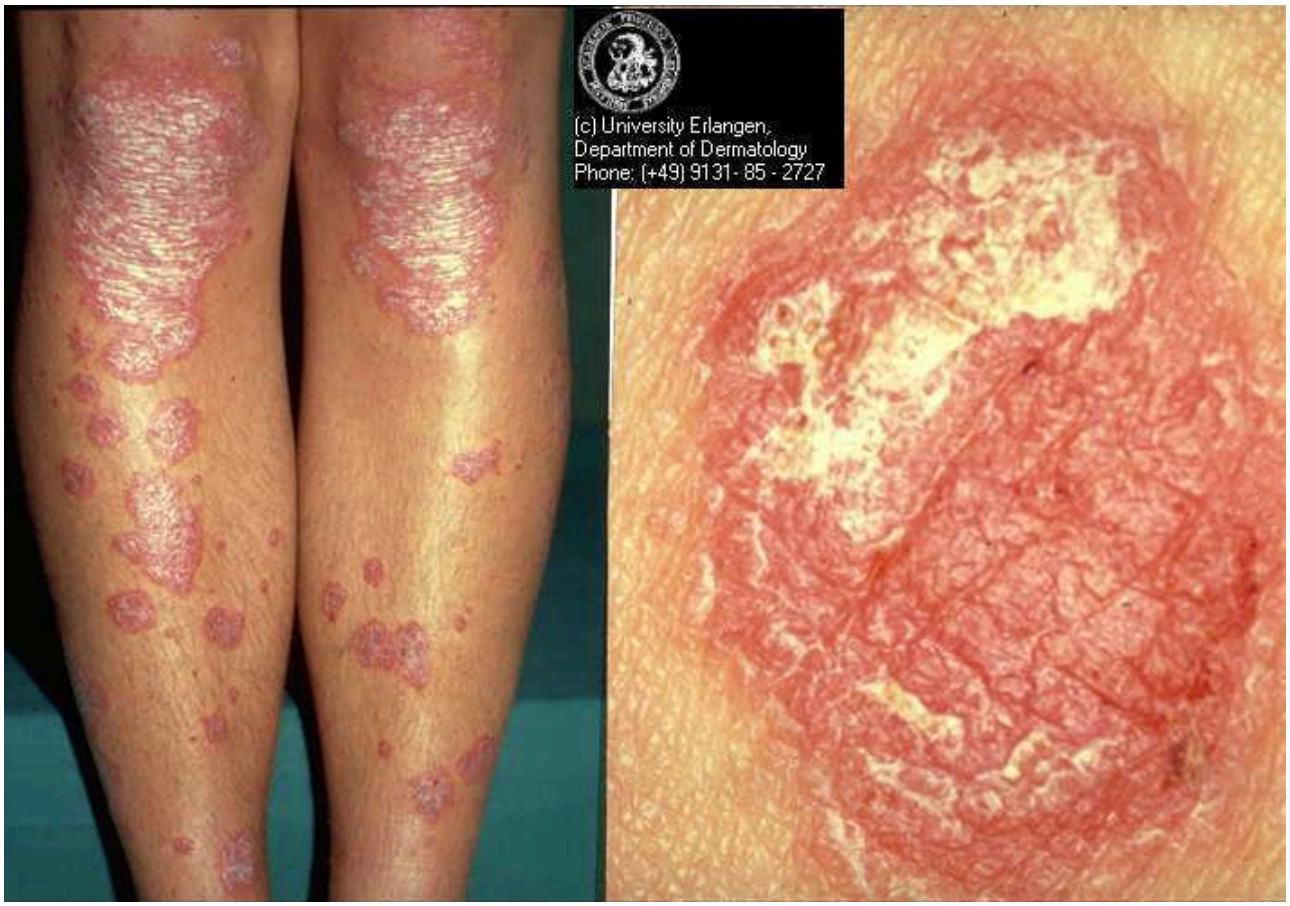
More long-term studies would help doctors and people with psoriasis decide on the best way to treat this chronic condition.

BACKGROUND

Description of the condition

Psoriasis is a chronic inflammatory skin disease with a prevalence ranging from between 1% and 2% in the UK and northern European populations (Hellgren 1967; Krueger 1984) to 0.1% to 0.3% in the Far East (Simons 1949) and China (Yip 1984). Psoriasis comprises multiple phenotypes and may be localised (e.g. to the skin-fold areas (inverse psoriasis), the palms, or the soles) or widespread. Types of widespread psoriasis include guttate, generalised pustular, and erythrodermic (Griffiths 2007). Chronic plaque psoriasis may be localised or widespread and accounts for 90% of psoriasis cases (Griffiths 2007); it is characterised by red patches of thickened skin (plaques) covered in silver scales (Figure 1). Any area of the body may be affected, but the main areas are the knees, elbows, lower back, and scalp. There is a wide spectrum of disease severity from a single plaque to involvement of more than 90% of the skin surface. Psoriasis may be classified as 'mild', 'moderate', or 'severe', although these categories are difficult to define precisely (Krueger 2000). Psoriatic arthritis accompanies the cutaneous (skin) manifestations of psoriasis in 5% to 30% of cases (Barisic-Drusko 1994; Krueger 1984; Salvarani 1995; Zanolli 1992). Recent improvements in the classification criteria may reduce the wide variation in reported prevalence of psoriatic arthritis (Taylor 2006). Psoriasis occurs in 5% of people with Crohn's disease (Lee 1990).

Figure 1. Chronic plaque psoriasis
Source: Dermis Dermatology Atlas Online (used with permission)

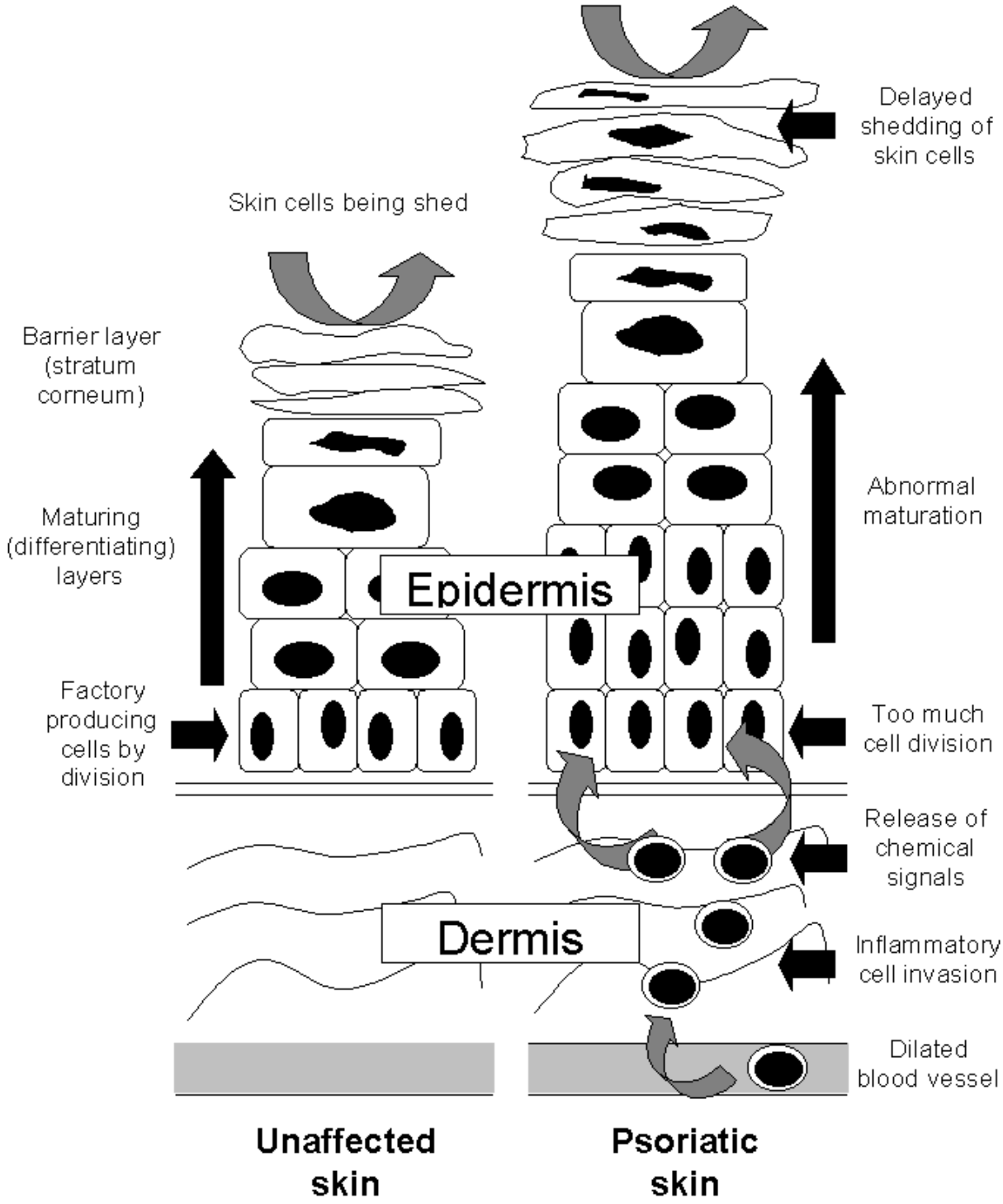


Causes

The way that psoriasis develops is complicated and appears to be influenced by many factors, including genetic changes, local trauma, infections, certain drugs (such as beta-blockers, lithium, chloroquine, and non-steroidal anti-inflammatory drugs (NSAIDs)), the duration of antipsoriatic treatments, endocrine factors, sunlight, alcohol, smoking, and stress (Tagami 1997). The skin lesions of psoriasis are shown in Figure 2, and they are characterised by cells multiplying too quickly (epidermal hyperproliferation), cells not maturing normally (abnormal keratinocyte differentiation), and the presence of cells that cause inflammation (a lymphocyte inflammatory infiltrate) (Barker 1991; Griffiths 2003; Stern 1997). Psoriasis is now recognised as an immune-mediated disorder, with tumour necrosis factor alpha (TNFα), dendritic cells, and T-cells all contributing to its pathogenesis (Griffiths 2007a). Several genes interact with environmental factors to induce the development of psoriasis, and different combinations of changes in several genes and environmental factors can produce the same clinical picture of psoriasis (Bhalerao 1998; Brandrup 1978; Farber 1974; Lomholt 1963; Willan 1808). A locus (plural = loci) is the specific location of a gene on a chromosome, and its position is defined using the letters 'p' (for a chromosome's short arm) and 'q' (for a long

arm). At least nine chromosomal psoriasis susceptibility loci were originally identified (Griffiths 2007a). The strongest association and linkage is to a locus within the major histocompatibility complex, the area affecting immune response (Genetic Analysis of Psoriasis Consortium 2010; Henseler 1992; Russell 1972; Svejgaard 1974; Tazi-Ahnini 1999a; Tazi-Ahnini 1999b; Trembath 1997). Other linkage studies have reported linkage to 4q and 17q (Matthews 1996; Tomfohrde 1994) and 16q and 20q (Nair 1997; Trembath 1997). Proinflammatory CD4-positive T helper cells produce interferon gamma (produced by Th1) or interleukin (IL)-17 (produced by Th17). These cells interact with dendritic cells, macrophages, mast cells, and neutrophils, causing inflammation (Ghoreschi 2007). A meta-analysis of 3 genome-wide association studies (GWAS) has identified 15 new susceptibility loci (Tsoi 2012) for psoriasis. This brings the total number of loci associated with psoriasis to 36. Several of these loci are involved in the regulation of the skin's innate immune response. They provide confirmation of the role of several existing biologic therapies as well as new targets for drug development.

Figure 2. The epidermis in the skin of people with and without psoriasis



Impact

Until identified as a single disease by von Hebra in 1841, psoriasis was thought to be a variant of leprosy and regarded as contagious (de Jong 1997). The misconception may persist: In a survey of people with psoriasis in 1997, almost three-quarters of respondents reported that others thought their condition was contagious, and a similar proportion feared swimming and taking part in sporting activities (Watts 1998). Psoriasis can lead to social isolation (van de Kerkhof 1997a), stigmatisation (Gupta 1998; van de Kerkhof 1997a), and fear of other people's reactions, adversely affecting the quality of daily life (Finlay 1994; Finlay 1995a; Finlay 1995b; Finlay 2001; McKenna 2003; Ortonne 2000; Richards 2003; Stern 1995).

Psychological distress induced by psoriasis may also impair the response to treatment (Fortune 2003).

Description of the intervention

Treatment of psoriasis should always be appropriate to its severity and importance to that individual: It should never be more unpleasant, intolerable, or dangerous than the disease itself (Camp 1992). Topical treatments include vitamin D analogues, topical corticosteroids, tar-based preparations, dithranol, salicylic acid, and topical retinoids (Baadsgaard 1995; Corbett 1976; Fredriksson 1980; Goeckerman 1931; Ingram 1953; Kragballe 1988; Kragballe 1989; Langner 1996; Staberg 1989; Unna 1916; Van de Kerkhof 1996a), but there is no evidence-based 'treatment ladder' by which to sequence treatments (Van de Kerkhof 2008). Emollients are generally used in a supportive role as an addition to topical treatments, to normalise hyperproliferation, differentiation, and to exert anti-inflammatory effects (Fluhr 2008). The two classes of topical treatment for psoriasis that are most commonly prescribed in developed countries are vitamin D analogues and topical corticosteroids, because they are considered more cosmetically acceptable than tar and dithranol preparations (Baadsgaard 1995; Kragballe 1988; Van de Kerkhof 1996a).

Topical corticosteroids (specifically glucocorticoids) are available in four potencies: mild, moderate, potent, and very potent, which are assessed using the vasoconstrictor assay (BMA 2012). The benefit of topical steroids is that in cream formulations, they are easy to apply, cosmetically acceptable, do not stain the skin, and rarely cause irritation. There are several adverse effects of corticosteroids, including cutaneous atrophy, rebound after discontinuation of treatment, and decreasing response to the drug (tachyphylaxis) (du Vivier 1975; Lee 1998; Kao 2003). Glucocorticoids (GC) exert their effects either via interaction with cell membranes (non-genomic effects) or downstream with the genome and via interaction with intracellular fluid in GC receptors and downstream with the genome (genomic effects). The genomic effects are of two types: "transrepression (inhibition of synthesis of regulatory proteins) and transactivation (induction of the synthesis of regulatory proteins)" (Bos 2008). Transactivation appears to mediate certain adverse reactions, such as cutaneous atrophy. Immunomodulation seems to be the result of GC-mediated transrepression, that is, silencing of proinflammatory genes, such as TNFα. Non-steroidal GC receptor ligands (selective GC receptor agonists) have recently been identified and may reduce the side-effects of GC without loss of immunosuppressive effects (Bos 2008).

The naturally occurring active metabolite of vitamin D, calcitriol (1a,25-dihydroxyvitamin D3) (Langner 1996), and two synthetic vitamin D analogues, calcipotriol (Kragballe 1988; Kragballe 1989; Staberg 1989) and tacalcitol (1a,24-dihydroxyvitamin D3) (Baadsgaard 1995; Van de Kerkhof 1996a), are effective when applied topically in psoriasis (Mason 2002a). These agents bind to vitamin D receptors (VDR), which in turn bind to vitamin D-responsive elements (VDRE) in multiple genes. 'Switching on' (transactivation of) these genes inhibits the multiplication of cells and stimulates their differentiation (Figure 2). VDRs also suppress the inflammatory component of psoriasis by inhibiting the production of proinflammatory cytokines (small proteins that affect cell-cell interaction), such as interleukin-1 (IL-1). Vitamin D analogues all have the potential to induce abnormally high levels of calcium in the blood serum (hypercalcaemia) and urine (hypercalciuria). Although calcipotriol ointment causes no elevation of total serum calcium when used at the recommended dose of 100 g per week (Mortensen 1993), there are significant elevations in both serum and urinary calcium when the dose is increased to 300 g per week (Bourke 1993a; Bourke 1994). Topical vitamin D analogues are cosmetically acceptable; they are not known to cause skin atrophy; and they are not usually associated with rebound when therapy is discontinued. However, at least 25% of people are reported to have little or no response to topical vitamin D analogues (Holick 1996; Mee 1998).

Urea or salicylic acid may be used to reduce thickness and scaling of the skin; combination with other products can improve their absorption. However, these can also irritate the skin. Topical immunosuppressants, such as methotrexate, and topical macrolactams, such as tacrolimus, are relatively new treatments, and their effectiveness, tolerability, and longer-term effects are less clear than with the more established products. This review also considers combination products involving any of the above treatments.

The Cochrane Library has three published Cochrane reviews of interventions for psoriasis. Owen 2000 assessed the impact of antistreptococcal interventions for guttate and chronic plaque psoriasis. The review found that "although both antibiotics and tonsillectomy have frequently been advocated for patients with recurrent guttate psoriasis or chronic plaque psoriasis, there is to date no good evidence that either intervention is beneficial." Chalmers 2000 reviewed all treatments, excluding antistreptococcal interventions, for guttate psoriasis. The review identified only one relevant trial and no evidence of the effectiveness of any topical interventions. Chalmers 2006 assessed interventions, including topical treatments, for chronic palmoplantar pustulosis (a disease that is closely related to psoriasis and used to be considered a variant of psoriasis). Chalmers 2006 found that topical steroids under hydrocolloid occlusion were effective in inducing remission. In addition, *The Cochrane Library* has four published Cochrane review protocols, which cover interventions for nail psoriasis (Velema 2009), interventions for scalp psoriasis (Jales 2012), phototherapy (Chen 2011), and the biological agent ustekinumab (Roberts 2011).

Why it is important to do this review

Chronic plaque psoriasis is a condition for which there is no known cure, and currently, available treatments may only temporarily clear the skin (Bonifati 1998; Griffiths 2004). Clinical practice varies between and within different countries. By focusing on topical treatments for psoriasis, either as monotherapy or in combination, this review assesses the relative effectiveness, tolerability, and safety of these treatments and so helps to determine how best to induce remission and delay recurrence in people receiving topical treatment. Table 1 provides a list of acronyms used in the review.

Structure of the Review

The structure of the review is provided to facilitate navigation:

- Objectives
- Methods
- Results
- ◦ Description of the studies
  - ◦ Risk of bias in the included studies
  - ◦ Effects of the interventions

- (1) Primary outcome measures
  - (a) Investigator's Assessment of Overall Global Improvement (IAGI)/Investigator's Global Assessment of Disease Severity (IGA)
  - (b) Total Severity Scores (TSS)
  - (c) Psoriasis Area and Severity Index (PASI)
  - (d) Patient Assessment of overall Global Improvement (PAGI)/Patient Global Assessment of Disease Severity (PGA)
  - (e) Combined end point (IAGI/TSS/PASI/PAGI)
- (2) Secondary outcome measures
  - (a) Withdrawal rates (total rate; withdrawal because of adverse events; withdrawal because of treatment failure)
  - (b) Adverse events (local and systemic)
    - (i) Findings from the main review
    - (ii) Findings from the separate search for additional studies of adverse events
  - (c) Quality of life measures
  - (d) Economic outcomes (not updated in 2011)
  - (e) Concordance or adherence with treatment (not updated in 2011)
- Discussion
- Authors' conclusions

Under 'Primary outcome measures', we report findings for each of the 19 analyses (including sensitivity analyses). We also do this under 'Secondary outcome measures' for subsections (a) and (b). We did not update the sections on Economic outcomes (2d) and Concordance (2e) in 2011 because of resource constraints.

OBJECTIVES

To compare the effectiveness, tolerability, and safety of topical treatments for chronic plaque psoriasis, relative to placebo, and to similarly compare vitamin D analogues (used alone or in combination) with other topical treatments.

METHODS

Criteria for considering studies for this review

Types of studies

We included randomised controlled trials in the review. Trials could be either placebo-controlled or head-to-head with a vitamin D preparation (head-to-head trials compare two active treatments with each other). The types of study design eligible for inclusion were as follows: parallel-group (between-patient), cross-over, and within-patient designs. For within-patient studies, where study participants serve as their own control, we included only those studies that clearly adopted a left-right design, and we excluded studies where multiple plaques were treated with more than two products. If no useful effectiveness, withdrawal, or adverse events data were available, either from the published paper or from sponsors or trialists, we excluded the study.

In addition to findings on adverse events from the main review, we undertook separate searches for additional safety and tolerability studies. The searches for longer-term adverse events included studies of any design that included humans (i.e. not only animals; either humans only or humans and animals). However, studies with fewer than 10 participants (including case reports) were not eligible for inclusion. We did not restrict the search for concordance/adherence studies by study design (i.e. non-randomised studies were eligible for inclusion).

Types of participants

People of any age with chronic plaque psoriasis affecting the body, limbs, scalp, or a combination of the aforementioned. We did not limit participant type by area of involvement, disease severity, or skin area treated.

Types of interventions

Topical treatments, including the following:

- vitamin D preparations, e.g. calcipotriol;
- corticosteroids, e.g. betamethasone valerate;
- coal tar;
- dithranol, also known as anthralin;
- salicylic acid;
- urea;
- topical retinoids;
- topical immunosuppressants, e.g. methotrexate;
- topical macrolactams, e.g. ascomycin derivatives, such as tacrolimus; and
- combination products, e.g. corticosteroids with coal tar or corticosteroids with vitamin D.

We compared topical treatments with vehicle (placebo). We also compared vitamin D analogues with other topical treatments. We selected vitamin D analogues for this comparison because they are first-line treatments in many developed countries (van de Kerkhof 1998). We based the potency of topical corticosteroids on classifications from a previous review (Mason 2002b).

The review included any topical treatment for psoriasis, except for products for which (a) no licence was obtained and (b) research into the product was discontinued. The reason for this exclusion criterion is that these products are unlikely to be of interest to people making decisions about health care, such as policy-makers, people with psoriasis, or clinicians. Although they may be of interest to researchers, lessons from the research into 'failed' molecules are likely to have been reflected in the development of subsequent products.

Trials of systemic or ultraviolet (UV) (phototherapy) treatments with adjunctive topical treatment were not eligible for inclusion in the review.

Types of outcome measures

Table 2 provides an overview of the effectiveness outcome measures included in the review. We provide details of how we used the primary outcomes to derive a 'combined end point' in the section 'Measures of treatment effect'.

Primary outcomes

1. Investigator's Assessment of Overall Global Improvement (IAGI)/Investigator's Global Assessment of Disease Severity (IGA).
2. Total Severity Scores (TSS).

3. Psoriasis Area and Severity Index (PASI).
4. Patient Assessment of overall Global Improvement (PAGI)/ Patient Global Assessment of Disease Severity (PGA).

Secondary outcomes

1. Withdrawal rates (total rate; withdrawal due to adverse events; withdrawal due to treatment failure).
2. Adverse events (local and systemic).
3. Quality of life measures.
4. Economic outcomes.
5. Concordance or adherence with treatment.

Search methods for identification of studies

We aimed to identify all relevant randomised controlled trials (RCTs) regardless of language or publication status (published, unpublished, in press, or in progress).

Electronic searches

Search strategies used for the previous version of the review (Mason 2009; see also Acknowledgements) were revised where appropriate and rerun. We did not restrict the searches by body area affected. The information specialists updated the search strategies to reflect changes in the interfaces and MeSH (Medical Subject) headings, as well as to incorporate terms for newly licensed products.

In February 2011, the following databases were searched for effectiveness RCTs of psoriasis treatments:

- the Cochrane Skin Group Specialised Skin Register (searched 8 February 2011) using the search strategy in Appendix 1;
- the Cochrane Central Register of Controlled Trials (CENTRAL) in *The Cochrane Library* (2011, Issue 2) using the search strategy in Appendix 2;
- MEDLINE via OVID (from 1948) using the strategy in Appendix 3;
- EMBASE via OVID (from 1980) using the strategy in Appendix 4;
- Science Citation Index (SCI) via the Institute for Scientific Information (ISI) Web of Knowledge interface (now known as Thomson Reuters) (from 2008) using the strategy in Appendix 5;
- Conference Proceedings Citation Index - Science (CPCI-S) via the ISI web of Knowledge interface (from 2008) using the strategy in Appendix 5;
- BIOSIS via the DialogClassic interface (from 1993) using the strategy in Appendix 6;
- Dissertation Abstracts via DialogClassic interface (from inception) using the strategy in Appendix 7;
- Inside Conferences via DialogClassic interface (from inception) using the strategy in Appendix 7;
- System for Information on Grey Literature in Europe (SIGLE) via WebSPIRS interface (search not updated) using the strategy in Appendix 8;
- National Research Register (NRR) (CD-ROM interface, issue 2004/4) using the strategy in Appendix 2; and
- the UK Clinical Research Network Study Portfolio (http://public.ukcrn.org.uk/search/) using the strategy in Appendix 2.

To comply with Cochrane policy (stipulating that reviews must be published within 12 months of the electronic searches being run), further searches for this update were run on 23, 24, and 29 August 2012. Although it was not possible to incorporate RCTs identified through this search within this review, we listed relevant references in the 'Characteristics of studies awaiting classification' tables. They will be incorporated into the next update of the review.

Searching other resources

References from published studies and reviews

We checked these for further references to relevant trials.

Unpublished literature

We routinely contacted trialists and companies for newly published studies and missing data.

The *meta*Register of Controlled Trials (http://www.controlled-trials.com/mrct/) was searched in August 2012 for ongoing and unpublished trials.

Adverse effects

On 2 February 2011, the following databases were searched for studies of adverse events of specific psoriasis treatments:

- MEDLINE via OVID (see Appendix 9); and
- EMBASE via OVID (see Appendix 10).

We limited searches to English-language papers published in the years between 2005 to 2011. In MEDLINE, the search was designed to omit records with the following publication types: 'note', 'comment', and 'editorial'.

We also considered relevant adverse effects studies identified during the screening for effectiveness trials.

These searches were updated in August 2012, identifying 537 new references. We will incorporate these studies into the next update of this review.

Concordance/adherence

We did not undertake searches for concordance/adherence in the 2011 review update because of resource constraints.

Language restrictions

There were no language restrictions when searching for effectiveness RCTs or concordance/adherence studies. We restricted searches for studies of adverse events to those published in English.

Data collection and analysis

Selection of studies

Two authors (AM and JM) screened titles and (where available) abstracts identified from the searches, and another author (MC) acted as an arbiter when necessary. In our protocol, we stated our intention that we would exclude studies meeting only some of the inclusion criteria stated above. However, this was infeasible, because we would have needed to cite large numbers of studies (over 1000). Therefore, we listed as excluded only those studies that we deemed potentially eligible for inclusion *and* for which we retrieved full papers, but which subsequently failed to meet the inclusion criteria.

For the separate search for studies exploring adverse events, we deemed studies as eligible if they addressed safety or tolerability issues, focused on drugs included in the main review, and were longer-term in follow-up (> 12 weeks). Short-term studies (with follow-up < 12 weeks) were eligible for inclusion only if they were designed specifically to consider adverse effects, tolerability, or safety. Studies that included fewer than 10 participants (including case reports) were not eligible for inclusion.

For the separate search for studies of concordance/adherence with treatment, studies were eligible if they addressed adherence with topical treatment in people with any type of psoriasis. This section was not updated because of resource constraints.

Data extraction and management

Applying methods from our original review (Mason 2002a), we summarised the major attributes of trials, including treatment forms, doses and duration, inclusion and exclusion criteria, level of blinding, within-patient or between-patient (parallel-group) design, method of generation of the randomisation sequence, concealment of allocation, numbers of participants randomised, baseline comparability, loss to follow up, primary and secondary outcomes, withdrawals, and adverse events. One reviewer (AM) extracted the data, and another reviewer (HH) checked these data.

We extracted data from trials on four primary outcomes:

1. IAGI (Investigator's Assessment of Global Improvement) or the IGA (Investigator's Global Assessment of Disease Severity).
2. TSS (Total Severity Score).
3. PASI (Psoriasis Area and Severity Index).
4. PAGI (Patient Assessment of Global Improvement) or the PGA (Patient Global Assessment of Disease Severity).

Where available, we also extracted data on quality of life, economic outcomes, and concordance/adherence.

In addition, we extracted data on withdrawal due to any reason, such as adverse events or treatment failure, as well as adverse events due to local and systemic effects.

For each outcome measure under a comparison, we included the same treatment options regardless of data availability (see Data and analyses). We did this for three reasons. Firstly, an inclusive approach makes clear that there is an absence of data, not that data have been omitted. Secondly, if data subsequently become available when the review is updated in future, the correct structure is in place for data entry. Thirdly, this approach ensures treatments are always ordered identically regardless of outcome.

Assessment of risk of bias in included studies

Assessment of methodological quality

The quality assessment included an evaluation of each included study, based on the following components, which are considered to be associated with biased estimates of treatment effect (Juni 2001):
(a) the method of generation of the randomisation sequence;
(b) the method of allocation concealment - we considered this 'adequate' if the assignment could not be foreseen;
(c) who was blinded/not blinded (participants, clinicians, outcome assessors); and
(d) how many participants were lost to follow up.

In addition, the quality assessment included the following:
(e) baseline assessment of the participants for age, sex, duration, and severity of psoriasis; and
(f) baseline comparability of intervention and control groups.

We recorded the information in the 'Characteristics of included studies' section.

Measures of treatment effect

Summarising primary outcomes with standardised mean differences

We extracted data on four primary outcome measures:

- IAGI (Investigator's Assessment of Global Improvement) or the IGA (Investigator's Global Assessment of Disease Severity)
- TSS (Total Severity Score)
- PASI (Psoriasis Area and Severity Index)
- PAGI (Patient Assessment of Global Improvement) or the PGA (Patient Global Assessment of Disease Severity)

Trials often reported more than one measure, but none of the trials reported all measures. We therefore devised a 'combined end point', which allowed more data to contribute to an overall analysis and facilitated treatment comparisons. We labelled this 'super' outcome as outcome (e) throughout the review.

We constructed the combined end point by taking IAGI (or IGA) data when available, and failing this, TSS, PASI, or PAGI (PGA) data in that order of availability. For PASI and TSS, some included trials reported change scores and others reported end point scores. In view of the mix of end point/change scores and of the variation in scale, we analysed findings using a standardised mean difference statistic (SMD) in a random-effects model. Table 2 summarises the characteristics of the outcome measures.

We also expressed SMDs in physical units adjusting by the appropriate pooled standard deviation estimate (Table 3).

Secondary outcomes

We summarised data on adverse events, quality of life measures, economic outcomes, and concordance as narratives. We summarised withdrawal data using the risk difference (RD) metric and pooled using a random-effects model. We felt this was more appropriate than a fixed-effect model since definitions of withdrawal and adverse events vary between trials.

Unit of analysis issues

Within-patient studies are statistically analogous to cross-over studies, and results should be adjusted by the correlation coefficient (Section 16.4.6, *Cochrane Handbook for Systematic Reviews of Interventions*; Higgins 2011). No study included in the review reported this statistic, and we did not have access to patient-level data, so could not estimate it directly.

On the subject of cross-over studies, the *Cochrane Handbook for Systematic Reviews of Interventions* states (Section 16.4.5; Higgins 2011) the following: "A common situation is that means and standard deviations (or standard errors) are available only for measurements on E [experimental group] and C [control group] separately. A simple approach to incorporating cross-over trials in a meta-analysis is thus to take all measurements from intervention

E periods and all measurements from intervention C periods and analyse these as if the trial were a parallel-group trial of E versus C. This approach gives rise to a unit-of-analysis error (see Chapter 9, Section 9.3) and should be avoided unless it can be demonstrated that the results approximate those from a paired analysis, as described in Section 16.4.4. The reason for this is that confidence intervals are likely to be too wide, and the trial will receive too little weight, with the possible consequence of disguising clinically important heterogeneity. Nevertheless, this incorrect analysis is conservative, in that studies are under-weighted rather than over-weighted. While some argue against the inclusion of cross-over trials in this way, the unit-of-analysis error might be regarded as less serious than some other types of unit-of-analysis error."

Consequently, we included within-patient studies as though they were parallel-group studies, accepting that they are under-weighted. To explore whether it was appropriate to combine these trials, we undertook two sensitivity analyses. First, we considered how effect size varied for within- and between-patient studies. If the magnitude of effect varied consistently between the two study designs, this strongly suggested a non-zero correlation coefficient and an appropriateness to separate the trials. Second, we used sensitivity analysis to explore the impact on pooled findings of varying the correlation coefficient (rho) for within-patient studies. This analysis used the generic inverse variance measure, with SMDs and their standard errors estimated from the formulae in the *Cochrane Handbook for Systematic Reviews of Interventions* (Section 16.4.6.4) (Higgins 2011). These estimated SMDs differ slightly from those that RevMan estimates for continuous outcomes, even when the correlation coefficient is zero (which is the assumption implicit in the latter model).

The analyses found no evidence that the magnitude of effect varied consistently. Within-patient trials did not consistently demonstrate smaller or larger effects than between-patient trials. Varying the value of rho had no significant effect on the findings: As rho increased, the effect size increased and the confidence intervals (usually) widened, but the magnitudes of changes were small and non-significant at the 5% level.

In the interests of statistical purity, these trials could (a) be reported separately or (b) be removed altogether. The drawback of option (a) is that it makes an already complex review even more complex and less accessible; the disadvantage of option (b) is that it removes data that might be of interest to clinicians and people with psoriasis. On balance, we preferred to report relevant randomised data wherever possible to help inform pragmatic decision-making.

Dealing with missing data

We routinely contacted trialists and companies for missing data.

Where studies did not report estimates of variance, we derived them from confidence intervals (CIs) or from P values where possible. Where we could not obtain estimates of variance, we imputed them deterministically by pooling the standard deviations of treatment cohorts fully reported in trials and adjusted for scale size.

We made separate imputations for each outcome measure (see Table 3):

- for within-patient studies;
- for between-patient (parallel-group) studies;
- for end point scores;
- for change scores; and
- for scalp trials.

Within-patient designs are statistically analogous to cross-over studies, and the precision of their findings within a meta-analysis needs adjustment for within-patient correlation. We attempted to explore this by sensitivity analysis.

Data synthesis

We analysed findings using a standardised mean difference statistic (SMD) in a random-effects model. However, this model cannot perfectly address all the sources of design complexity that arise when summarising findings across studies. Three of the main sources of complexity are listed below. Other sources of complexity include variation in trial duration, disease severity, participant demographics, treatment application method, dosing frequency, drug potency and vehicle.

Study design (within- versus between-patient)

Trials were either between-patient or within-patient designs. The former randomise participants into separate (parallel) groups; the latter randomise treatments to the left or right side of the same participant. Within- and between-patient trials have different variance structures. Moreover, the two responses (left and right) of within-patient studies may be correlated (See Unit of analysis issues for further details).

Absence of a simple one-to-one correspondence between papers, trials, and comparisons

There were instances of single papers reporting either multiple trials or multiple analyses within a single trial. Therefore, simple counts of numbers of participants and numbers of studies contributing data to the analysis were misleading, and we made adjustments accordingly (Table 4). Thus, these numbers may not match the numbers estimated in RevMan, which does not account for these factors.

Body area targeted for treatment

Whereas the majority of trials investigated chronic plaque psoriasis on the body, some trials focused on scalp psoriasis; some reported findings for both scalp and body psoriasis; and some were of inverse (flexural) or facial psoriasis. One trial of body and scalp psoriasis reported overall outcomes (IAGI/PAGI), a scalp-only outcome (TSS), and a body-only outcome (modified PASI) (Van de Kerkhof 2002a). Ortonne 2010 reported findings separately for treatment of the body and treatment of the face. We previously used sensitivity analysis to investigate the scalp psoriasis trials (Mason 2009), but in this update we analysed trials of inverse psoriasis (comparisons 16 and 17) and scalp trials (comparisons 18 and 19) separately from the trials of body psoriasis (see Sensitivity analysis).

Subgroup analysis and investigation of heterogeneity

We examined findings by agent class (as our primary analysis) and individual topical agent (within-class analysis).

When comparing trials both within and across therapeutic classes, the summary estimates may demonstrate substantial

heterogeneity. Ideally, we would seek to identify the reasons for individual differences, but publications rarely report sufficient detail to make a robust investigation feasible. Reasons might include differences in trial design, length of follow-up, disease severity, participant selection, adherence, adequacy of concealment of allocation, adequacy of blinding, and source of funding (Mason 2002a).

The *Cochrane Handbook for Systematic Reviews of Interventions* explicitly endorses the combination of 'apples and oranges' "if they are used to contribute to a wider question about fruit" (Section 9.5.1; Higgins 2011). Our purpose was to identify whether classes of topical treatments work and are safe. To this end, there is a fundamental difference between heterogeneity that makes it uncertain whether individual people with psoriasis will derive any benefit from a treatment and heterogeneity that makes the size of a positive benefit imprecise. Clinicians and those with psoriasis will still value information about a treatment that is beneficial even though its magnitude is poorly understood. However, we clearly stated the presence of heterogeneity where it occurred and used the *Cochrane Handbook for Systematic Reviews of Interventions* as a guide to interpretation (Section 8.5.2; Higgins 2011).

Sensitivity analysis

We used a meta-analysis with a random-effects estimation both for measures of effect and for pooling of risk differences for adverse events. We quantified heterogeneity using the I^2 statistic. If we identified outliers, we undertook a sensitivity analysis to investigate the implications of their exclusion on the pooled summary statistics. In addition, we undertook sensitivity analyses to investigate the impact of within-patient versus between-patient trials, and to explore the impact on pooled findings of varying the correlation coefficient (see Unit of analysis issues). In some comparisons, there were no, or relatively few, studies that included both within-patient and between-patient designs, few participants contributing data, or both. We used the following criteria to help decide whether we should have included an analysis in the sensitivity analysis:

- frequently-used products in clinical practice; and
- for within-/between-patient sensitivity analysis: whether it included both within-patient and between-patient designs

Where at least two within-patient trials were included in a pooled comparison, we explored the potential influence of the correlation coefficient.

Based on these criteria, we selected six comparisons (analyses 1, 2, 3, 4, 7, and 18) for sensitivity analysis. To ensure sufficient data were available, we analysed the combined end points. These analyses cover vitamin D analogues, dithranol, and corticosteroids, which are amongst the most frequently used products in clinical practice.

Other

We involved a consumer throughout the review process to help ensure the readability of the final review.

RESULTS

Description of studies

Results of the search

For this update, the RCT searches identified 3749 records:

- MEDLINE: 1312
- EMBASE: 2008
- SCI: 253
- BIOSIS: 44
- Dissertation Abstracts: 1
- Inside Conferences: 0
- CENTRAL: 70
- UK Clinical Research Network: 20
- Skin Group Specialised Register: 41

The total number of new records assessed after deduplication against each other and previously identified records was 2637.

We added records from the searches in February 2011 to those identified from searches run in 2008 (see Mason 2009). The total number of records screened for this review over time is now 5414.

From the 2011 searches, we retrieved 148 papers and screened these for eligibility. (Some papers were multiple reports of the same trial).

In 40 trials (some of which were consequently excluded), some or all outcome data were missing. We contacted trialists or sponsors to request missing data, receiving data for 25 of these trials. We excluded trials that reported no useable outcome data. We did not contact trialists or sponsors for missing adverse events or withdrawal data, although some sponsors provided this spontaneously.

We included 48 new randomised controlled trials in the updated review. Compared with the previous version of this review (Mason 2009), studies were larger (mean number of participants: 284 versus 164), had a longer treatment duration (10 weeks versus 6 weeks) and follow up (11 weeks versus 8 weeks), and were more likely to be parallel-group in design (88% versus 63%). The new studies were also more likely to include an active control group (60% versus 43%) and patient-reported outcomes (44% versus 24%), and there were relatively more scalp trials (21% versus 12%). The 48 trials provided evidence on 7 new active treatments.

Included studies

The updated review included 177 studies, with 34,808 participants.

The number of included studies counted by RevMan is 190, because we entered each study reporting a placebo and an active comparison into the 'Characteristics of included studies' table as two studies.

Of the included studies, 106 of these were placebo-controlled; 84 compared treatments head-to-head, with 15 trials reporting both placebo-controlled and head-to-head comparisons. The 15 trials reporting both head-to-head and placebo comparisons contributed only once to the analysis of study characteristics, unless the trial involved entirely distinct participants in its placebo-controlled and active-controlled analyses. For example, the trial by

Guenther 2002 compared treatments against each other (Guenther 2002 (H)) and against placebo (Guenther 2002 (P)). This study contributed only once to the analysis of study characteristics (number of participants, proportion of males, etc). However, two trials reported placebo and head-to-head analyses involving entirely separate participants (Barker 1999 (H) and Barker 1999 (P); Grattan 1997 (H) and Grattan 1997 (P)). Therefore, the total number of studies contributing data to the analysis of study characteristics and quality assessment was 177 (106 placebo + 84 head-to-head -15 double-counted trials (with placebo and active comparators) and 2 trials that each report 2 separate studies (Barker 1999 (H) and Barker 1999 (P); Grattan 1997 (H) and Grattan 1997 (P)).

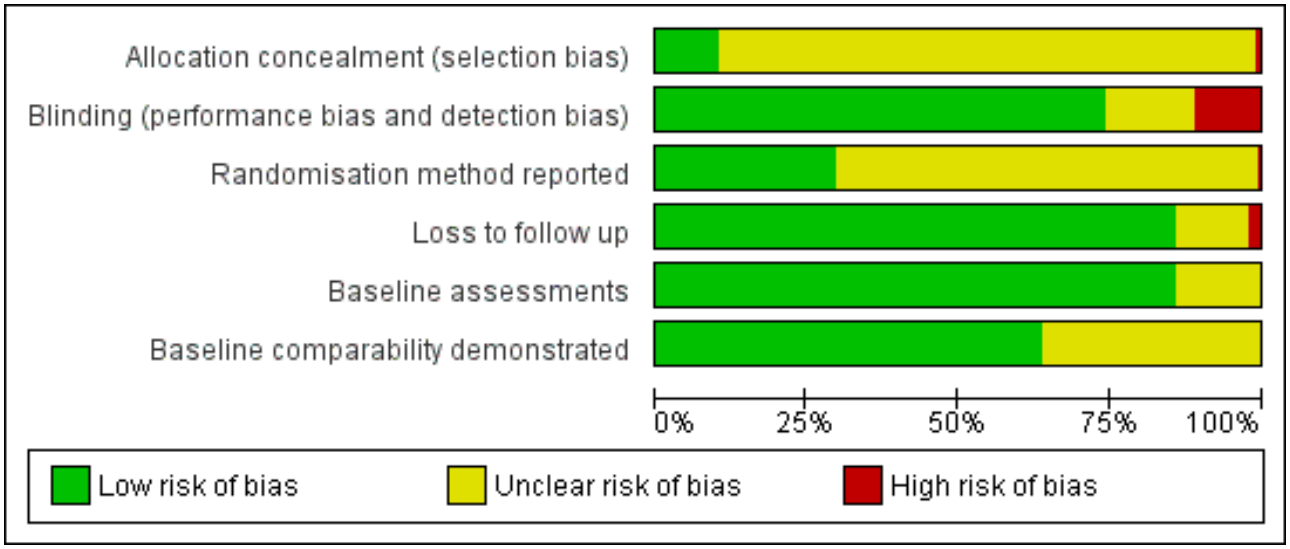
There were 26 trials of scalp psoriasis (Barrett 2005; Buckley 2008; Cook-Bolden 2010; Duweb 2000; Elie 1983; Ellis 1988; Franz 1999; Franz 2000; Green 1994; Jarratt 2004; Jemec 2008 (H) and Jemec 2008 (P); Kiss 1996; Klaber 1994; Klaber 2000b; Köse 1997; Kragballe 2009; Lepaw 1978; Luger 2008; Olsen 1991; Pauporte 2004; Poulin 2010; Reygagne 2005; Shuttleworth 1998; Tyring 2010; Van de Kerkhof 2002a; Van de Kerkhof 2009). Six trials investigated inverse psoriasis, facial psoriasis, or both (Gribetz 2004; Kreuter 2006 (H) and Kreuter 2006 (P); Lebwohl 2004; Liao 2007; Ortonne 2003; Ortonne 2010). One trial evaluated psoriasis in children (Oranje 1997). Most trials were conducted in ambulatory care settings, but four trials were of hospitalised participants (Grattan 1997 (H) and Grattan 1997 (P); Kragballe 1991a; Monastirli 2000; Van der Vleuten 1995).

One hundred and twenty-three trials adopted a between-patient (parallel-group) design; 53 were within-patient studies; and one trial used both designs (Henneicke-v. Z. 1993). The trial by Levine (Levine 2010 (H) and Levine 2010 (P)) was a within-patient trial that randomised participants to two of seven treatment options. Therefore, the pair-wise comparisons we analysed (e.g. calcipotriol versus placebo) included a mixture of within- and between-patient designs: Some participants received calcipotriol on one side and placebo on the other; other participants received calcipotriol on one side and another active treatment on the other side.

The 177 studies included 34,808 participants. Of these studies, 133 provided data on the age of participants. The mean age of all participants for which studies provided data was 47.2 years (range = 2 to 97 years) (N = 28,921). Data on the gender of participants (N = 28,941) were available from 140 studies. Overall, participants were more likely to be male; the mean proportion of males was 56.7% (range = 30% to 100%).

Almost half the studies (77/177 = 44%) did not clearly report the overall baseline severity of study participants (e.g. participants with mild to moderate disease) (Figure 3). One hundred studies explicitly reported baseline severity or reported sufficient information on global severity scores, such as the mean and variation in baseline PASI or the percentage of body surface area (BSA) affected, to allow us to infer global severity using guidance on the interpretation of severity scores (Finlay 2005; Krueger 2000). In the 100 trials where severity was assessable, we classified participant severity as mild (5 studies), mild to moderate (36 studies), mild to severe (6) or very severe (2 studies), moderate (12 studies), moderate to severe (27 studies), moderately severe (2 studies), moderately severe to very severe (2 studies), and severe (8 studies).

Figure 3. Risk of bias graph: review authors' judgements about each risk of bias item presented as percentages across all included studies.



Seventy-seven studies provided insufficient information to allow an assessment of clinical severity to be made; we could not make assessments of the clinical characteristics of participants in studies reporting only the mean PASI (with no information about variation) or reporting only localised (e.g. TSS) scores. One example of a study that included participants with a wide range of severity scores is the trial by Cunliffe 1992, where the mean baseline PASI was 9.0 (suggesting moderately severe disease, according to Finlay 2005), but where individual participant scores ranged from 0.6 to 41.2. Another example is the study by Olsen 1996 (1), where participant BSA involvement averaged 12%, but ranged from 1% to 80%. It is unclear how participant severity was distributed within these ranges (i.e. whether these extremes were 'outliers' or whether a sizeable proportion of participants were clustered at the extreme ends of the distribution).

Even where trialists classified participant severity, it was not always clear that this was consistent with published guidance, which itself does not always provide consistent messages. For example, Finlay 2005 states that a PASI score > 10, a BSA involvement > 10%, or Dermatology Life Quality Index (DLQI) score > 10 constitutes severe disease. However, Krueger 2000 argues that BSA is unreliable as an indicator of severity, which is better proxied by quality of life assessments. However, the included studies rarely assessed quality of life. Given this lack of clarity and the absence of adequate severity data in around half (44%) of the included studies, we could not use sensitivity analysis to investigate the impact of baseline participant severity, nor could we reliably use severity to investigate inter-study heterogeneity.

All 177 studies provided data on treatment duration (mean: 7 weeks; range = 1 to 52) and follow-up duration (mean: 9 weeks; range = 2 to 52), where 'follow-up duration' was defined as including the treatment period. Commonly used outcomes assessed by the studies included the following:

- individual signs (erythema, scaling, induration) (105/177 studies = 59%);
- Total Severity Score, Total Sign Score, or equivalent (83 studies = 47%);
- PASI (65 studies = 37%);
- IAGI/IGA (113 studies = 64%); and
- PAGI/PGA (52 studies = 29%).

Outcome measures employed by small numbers (< 5) of trials included the following;

- Local Psoriasis Severity Index (scale not reported);
- Jacoby assessment score (0 to 7 score transformed to % clinical improvement); and
- investigator assessment of skin staining.

Trials seldom assessed quality of life (9 trials = 5%).

Participant-reported outcomes included the following:

- overall participant assessment (relative efficacy, speed of response, irritation, staining, ease of application);
- participant global assessment of acceptability of treatment, participant assessment of likely adherence; and
- participant assessment of cosmetic acceptability.

We grouped placebo-controlled trials by type of treatment (e.g. vitamin D products) and grouped head-to-head trials in a similar way (e.g. vitamin D versus potent corticosteroid). We included 19 comparisons in the review. Since many trials did not specify participants' disease severity, it was not possible to use severity to inform pooling decisions. The primary analysis explored the results of pooling within these 19 comparison groups using a random-effects model. In addition, we undertook sensitivity analyses for five comparisons using the 'combined end point'. These analyses used pooled data to explore within- and between-patient trial variation.

In 90% (159/177) of the studies included in the review, participants applied their own treatments. Nurses applied treatments in 1 trial (Geilen 2000); participants' parents delivered some care in a trial of childhood psoriasis (Oranje 1997); and the delivery method was unclear in 16 studies.

Excluded studies

We excluded 43 studies, of which we had newly added 16 studies in this update of the review (see 'Characteristics of excluded studies' tables). The most common reasons for exclusion from the update were that the study did not report adequate data and requests for missing data from trialists or sponsors were unsuccessful (N = 5), or that the study did not provide a comparison of interest (N = 6). Two studies were not randomised (Kaur 2004; Vena 2005); one study assessed multiple plaques (Buder 2010); and two evaluated unlicensed products that were not subsequently marketed (Agrawal 2010; Rhemus 2006). We also excluded trials of nail psoriasis that we had previously included (Mason 2009), as the topic is now covered by a separate Cochrane review (de Vries 2013).

Studies awaiting classification

Update searches were run on 23, 24, and 29 August 2012. For each database searched, we have shown below the numbers of records identified. The total number of new records assessed (after deduplication against each other and previously identified records) was 1865. Relevant studies from these searches (10 references) are listed in the Studies awaiting classification section, but we did not include them in the main review.

- MEDLINE: 1203
- EMBASE: 1140
- SCI: 129
- BIOSIS: 37
- Dissertation Abstracts: 1
- Inside Conferences: 0
- CENTRAL: 26
- UK Clinical Research Network: 0
- Skin Group Specialised Register: 67

Ongoing studies

The *meta*Register of Controlled Trials was searched for ongoing and unpublished trials during the final searches for this review in August 2012 http://www.controlled-trials.com/mrct/ using the following phrases:

- "psor* AND topical NOT completed", which retrieved 127 hits;
- "psor* AND calcipot% NOT completed", which retrieved 7 hits;
- "psor* AND vitamin D NOT completed", which retrieved 21 hits;
- "(psor* AND topical AND corticost%) NOT completed", which retrieved 63 hits; and
- "psor* AND tar NOT completed", which retrieved 8 hits.

In total, we identified 10 potentially relevant trials. We provide details in the 'Characteristics of ongoing studies' tables.

Risk of bias in included studies

We extracted and tabulated data on six quality indicators. Summary findings are presented narratively, with characteristics for all studies presented in the 'Characteristics of included studies' tables. Figure 3 is a graphical representation of the overview of the risk of bias. All included trials were randomised, but only 47/177 (27%) clearly reported the method used to randomise participants.

Concealment of treatment allocation was explicitly adequate in 15 trials, but most trials (151/177 = 85%) blinded participants to treatment allocation. Most (164/77 = 93%) trials reported loss to follow up data, and 142 trials (80%) demonstrated that groups were comparable at baseline.

Allocation

Of the 177 studies assessed for quality, 15 (8.5%) explicitly achieved adequate concealment of treatment allocation (low risk of bias). Concealment was unclear in the majority of studies (160 studies = 90.4%), so the risk of bias was also unclear. Concealment was inadequate in 2 studies (1.1%) (high risk of bias) (Figure 3).

Blinding

Most (131/177 = 74%) studies were double-blind, with 20 studies adopting a single-blind (investigator-only) approach. Eighteen studies were 'open' (no blinding), and in the remaining 8 studies, the blinding approach adopted was unclear (Figure 3). Twenty trials explicitly stated that the outcome assessor was blinded to treatment allocation. However, the outcome assessor will also have been blinded in double-blind trials where the investigator also assessed outcomes.

Incomplete outcome data

We defined 'loss to follow up' as the number of enrolled participants who failed to contribute data for the analysis.

Of the 177 studies assessed for quality, 13 (7%) provided no data on loss to follow up. For the remaining 164 studies, the mean percentage loss to follow up was 6.1% (range = 0% to 31.5%). Fifty-one studies reported that there was no loss to follow up. Four studies lost more than 25% of their participants to follow-up, and we classified them as having high risk of bias for this dimension (Henneicke-v. Z. 1993; Lin 2007; Maier 2004; Weinstein 2003) (see Figure 3).

Where studies did not report estimates of variance, we derived them from confidence intervals (CIs) or from P values where possible. Where we could not obtain estimates of variance, we imputed them (see Table 3). In total, we imputed estimates of variance for at least 1 outcome measure in 45 studies (7 of which were scalp trials); details are in the notes section of the 'Characteristics of included studies' tables.

Other potential sources of bias

Method of generation of the randomisation sequence

Only randomised controlled trials were eligible for inclusion in the review. However, 130 studies (73%) did not clearly report the randomisation method used. Fourteen studies reported a block randomisation design, and 27 studies used computerised methods (5 studies used both). Four reported that sequential allocation had been used (3 of these studies were published in the 1970s); 1 study used the toss of a coin; and another study used a sealed envelope method. It could be argued that we should have excluded trials with sequential allocation from the review, but this might discriminate against studies with better reporting methods in favour of those not stating the randomisation method.

Baseline assessment of the participants for age, gender, and clinical characteristics

We coded studies as follows: y (baseline assessments for age, gender, and clinical characteristics), p (at least one type of assessment), and NR (not reported or unclear). Most studies (121/177 = 68.4%) provided baseline assessments of age, gender, and clinical characteristics. Forty-three studies (24.3%) provided a partial assessment, and 13 studies (7.3%) reported no relevant data.

Baseline comparability of intervention and control groups

We coded studies as follows: y (comparability demonstrated, low risk of bias), p (comparability partially demonstrated, risk of bias unclear), and NR (comparability not demonstrated or unclear, risk of bias unclear or high, depending on whether groups were clearly non-comparable). Studies could demonstrate comparability by reporting data for each group, by reporting the outcome of statistical tests (e.g. P values), or both. One hundred and sixteen studies (65.5%) demonstrated that the groups were comparable at baseline; 27 studies (15.3%) demonstrated partial comparability; and 34 studies (19.2%) did not clearly demonstrate comparability between the groups. No study found that groups were non-comparable (high risk of bias).

Data extraction method for the review

To minimise errors and reduce potential biases being introduced by review authors, the recommended approach is that data extraction should be undertaken independently by at least two people, preferably from complementary disciplines (Section 7.6.2, Higgins 2011). However, in this review, one reviewer (AM) extracted the data, and another reviewer (HH) checked these data.

Effects of interventions

Primary outcome measures

The review analyses 19 comparisons. Of these, 8 are topical treatment versus placebo analyses, and 11 are head-to-head analyses of a topical treatment against a vitamin D analogue (i.e. 1 commonly used class of treatments). Some analyses are a 'catch all' category; for example, analysis 6 includes 'Other treatment versus placebo', which covers 26 treatments for body psoriasis for which there is less research evidence (both in terms of numbers of studies and numbers of participants contributing data). Similarly, analysis 15 incorporates 12 head-to-head comparisons of vitamin D analogues for body psoriasis that are not easily classified under the other head-to-head comparisons. Scalp trials (comparisons 18 and 19) and trials of inverse psoriasis (comparisons 16 and 17) are analysed separately from the trials of body psoriasis.

Table 4 summarises the 19 analyses. Table 2 gives details of the outcome measures considered. The number of participants and number of studies are adjusted manually from those reported in the Tables and Figures to allow for within-patient studies, studies contributing more than once to a single analysis, and studies contributing to multiple analyses. Therefore, numbers of participants and studies reported sometimes differ from the numbers estimated by RevMan.

For each of the 19 analyses, we analysed data on 5 effectiveness outcome measures, where available. The fifth measure is a

'combined end point' that uses data from the four primary outcome measures.

(a) Investigator's Assessment of Overall Global Improvement (IAGI)/Investigator's Global Assessment of Disease Severity (IGA)

Analysis 1: Vitamin D analogues versus placebo

This comparison included eight vitamin D analogues for body psoriasis (see Analysis 1.1 and Table 5). Twenty trials with 3771 participants reported IAGI data on 7 of these treatments. Thirteen trials were between-patient design, and 7 were within-patient studies. Treatment duration ranged from 4 weeks to 12 weeks. The pooled SMD across all treatments was -0.95 (95% CI -1.17 to -0.74; I^2 statistic = 89.0%), but there was considerable variation between treatments, so we removed pooling across subgroups. Six treatments were significantly more effective than placebo, with the effect size ranging from -0.67 (becocalcidiol twice daily) to -1.66 (paricalcitol once daily). There was considerable between-study variation in the IAGI SMD for calcitriol. The pooled effect was -1.03 (95% CI -1.71 to -0.36), but this ranged from -0.26 (95% CI -0.99 to 0.47) for Langner 2001 (P) to -3.11 (95% CI -3.57 to -2.66) for Perez 1996. The magnitude of the IAGI SMD for the Perez study was the highest across all comparisons and treatments. For the 'combined end point' of this analysis, we explored the impact of removing this trial from the pooled findings using sensitivity analysis. The presence of considerable heterogeneity within this subgroup means that the estimated average benefit should be interpreted with caution (Higgins 2011).

Analysis 2: Corticosteroid (potent) versus placebo

This comparison included 10 potent corticosteroids for body psoriasis (see Analysis 2.1 and Table 6), although no effectiveness data were available for budesonide. Nine studies with 1867 participants reported IAGI data on 6 of these 10 treatments. Eight trials were between-patient design, and one was a within-patient study (Stein 2001). Treatment duration ranged from 3 to 12 weeks. The SMD across all 6 treatments for IAGI was -1.00 (95% CI -1.18 to -0.82; I^2 statistic = 57.6%). All six treatments performed statistically significantly better than placebo.

Analysis 3: Corticosteroid (very potent) versus placebo

This comparison included three very potent corticosteroids for treatment of psoriasis of the body (see Analysis 3.1 and Table 7). Five studies with 515 participants reported IAGI data on 2 of the 3 treatments. There were four between-patient trials and 1 within-patient study (Beutner 2006). Treatment duration ranged from two to four weeks. The IAGI SMD across both treatments was -1.87 (95% CI -2.38 to -1.36; I^2 statistic = 78.7%). Both clobetasol propionate and halobetasol performed statistically significantly better than placebo. In Analysis 18.1, we present placebo-controlled scalp trials of very potent corticosteroids.

Analysis 4: Dithranol versus placebo

Our review did not identify any study comparing dithranol against placebo and which reported IAGI data.

Analysis 5: Vitamin D combination products versus placebo

This comparison included treatment with combined calcipotriol and betamethasone dipropionate used either once or twice daily on the body (see Analysis 5.1 and Table 8). Five parallel-group studies with 2058 participants contributed data on both dosing options. Treatment duration ranged from four to eight weeks. The IAGI SMD across treatments was -1.44 (95% CI -1.76 to -1.12; I^2 statistic = 89.4%), with twice-daily combination treatment (SMD -1.90; 95% CI -2.09 to -1.71) achieving a significantly larger effect than once-daily treatment (SMD -1.21; 95% CI -1.50 to -0.91). However, the difference between once- and twice-daily dosing was not statistically significant when benefit was assessed using the PASI (see Analysis 5.3). In Analysis 18.1, we report placebo-controlled trials of combination vitamin D/steroid treatments for scalp psoriasis.

Analysis 6: Other treatment versus placebo

This comparison comprised all other treatments for psoriasis of the body not included in the first five analyses; therefore, we removed pooling. None of the studies assessed the same treatment, which means that findings should be interpreted with caution.

In total, we included 26 treatments in this analysis (see Analysis 6.1 and Table 9). Eight studies with 364 participants reported IAGI data on 8 of these 26 treatments. Four trials were between-patient design, and four were within-patient studies. Treatment duration ranged from 3 to 12 weeks.

Four treatments performed statistically significantly better than placebo: anti-IL-8 monoclonal antibody cream; betamethasone 17-valerate 21-acetate plus tretinoin plus salicylic acid, indigo naturalise 1.4% ointment, and methotrexate gel. The effect size for the IAGI ranged from -0.56 (Sutton 2001; methotrexate gel) to -2.14 (Lin 2008; indigo naturalise 1.4% ointment).

In four treatments, the difference relative to placebo was not statistically significant: hexafluoro-1,25-dihydroxyvitamin D3, kukui nut oil, oleum horwathiensis, and platelet aggregation activating factor (PAF). No treatment was statistically significantly less effective than placebo.

Analysis 7: Vitamin D analogues versus corticosteroid (potent)

This comparison included eight vitamin D analogue-potent corticosteroid contrasts for body psoriasis (see Table 10). Eight studies with 2655 participants reported IAGI data for 6 of the 8 intervention-comparator contrasts (see Analysis 7.1). Seven trials were between-patient design, and one was a within-patient study (Medansky 1996). Treatment duration ranged from three to eight weeks. Overall, there was no statistically significant difference between vitamin D analogues and potent corticosteroids: The SMD across all 6 treatments for IAGI was 0.17 (95% CI -0.04 to 0.37; I^2 statistic = 83.4%). In light of the high level of heterogeneity and inconsistency across treatments (Higgins 2011). We removed pooling. Vitamin D analogues performed statistically significantly better than one potent corticosteroid. This finding came from a single between-patient study in which 99 participants contributed data (Bruce 1994). The SMD for calcipotriol against fluocinonide 0.05% ointment was -0.58 (95% CI -0.99 to -0.18; I^2 statistic = NA). Calcipotriol was statistically significantly less effective than both diflorasone diacetate 0.05% ointment (SMD 0.27; 95% CI 0.02 to 0.52) and betamethasone dipropionate (SMD 0.43; 95% CI 0.28 to 0.58; I^2 statistic = 50.3%). We found no statistically significant difference between calcipotriol and betamethasone valerate, calcitriol and betamethasone dipropionate, or calcitriol and betamethasone valerate.

Analysis 8: Vitamin D analogues versus corticosteroid (very potent)

This comparison included one vitamin D analogue, calcipotriol ointment, versus a very potent corticosteroid contrast, clobetasol propionate foam, for psoriasis of the body (see Table 11 and Analysis 8.1). One study with 42 participants reported IAGI data. Koo 2006 was a between-patient study with a treatment duration of two weeks, which found no significant difference between the treatments (SMD 0.19; 95% CI -0.42 to 0.80).

Analysis 9: Vitamin D combined with corticosteroid versus corticosteroid

This comparison considered vitamin D analogues-steroid combination against potent or very potent corticosteroids for body psoriasis (see Analysis 9.1 and Table 12). The comparison included three contrasts: calcipotriol plus betamethasone dipropionate versus betamethasone dipropionate, calcipotriol plus betamethasone dipropionate versus clobetasol propionate, and calcipotriol plus clobetasol propionate versus clobetasol propionate.

Four between-patient trials reported IAGI data for 1991 participants on 2 of the 3 intervention-comparator contrasts. Treatment duration ranged between two and eight weeks. As these treatment comparisons were very different, we only pooled subtotals. In all but one trial (Fleming 2010 (H)), combination treatment was significantly more effective than corticosteroid alone. Three of the four trials compared calcipotriol/betamethasone dipropionate against betamethasone dipropionate (SMD -0.40; 95% CI -0.52 to -0.27; I^2 statistic = 41.8%), and one trial compared combined treatment with calcipotriol and clobetasol against clobetasol alone (SMD -0.69; 95% CI -1.22 to -0.15).

Analysis 10: Vitamin D alone or in combination versus dithranol

This comparison considered vitamin D analogues against dithranol (Analysis 10.1 and Table 13). We identified three intervention-comparator contrasts: calcipotriol versus dithranol, calcitriol versus dithranol, and tacalcitol versus dithranol. Five between-patient trials reported IAGI data for 1108 participants on 2 of these 3 intervention-comparator contrasts. Treatment duration ranged from 8 weeks to 12 weeks. There was some variation in the dithranol regimens employed by trials and in the baseline severity of trial participants. These factors may help explain the high level of heterogeneity found in the pooled results.

The SMD for the IAGI was -0.24 (95% CI -0.72 to 0.25; I^2 statistic = 93.0%). The presence of considerable heterogeneity means that the estimated average benefit should be treated with caution and pooling was therefore removed (Higgins 2011). Data from four trials contributed to the SMD for the calcipotriol versus dithranol: -0.43 (95% CI -0.85 to -0.01; I^2 statistic = 89.3%), indicating that calcipotriol was statistically significantly more effective than dithranol. Three of these four trials found a significant difference in favour of calcipotriol (Berth Jones 1992b; Christensen 1999; Wall 1998), but the trial by Van de Kerkhof 2006 found outpatient treatment with short contact dithranol to be significantly more effective than calcipotriol alone.

Data from one trial contributed to the SMD for the calcitriol versus dithranol: 0.51 (95% CI 0.13 to 0.88; I^2 statistic = NA), indicating that dithranol was statistically significantly more effective than calcitriol.

Analysis 11: Vitamin D alone or in combination versus other vitamin D analogue

Our review identified three intervention-comparator contrasts in this comparison: calcipotriol versus calcitriol, calcipotriol versus tacalcitol, and calcipotriol versus maxacalcitol for body psoriasis (see Analysis 11.1 and Table 14). Three trials involving 498 participants contributed IAGI data for all 3 intervention-comparator contrasts (one trial for each contrast). Two trials were between-patient, and one was within-patient in design (Barker 1999 (H)). Treatment duration ranged from 8 to 12 weeks. The SMD for the IAGI was -0.06 (95% CI -0.51 to 0.38; I^2 statistic = 82.2%). The presence of substantial heterogeneity reflects differences in the findings from the two intervention-comparator contrasts underlying this statistic. We found a statistically significant difference in favour of calcipotriol in the analysis against tacalcitol (SMD -0.47; 95% CI -0.73 to -0.21), but there was no significant difference relative to calcitriol (SMD 0.00; 95% CI -0.25 to 0.25) or between calcipotriol and maxacalcitol (SMD 0.43; 95% CI -0.12 to 0.98). In light of the inconsistency of results across treatments, we only pooled subtotals (Higgins 2011).

Analysis 12: Vitamin D alone or in combination versus vitamin D + corticosteroid

Our review identified 12 intervention-comparator contrasts for body psoriasis, involving 3 vitamin D analogues, 2 combination products, and 7 different corticosteroids (see Analysis 12.1 and Table 15). Eleven parallel-group trials involving 4791 participants contributed IAGI data for 9 of these 12 intervention-comparator contrasts. Treatment duration ranged from two to eight weeks. There were no IAGI data for three contrasts: calcipotriol versus calcipotriol plus diflucortolone valerate, calcipotriol versus calcipotriol plus fluocinonide acetonide, and calcitriol versus calcitriol plus diflucortolone valerate.

Overall, vitamin D alone appeared to be less effective than vitamin D plus corticosteroid: The SMD for the IAGI was 0.48 (95% CI 0.32 to 0.65; I^2 statistic = 86.9%). This finding applied to all but two of the intervention-comparator contrasts: There was no statistically significant difference between twice-daily calcipotriol and a regimen of calcipotriol (morning) plus betamethasone valerate (night time) (SMD 0.27; 95% CI -0.19 to 0.74) (Kragballe 1998b), or between once-daily calcipotriol and once-daily treatment with a combined product containing calcipotriol and hydrocortisone (SMD 0.14; 95% CI -0.06 to 0.33) (Ortonne 2010). The study by Ortonne 2010 also reported findings separately for the face (see Analysis 17.1).

In light of the observed heterogeneity between the intervention-comparator contrasts, we only pooled subtotals (Higgins 2011).

Analysis 13: Vitamin D alone or in combination versus other treatments: complex regimens

This comparison summarises findings on complex regimens for body psoriasis, defined here as treatment sequences that do not consist of a simple head-to-head comparison between two active treatments (see Analysis 13.1 and Table 16). We identified 12 intervention-comparator contrasts, and IAGI data were available for 10 of these. Data from 2755 participants contributed to the IAGI analysis, based on findings from seven trials. Six of the trials were between-patient (parallel-group) in design, and one was a within-patient study (Austad 1998). Trial duration varied between 6 and 12 weeks. As the interventions and comparators were highly variable

and because two trials each contributed three pair-wise contrasts, we did not pool the data.

Six intervention-comparator contrasts for which IAGI data were available found a significant difference between regimens. A two-week regimen with clobetasol propionate followed by four weeks' treatment with calcipotriol was more effective than six weeks of monotherapy with calcipotriol (SMD 0.60; 95% CI 0.18 to 1.02). All treatments were applied twice-daily in this within-patient study (Austad 1998).

The remaining five more effective regimens all involved once-daily treatment with a combined product containing calcipotriol and betamethasone dipropionate, and the same study (White 2006 (P)) reported three contrasts. This study involved an initial 'treatment' phase consisting of 4 weeks' treatment with the combined product, followed by an 8-week maintenance phase. In one maintenance phase, participants received placebo ointment for 8 weeks. This was significantly less effective than maintenance with once-daily calcipotriol (SMD 0.27; 95% CI 0.12 to 0.41), and it was also less effective than maintenance with once-daily calcipotriol on weekdays and the combined product at the weekend (SMD 0.51; 95% CI 0.37 to 0.66). When these two comparator regimens were compared directly (White 2006 (H)), the alternating regimen using weekday/weekend treatments during the maintenance phase was significantly more effective than once-daily calcipotriol for maintenance (SMD 0.26; 95% CI 0.11 to 0.40). Kragballe 2004 compared 3 12-week treatment regimens, 2 of which were 'complex'. When we compared these complex regimens, eight weeks' once-daily combination treatment with calcipotriol and betamethasone dipropionate, followed by four weeks of once-daily calcipotriol was significantly less effective than a regimen consisting of four weeks' once-daily combination treatment, followed by eight weeks of once-daily calcipotriol on weekdays and the combined product at weekends (SMD 0.24; 95% CI 0.08 to 0.40). A separate trial compared 8 weeks with tacalcitol to combination ointment for 4 weeks, followed by calcipotriol for 4 weeks (Ortonne 2004). Participants applied all treatments once daily (at night time). Monotherapy with tacalcitol was significantly less effective than the complex regimen (SMD 0.54; 95% CI 0.36 to 0.72).

In 4 of the 10 intervention-comparator contrasts for which IAGI data were available, there was no significant difference in effect. The study by Kragballe 2004 (see paragraph above) found no difference between twice-daily calcipotriol and the two comparator complex regimens. One regimen consisted of eight weeks' once-daily treatment with a combined product containing calcipotriol and betamethasone dipropionate, followed by four weeks of once-daily calcipotriol. Relative to calcipotriol monotherapy, the SMD for the IAGI was -0.12 (95% CI -0.29 to 0.04). When compared with a regimen consisting of four weeks' once-daily treatment with a combined product containing calcipotriol and betamethasone dipropionate, followed by eight weeks of once-daily calcipotriol on weekdays and the combined product at weekends, twice-daily calcipotriol appeared to be slightly less effective, although the difference was not statistically significant (SMD 0.13; 95% CI -0.04 to 0.29).

Yang 2009 compared a six-week course of twice-daily calcipotriol with a complex routine using halometasone and calcipotriol. For two weeks participants applied halometasone in the morning and calcipotriol at night; over the next two weeks, halometasone was applied twice daily at weekends and calcipotriol twice daily during the week. For the final two weeks, treatment reverted to twice-daily calcipotriol. Although there was a trend in favour of the complex regimen (SMD 0.41; 95% CI -0.05 to 0.86), the difference was not statistically significant.

Lahfa 2003 compared two different vitamin D products combined with a very potent corticosteroid. In the initial phase, participants applied dual therapy (clobetasol propionate in the mornings and the vitamin D analogue (calcipotriol or calcitriol) at night) until achieving clearance or marked improvement or until 4 weeks had elapsed. Participants then switched to a monotherapy maintenance phase with the vitamin D product for the remainder of the 12-week study period. The IAGI results showed the 2 treatment regimens to be equivalent: -0.19 (95% CI -0.54 to 0.16).

Analysis 14: Vitamin D alone or in combination versus other treatment: long-term studies (> 24 weeks)

This comparison included active-controlled studies of psoriasis of the body that were at least 24 weeks in duration (see Analysis 14.1 and Table 17). One longer-term placebo-controlled trial of the body (Katz 1991a) and two long-term scalp trials (Luger 2008; Poulin 2010) did not meet the inclusion criteria for this comparison, and they are evaluated elsewhere (Analysis 2, Analysis 19, and Analysis 18, respectively).

One trial was included in this comparison; Kragballe 2006 was a between-patient trial that compared three 52-week regimens with all treatments used once daily:

- first, combination treatment with calcipotriol and betamethasone dipropionate;
- second, alternating treatment with combination therapy for 4 weeks, then calcipotriol for 4 weeks; and
- third, combination therapy for 4 weeks, then calcipotriol for 48 weeks.

In total, 297 participants contributed IGA data to the analysis. Data were unsuitable for pooling because the same participants contributed to more than one analysis.

According to the investigators' assessment, there was no significant difference between the three long-term regimens. One year's combination therapy was not significantly better than either the alternating regimen (SMD -0.09; 95% CI -0.36 to 0.18) or the regimen of treatment with 4 weeks of combination therapy followed by 48 weeks of calcipotriol (SMD -0.18; 95% CI -0.47 to 0.10). In both these comparisons, combination therapy achieved a larger absolute benefit, but the difference was not statistically significant. When alternating therapy was compared with the regimen of 4 weeks' combination therapy followed by 48 weeks of calcipotriol, the SMD for the IAGI also indicated the two regimens were not statistically significantly different: -0.09 (95% CI -0.37 to 0.19).

Analysis 15: Vitamin D analogues versus other treatment

This comparison incorporated all other vitamin D head-to-head comparisons of treatments for psoriasis of the body (excluding inverse psoriasis) that had not already been included (see Analysis 15.1 and Table 18). We included 12 intervention-comparator contrasts, with IAGI data available for 6 of these contrasts. Eight between-patient trials and 2 within-patient trials provided data for 1386 participants. Trial duration ranged between 4 and 12 weeks.

In light of the pharmacological diversity amongst the comparators, we only pooled data within subgroups.

According to the investigator's global assessment, twice-daily calcipotriol was significantly more effective than coal tar polytherapy (SMD -0.59; 95% CI -0.87 to -0.31; I^2 statistic = 0%). Once-daily vitamin D was significantly less effective than a twice-daily application (SMD -0.24; 95% CI -0.38 to -0.09; I^2 statistic = 0%). This contrast included a comparison of once- versus twice-daily dosing of calcipotriol (SMD -0.27; 95% CI -0.48 to -0.06) and a dosing comparison combination treatment with calcipotriol and betamethasone dipropionate (SMD -0.20; 95% CI -0.41 to 0.00).

In the remaining four intervention-comparator contrasts, no significant difference was found between twice-daily calcipotriol and the comparators. This finding held for the comparison against coal tar monotherapy (SMD -0.53; 95% CI -1.74 to 0.68; I^2 statistic = 91.1%), against betamethasone dipropionate ointment and salicylic acid (SMD -0.06; 95% CI -0.33 to 0.22; I^2 statistic = NA), against tacrolimus ointment (SMD -0.22; 95% CI -0.60 to 0.16; I^2 statistic = NA), and against vitamin B12 cream (SMD -0.55; 95% CI -1.33 to 0.24; I^2 statistic = NA).

Two of the three trials comparing calcipotriol with coal tar monotherapy found a significant difference in favour of calcipotriol; the other trial found a significant difference in favour of coal tar (Alora-Palli 2010). This apparent contradiction may reflect different formulations of coal tar, treatment durations, or different baseline disease severity.

Analysis 16: Flexural/facial psoriasis: placebo-controlled trials

This comparison included placebo-controlled trials of topical treatments for inverse or facial psoriasis (see Analysis 16.1 and Table 19). Evidence on four treatments was found in this comparison: the potent steroid betamethasone valerate; the vitamin D analogue calcipotriol; and two topical calcineurin inhibitors, pimecrolimus and tacrolimus. We only found one trial that evaluated tacrolimus ointment (Lebwohl 2004), but the study did not report any effectiveness data suitable for this review. However, the study did contribute data on adverse events and withdrawal rates.

IAGI outcome data were available for one of the four topical treatments for inverse psoriasis. One 8-week between-patient study with 47 participants (Gribetz 2004) reported placebo-controlled data on pimecrolimus 1% cream, which demonstrated a statistically significant difference in favour of twice-daily pimecrolimus (SMD -1.07; 95% CI -1.69 to -0.45).

Analysis 17: Flexural/facial psoriasis: vitamin D alone or in combination versus other treatment

This comparison included head-to-head trials of treatments for inverse psoriasis, which compared vitamin D with an active control (see Analysis 17.1 and Table 20). We identified five intervention-comparator contrasts. Four treatments were compared with calcipotriol: once-daily betamethasone valerate, combined treatment with calcipotriol and hydrocortisone, calcitriol, and pimecrolimus. Calcitriol was compared with tacrolimus.

Two between-patient studies contributed IAGI data from 457 study participants on 2 of the 5 intervention-comparator contrasts. Trial duration ranged from six to eight weeks. When applied once daily to inverse psoriasis, calcipotriol was significantly less effective than combined treatment with calcipotriol and hydrocortisone (SMD 0.30; 95% CI 0.11 to 0.50) (Ortonne 2010). However, there was no significant difference in effect between twice daily treatment with calcitriol and tacrolimus (SMD 0.42; 95% CI -0.15 to 0.98) (Liao 2007).

Analysis 18: Scalp psoriasis: placebo-controlled trials

This comparison included placebo-controlled trials of treatments for scalp psoriasis (see Analysis 18.1 and Table 21). We included evidence on 11 treatments in this comparison, with IAGI data available for 9 treatments. Ten trials, 9 of which were between-patient studies, contributed data from 2472 participants. One study was a within-patient trial (Lepaw 1978). Trial duration ranged between two and eight weeks. IAGI data were not available for betamethasone valerate or ciclopirox olamine shampoo.

Eight treatments for scalp psoriasis that were assessed using the IAGI scale were significantly more effective than placebo. The least effective treatment was calcipotriol (SMD -0.72; 95% CI -1.28 to -0.16; I^2 statistic = 69.2%), and the most effective treatment was clobetasol propionate (SMD -1.73; 95% CI -1.99 to -1.48; I^2 statistic = 14.3%). Combination treatment with calcipotriol and betamethasone dipropionate was also effective (SMD -0.97; 95% CI -1.61 to -0.32; I^2 statistic = 90.2%). Data from the three very potent corticosteroids were pooled (amcinonide, clobetasol propionate, halcinonide). The SMD across these treatments was -1.57 (95% CI -1.85 to -1.28; I^2 statistic = 49.7%). Only salicylic acid was not significantly more effective than placebo (SMD -0.86; 95% CI -1.79 to 0.06).

Analysis 19: Scalp psoriasis: vitamin D alone or in combination versus other treatment

This comparison included head-to-head trials of treatments for scalp psoriasis in which one of the interventions was a vitamin D product (used either as monotherapy or in combination with another product) (see Analysis 19.1 and Table 22). We identified six intervention-comparator contrasts, and IAGI data were available for five of these contrasts. All studies were parallel-group in design (between-patient). Ten studies contributed IAGI data from 5175 participants, and trial duration ranged from 4 to 52 weeks.

Vitamin D for scalp psoriasis was significantly less effective than potent steroids, either alone or in combination with vitamin D. Specifically, calcipotriol was less effective than three comparator treatments: betamethasone dipropionate (SMD 0.48; 95% CI 0.32 to 0.64; I^2 statistic = 60.4%), betamethasone valerate (SMD 0.37; 95% CI 0.20 to 0.55; I^2 statistic = 0%), and combination treatment with calcipotriol and betamethasone dipropionate (SMD 0.64; 95% CI 0.44 to 0.84; I^2 statistic = 82.3%). Combination treatment (calcipotriol/betamethasone dipropionate) was significantly more effective than betamethasone dipropionate alone (SMD -0.18; 95% CI -0.26 to -0.10; I^2 statistic = 0%). The efficacy of calcipotriol and coal tar polytherapy was similar: SMD -0.24 (95% CI -0.73 to 0.25; I^2 statistic = 91.1%).

(b) Total Severity Scores (TSS)

Analysis 1: Vitamin D analogues versus placebo

Our review included eight vitamin D analogues for body psoriasis in this comparison (see Analysis 1.2 and Table 5). Nineteen studies reported TSS data with 2647 participants contributing data. Nine

trials were between-patient design, and 10 were within-patient studies. Treatment duration ranged from 4 weeks to 12 weeks. The average effect size across all 8 treatments for TSS was -1.04; (95% CI -1.33 to -0.74; I^2 statistic = 93.0%), but two of these treatments were not significantly more effective than placebo. The high level of heterogeneity means that the estimated average benefit should be treated with caution; there was considerable variation between effective treatments, with the TSS ranging from -0.46 (becocalcidiol twice daily) to -2.15 (paricalcitol once daily). Therefore, we removed pooling across subgroups (Higgins 2011).

Four studies contributed data for the SMD for the TSS of calcitriol (SMD -1.22; 95% CI -2.38 to -0.07), but there was considerable heterogeneity within the subgroup (I^2 statistic = 98.3%). One of the studies (Van de Kerkhof 1989) found no statistically significant difference between calcitriol and placebo (SMD -0.06; 95% CI -0.94 to 0.81), whereas the study by Perez 1996 found a large and statistically significant difference (-4.03; 95% CI -4.56 to -3.50). We considered this finding in more detail in the 'combined end point' section (e) below.

Analysis 2: Corticosteroid (potent) versus placebo

Our review included 10 potent corticosteroids for body psoriasis in this comparison (see Analysis 2.2 and Table 6). Seven studies reported TSS data contributed by 553 participants on 8 of these 10 treatments. Six trials were between-patient studies, and there was one within-patient design (Ormerod 1997). Treatment duration ranged from 2 to 12 weeks. The average effect size across all 8 treatments for TSS was -0.77 (95% CI -1.01 to -0.52; I^2 statistic = 46.7%). We found all treatments, except for diflorasone diacetate, to be statistically significantly superior to placebo: SMD -0.32; 95% CI -0.73 to 0.09).

Analysis 3: Corticosteroid (very potent) versus placebo

Of the three very potent corticosteroids for body psoriasis included in this comparison, TSS data were available only for clobetasol propionate (see Analysis 3.2 and Table 7). Three studies, all of which were between-patient trials, reported TSS data for 545 participants. Treatment duration ranged from two to four weeks. The SMD for the TSS was -1.35 (95% CI -1.80 to -0.89; I^2 statistic = 75.3%). In Analysis 18.2, we reported TSS data on the use of very potent steroids on the scalp.

Analysis 4: Dithranol versus placebo

This comparison considered dithranol against placebo (see Analysis 4.2 and Table 23). Three within-patient trials reported TSS data for 47 participants. Treatment duration ranged from three to eight weeks. The SMD for the TSS was -1.06 (95% CI -1.66 to -0.46; I^2 statistic = 37.4%).

Analysis 5: Vitamin D combination products versus placebo

Our review did not identify any trial reporting TSS data for this comparison.

Analysis 6: Other treatment versus placebo

This comparison comprised all other treatments for body psoriasis that were not included in the first five comparisons. None of the studies assessed the same treatment, which means that findings should be interpreted with caution.

In total, we included 26 treatments in this analysis (see Analysis 6.2 and Table 9). Seventeen studies with 907 participants reported TSS data on 17 of these 26 treatments. Five trials were between-patient design, and 12 were within-patient studies. Treatment duration ranged from 3 to 12 weeks.

Ten treatments performed significantly better than placebo: anti-IL-8 monoclonal antibody cream, calcipotriene 0.005% ointment + nicotinamide, fish oil plus occlusion, hexafluoro-1,25-dihydroxyvitamin D3, indigo naturalise 1.4% ointment, methotrexate gel, mycophenolic acid ointment, oleum horwathiensis, PTH (1-34) in Novasome cream®, and tazarotene. The effect size for the TSS ranged from -0.48 (Levine 2010 (P); calcipotriene 0.005% ointment + nicotinamide) to -2.31 (Holick 2003; PTH (1-34) in Novasome cream®).

In seven treatments, the difference relative to placebo was not statistically significant: kukui nut oil, NG-monomethyl-L-arginine (L-NMMA) cream, nicotinamide 1.4%, polymyxin B cream, topical sirolimus, topical tacrolimus, and tar.

Analysis 7: Vitamin D analogues versus corticosteroid (potent)

There were eight vitamin D analogue-potent corticosteroid comparisons for body psoriasis (see Analysis 7.2 and Table 10). Six studies with 891 participants reported TSS data for 5 of the 8 intervention-comparator contrasts. Two trials were between-patient design, and four were within-patient studies. Treatment duration ranged from three to six weeks. The SMD across all 5 treatments for TSS indicated that there was no significant difference between the vitamin D derivatives and potent corticosteroid: SMD 0.11 (95% CI -0.22 to 0.44; I^2 statistic = 86.7%). However, there was considerable variation between the individual contrasts underlying the pooled effect. In light of this heterogeneity, we removed pooling (Higgins 2011).

In two of the five vitamin D-potent corticosteroid comparisons, the vitamin D analogue performed statistically significantly better than the potent corticosteroid: The SMD for calcipotriol against fluocinonide 0.05% ointment was -0.50 (95% CI -0.92 to -0.07; I^2 statistic = NA) (Bruce 1994). Similarly, the comparison of calcipotriol against betamethasone valerate showed a significant difference in favour of calcipotriol (SMD -0.26; 95% CI -0.41 to -0.11), a finding also based on a single study (Kragballe 1991a).

In three comparisons, the vitamin D analogue was statistically significantly less effective than the potent corticosteroid: calcipotriol versus diflorasone diacetate (SMD 0.40; 95% CI 0.15 to 0.65), calcitriol versus betamethasone dipropionate (SMD 0.27; 95% CI 0.02 to 0.51), and tacalcitol versus betamethasone valerate (SMD 0.41; 95% CI 0.09 to 0.74).

Analysis 8: Vitamin D analogues versus corticosteroid (very potent)

Our review did not identify any study of psoriasis of the body that compared vitamin D analogues against very potent corticosteroids and that reported TSS data.

Analysis 9: Vitamin D combined with corticosteroid versus corticosteroid

This comparison considered vitamin D analogues-steroid combination against potent or very potent corticosteroid for body psoriasis (see Analysis 9.2 and Table 12). One four-week between-patient trial reported TSS data for 122 participants with moderate

to severe psoriasis (Menter 2009). The combined treatment with calcipotriol and betamethasone dipropionate was found to be significantly less effective than clobetasol propionate spray alone (0.45; 95% CI 0.09 to 0.81).

Analysis 10: Vitamin D alone or in combination versus dithranol

This comparison considered vitamin D analogues against dithranol (see Analysis 10.2 and Table 13). We identified three intervention-comparator contrasts: calcipotriol versus dithranol, calcitriol versus dithranol, and tacalcitol versus dithranol. Three between-patient trials and 1 within-patient trial (Grattan 1997 (H)) reported TSS data for 386 participants. Treatment duration ranged from four weeks to eight weeks. There was some variation in the dithranol regimens employed by trials and in the baseline severity of trial participants. These factors may help explain the substantial heterogeneity found in the pooled results (Higgins 2011).

The SMD for the TSS was -0.27 (95% CI -0.73 to 0.20; I^2 statistic = 80.6%). Data from two trials contributed to the SMD for the calcipotriol versus dithranol: -0.54 (95% CI -1.16 to 0.08; I^2 statistic = 71.2%) (Christensen 1999; Grattan 1997 (H)). Data from one trial contributed to the SMD for the calcitriol versus dithranol: 0.13 (95% CI -0.24 to 0.50; I^2 statistic = NA) (Hutchinson 2000). Data from one trial contributed to the SMD for the tacalcitol versus dithranol: -0.18 (95% CI -0.60 to 0.25; I^2 statistic = NA) (Farkas 1999). Therefore, neither the summary statistic for the TSS nor the pooled data for individual intervention-comparator contrasts provided evidence of a statistically significant advantage of a vitamin D analogue over dithranol or vice versa.

Analysis 11: Vitamin D alone or in combination versus other vitamin D analogue

Our review identified three intervention-comparator contrasts for body psoriasis in this comparison: calcipotriol versus calcitriol, calcipotriol versus tacalcitol, and calcipotriol versus maxacalcitol (see Analysis 11.2 and Table 14). Three trials involving 563 participants contributed TSS data for all 3 of these intervention-comparator contrasts. Two trials were between-patient, and one was within-patient in design (Barker 1999 (H)). Treatment duration ranged from 8 to 12 weeks. The SMD for the TSS indicated that there was a statistically significant difference in favour of calcipotriol: SMD -0.31; 95% CI -0.55 to -0.06; I^2 statistic = 46.9%. When assessed by the TSS, calcipotriol was statistically significantly more effective than calcitriol (SMD -0.32; 95% CI -0.57 to -0.07). This finding contrasts with the IAGI assessment from the same study, which found no significant difference (see Ji 2008; Analysis 11.1). Calcipotriol was also significantly more effective than tacalcitol (SMD -0.45; 95% CI -0.68 to -0.22) and similar in efficacy relative to maxacalcitol (SMD 0.13; 95% CI -0.41 to 0.68).

Analysis 12: Vitamin D alone or in combination versus vitamin D + corticosteroid

Our review identified 12 intervention-comparator contrasts for body psoriasis, involving 3 vitamin D analogues, 2 combination products, and 7 different corticosteroids (see Analysis 12.1 and Table 15). One 4-week parallel-group trial contributed TSS data from 301 participants for 1 of these 12 intervention-comparator contrasts (Huang 2009). Twice-daily calcipotriol was found to be statistically significantly less effective than once-daily treatment with a combined product containing calcipotriol and betamethasone dipropionate (SMD 0.25; 95% CI 0.03 to 0.48).

Analysis 13: Vitamin D alone or in combination versus other treatments: complex regimens

This comparison summarises findings on complex regimens for body psoriasis, defined here as treatment sequences that do not consist of a simple head-to-head comparison between two active treatments (see Analysis 13.2 and Table 16). We identified 12 intervention-comparator contrasts and TSS data were available for one of these. Data from 1 6-week within-patient trial with 46 participants (Austad 1998) contributed to the TSS analysis. Austad 1998 compared six weeks of twice-daily calcipotriol with a regimen of two weeks' treatment with clobetasol propionate followed by four weeks with calcipotriol. The complex regimen was significantly more effective than monotherapy with calcipotriol (SMD 0.63; 95% CI 0.21 to 1.05).

Analysis 14: Vitamin D alone or in combination versus other treatment: long-term studies (> 24 weeks)

We did not identify any relevant study that provided TSS data for this comparison.

Analysis 15: Vitamin D analogues versus other treatment

This comparison incorporated all other vitamin D head-to-head comparisons of treatments for psoriasis of the body (excluding inverse psoriasis) that had not already been included (see Analysis 15.2 and Table 18). We included 12 intervention-comparator contrasts, with TSS data available for 6 of these contrasts. Five between-patient trials and 2 within-patient trials provided data from 898 participants. Trial duration ranged between 6 and 12 weeks. In light of the pharmacological diversity of the comparators, we only pooled data within subgroups.

According to the TSS assessment, twice-daily calcipotriol was significantly more effective than coal tar polytherapy (SMD -0.51; 95% CI -0.86 to -0.16; I^2 statistic = NA). In the remaining five intervention-comparator contrasts, we found no significant difference between twice-daily calcipotriol and the comparators.

Analysis 16: Flexural/facial psoriasis: placebo-controlled trials

This comparison included placebo-controlled trials of topical treatments for inverse or facial psoriasis (see Analysis 16.2 and Table 19). Evidence on four treatments was found in this comparison: the potent steroid betamethasone valerate; the vitamin D analogue calcipotriol; and two topical calcineurin inhibitors, pimecrolimus and tacrolimus. We found only one placebo-controlled trial that evaluated tacrolimus ointment (Lebwohl 2004), but the study did not report any effectiveness data suitable for this review. However, the study did contribute data on adverse events and withdrawal rates.

TSS data were available for one of the four topical treatments for inverse psoriasis. One 8-week between-patient study contributed data on pimecrolimus 1% cream from 57 participants (Gribetz 2004), 10 participants more than those with an investigator's assessment (see Analysis 16.1). Findings from the TSS were consistent with those of the IAGI: the SMD for the TSS also found a statistically significant difference in favour of twice-daily pimecrolimus (SMD -1.37; 95% CI -1.95 to -0.79).

Analysis 17: Flexural/facial psoriasis: vitamin D alone or in combination versus other treatment

This comparison included head-to-head trials of treatments for inverse psoriasis, which compared vitamin D with an active control (see Analysis 17.2 and Table 20). We identified five intervention-comparator contrasts. Four treatments were compared with calcipotriol: once-daily betamethasone valerate, combined treatment with calcipotriol and hydrocortisone, calcitriol, and pimecrolimus. Calcitriol was compared with tacrolimus.

Two 6-week studies contributed TSS data from 124 study participants on 2 of the 5 intervention-comparator contrasts. Calcipotriol was significantly less effective than calcitriol (SMD 0.61; 95% CI 0.28 to 0.94) (Ortonne 2003). In this within-patient study, participants applied treatments twice daily to 'sensitive areas', including the face, hairline, retro-auricular, and flexural areas. When they applied treatments to the facial and genitofemoral areas, there was no significant difference in effect between twice-daily treatment with calcitriol and tacrolimus (SMD 0.29; 95% CI -0.27 to 0.85) (Liao 2007). In this between-patient study, participants applied both treatments twice daily.

Analysis 18: Scalp psoriasis: placebo-controlled trials

This comparison included placebo-controlled trials of treatments for scalp psoriasis (see Analysis 18.2 and Table 21). We included evidence on 11 treatments in this comparison, with TSS data available for 10 treatments. Twelve between-patient trials contributed data from 2897 participants. Trial duration ranged between two and eight weeks. TSS data were not available for halcinonide (classed as a very potent corticosteroid).

Eight of the 10 treatments for scalp psoriasis that were assessed using the TSS scale were significantly more effective than placebo. The least effective treatment was calcipotriol (SMD -0.44; 95% CI -0.64 to -0.25; I^2 statistic = 0%), and the most effective were the 2 very potent steroids, amcinonide (SMD -1.58; 95% CI -1.98 to -1.18) and clobetasol propionate (SMD -1.53; 95% CI -1.77 to -1.28; I^2 statistic = 46.3%). Combination treatment with calcipotriol and betamethasone dipropionate was also effective (SMD -0.92; 95% CI -1.42 to -0.43; I^2 statistic = 83.2%).

We pooled data from the two potent corticosteroids, betamethasone valerate and betamethasone dipropionate (SMD -1.13; 95% CI -1.44 to -0.81; I^2 statistic = 52.2%). We also pooled data from the two very potent corticosteroids, amcinonide and clobetasol propionate (SMD -1.55; 95% CI -1.73 to -1.37; I^2 statistic = 19.6%).

Two treatments were not significantly different to placebo: ciclopirox olamine shampoo (SMD -0.07; 95% CI -0.82 to 0.68) and salicylic acid (SMD -0.57; 95% CI -1.47 to 0.32).

Analysis 19: Scalp psoriasis: vitamin D alone or in combination versus other treatment

This comparison included head-to-head trials of treatments for scalp psoriasis in which one of the interventions was a vitamin D product (used either as monotherapy or in combination with another product) (see Analysis 19.2 and Table 22).

We identified six intervention-comparator contrasts, and TSS data were available for all six of these contrasts. All studies were parallel-group in design (between-patient). Eleven studies contributed TSS data from 4877 participants, and trial duration ranged from 4 to 8 weeks.

Based on Total Severity Scores, calcipotriol was significantly less effective than betamethasone dipropionate (SMD 0.45; 95% CI 0.28 to 0.63; I^2 statistic = 66.3%), clobetasol propionate (SMD 0.37; 95% CI 0.05 to 0.69; I^2 statistic = NA), and combination treatment with calcipotriol and betamethasone dipropionate (SMD 0.70; 95% CI 0.56 to 0.84; I^2 statistic = 49.6%). There was no statistically significant difference between calcipotriol and betamethasone valerate (SMD 0.09; 95% CI -0.09 to 0.27; I^2 statistic = 0%). Combination treatment (calcipotriol/betamethasone dipropionate) was significantly more effective than betamethasone dipropionate alone (SMD -0.19; 95% CI -0.27 to -0.11; I^2 statistic = 0%). The efficacy of calcipotriol and coal tar polytherapy was not significantly different (SMD -0.30; 95% CI -0.84 to 0.24; I^2 statistic = 93.1%).

(c) Psoriasis Area and Severity Index (PASI)

Analysis 1: Vitamin D analogues versus placebo

Our review included eight vitamin D analogues for body psoriasis in this comparison (see Analysis 1.3 and Table 5). Nine studies reported PASI data, with 2357 participants contributing data on 2 (calcipotriol and tacalcitol) of these 8 treatments. Eight trials were between-patient design, and one was a within-patient study (Dubertret 1992). Treatment duration ranged from three weeks to eight weeks. The average effect size across the 2 treatments for PASI was SMD -0.58 (95% CI -0.71 to -0.45; I^2 statistic = 42.3%).

Analysis 2: Corticosteroid (potent) versus placebo

Our review included 10 potent corticosteroids for body psoriasis in this comparison (see Analysis 2.3 and Table 6). Three between-patient studies reported PASI data from 1158 participants on once-daily or twice-daily doses of betamethasone dipropionate (2 of the 10 potent steroid regimens considered in this group). Trial duration ranged between four and eight weeks. The average PASI effect size across both application frequencies was -0.97 (95% CI -1.31 to -0.62; I^2 statistic = 79.6%).

Analysis 3: Corticosteroid (very potent) versus placebo

Our review did not identify any study that compared very potent corticosteroids against placebo and also reported PASI data. This may be because whole-body application of very potent corticosteroids is not recommended, so a whole-body assessment measure like the PASI is inappropriate.

Analysis 4: Dithranol versus placebo

Our review did not identify any study that compared dithranol against placebo and also reported PASI data.

Analysis 5: Vitamin D combination products versus placebo

This comparison included treatment with combined calcipotriol and betamethasone dipropionate used either once or twice daily on the body (see Analysis 5.3 and Table 8). Five parallel-group studies with 2056 participants contributed PASI data on both dosing options. Treatment duration ranged from four to eight weeks. The PASI SMD across treatments was -1.24 (95% CI -1.53 to -0.95; I^2 statistic = 87.6%). Although twice-daily combination treatment (SMD -1.41; 95% CI -1.86 to -0.97) achieved a larger effect

than once-daily treatment (SMD -1.14; 95% CI -1.57 to -0.70), the difference was not statistically significant at the 5% level. This finding contrasts with the assessment of the relative benefit of once- versus twice-daily dosing using the IAGI metric (see Analysis 5.1).

Analysis 6: Other treatment versus placebo

This comparison comprised all other treatments for body psoriasis that were not included in the first five comparisons; therefore, we removed pooling. None of the studies assessed the same treatment, which means that findings should be interpreted with caution.

In total, we included 26 treatments in this analysis (see Analysis 6.3 and Table 9). Nine studies with 529 participants reported PASI data on 9 of these 26 treatments. Eight trials were between-patient studies, and one was within-patient in design (Vali 2005). Treatment duration ranged from 2 to 12 weeks.

Six treatments performed statistically significantly better than placebo: aloe vera extract, betamethasone 17-valerate 21-acetate plus tretinoin plus salicylic acid, a herbal skin care product, *Mahonia aquifolium*, methotrexate gel, and theophylline ointment. Effects sizes ranged from -0.54 (95% CI -0.99 to -0.10) for the betamethasone 17-valerate 21 product (Santoianni 2001) to -2.96 (95% CI -4.19 to -1.74) for the herbal skin care treatment (Maier 2004).

In three treatments, we found no statistically significant difference relative to placebo in the PASI assessments. These comprised topical caffeine (Vali 2005), dead sea salts emollient lotion (Cheesbrough 1992), and kukui nut oil (Brown 2005).

Analysis 7: Vitamin D analogues versus corticosteroid (potent)

Our review identified eight vitamin D analogue-potent corticosteroid comparisons for body psoriasis (see Analysis 7.3 and Table 10). Nine studies with 3185 participants reported PASI data for 4 of the 8 intervention-comparator contrasts. Seven trials were between-patient design, and two were within-patient studies. Treatment duration ranged from four to eight weeks. The PASI SMD across all four intervention-comparator contrasts indicated that there was no statistically significant difference between the vitamin D derivatives and potent corticosteroid (SMD 0.12; 95% CI -0.07 to 0.32; I^2 statistic = 86.2%).

In one vitamin D analogue versus potent corticosteroid comparison, the vitamin D analogue performed statistically significantly better than the potent corticosteroid: four studies contributed data to analysis of calcipotriol versus betamethasone valerate (SMD -0.12; 95% CI -0.22 to -0.02; I^2 statistic = 0%).

In two intervention-comparator contrasts, the vitamin D analogue was statistically significantly less effective than the potent corticosteroid: Betamethasone dipropionate was more effective than both calcipotriol (SMD 0.36; 95% CI 0.22 to 0.51; I^2 statistic = 49.6%) and calcitriol (SMD 0.39; 95% CI 0.14 to 0.63; I^2 statistic = NA).

We found no statistically significant difference between calcipotriol and desoxymetasone.

Analysis 8: Vitamin D analogues versus corticosteroid (very potent)

This comparison considered vitamin D analogues against very potent corticosteroids for treating psoriasis of the body (see Analysis 8.3 and Table 11). We found data on one intervention-comparator contrast: calcipotriol versus clobetasol propionate. One between-patient trial reported PASI data for 40 participants. This trial had a treatment duration of six weeks (Landi 1993). The SMD for the PASI indicated that there was no statistically significant difference between the very potent corticosteroid and the vitamin D analogue: SMD -0.32 (95% CI -0.95 to 0.30; I^2 statistic = NA).

Analysis 9: Vitamin D combined with corticosteroid versus corticosteroid

This comparison considered vitamin D analogue-steroid combination against potent or very potent corticosteroid for body psoriasis (Table 12). Three between-patient trials reported PASI data for 1876 participants (see Analysis 9.3). All 3 trials compared combination treatment with calcipotriol and betamethasone dipropionate with betamethasone dipropionate as monotherapy, but varied in their treatment duration (4 to 8 weeks). The SMD for the PASI was -0.44 (95% CI -0.55 to -0.33; I^2 statistic = 22.4%), indicating a significantly greater effect for combination treatment.

Analysis 10: Vitamin D alone or in combination versus dithranol

This comparison considered vitamin D analogues against dithranol (see Analysis 10.3 and Table 13). We identified three intervention-comparator contrasts: calcipotriol versus dithranol, calcitriol versus dithranol, and tacalcitol versus dithranol. Five between-patient trials reported PASI data for 796 participants. Treatment duration ranged from 8 to 12 weeks. There was some variation in the dithranol regimens employed by trials and in the baseline severity of trial participants. These factors may explain the considerable level of heterogeneity found in the pooled results (Higgins 2011).

The SMD for the PASI was 0.36 (95% CI -0.33 to 1.04; I^2 statistic = 94.5%). Data from three trials contributed to the SMD for the calcipotriol versus dithranol: 0.73 (95% CI -0.55 to 2.00; I^2 statistic = 97.2%) (Berth Jones 1992b; Monastirli 2000; Van de Kerkhof 2006). One of these three trials found a large and statistically significant difference in favour of calcipotriol (Berth Jones 1992b); Monastirli 2000 found a significant difference in favour of dithranol, and the trial by Van de Kerkhof 2006 found no difference between the two treatments. In the light of this heterogeneity, we removed all pooling from this comparison.

Analysis 11: Vitamin D alone or in combination versus other vitamin D analogue

Our review identified three intervention-comparator contrasts for body psoriasis in this comparison: calcipotriol versus calcitriol, calcipotriol versus tacalcitol, and calcipotriol versus maxacalcitol (see Analysis 11.3 and Table 14). One between-patient trial involving 15 participants contributed PASI data for the comparison of calcipotriol and calcitriol (Bourke 1997). Treatment duration was eight weeks. Although there was a trend towards a greater effect for calcipotriol, the SMD for the PASI was not statistically significant: -1.11 (95% CI -2.22 to 0.01; I^2 statistic = NA).

Analysis 12: Vitamin D alone or in combination versus vitamin D + corticosteroid

Our review identified 12 intervention-comparator contrasts, involving 3 vitamin D analogues, 2 combination products, and 7

different corticosteroids (see Analysis 12.3 and Table 15). Sixteen trials involving 5703 participants contributed PASI data for 11 of these 12 intervention-comparator contrasts. Fifteen trials were between-patient, and 1 was within-patient in design (Salmhofer 2000). Treatment duration ranged from 2 to 12 weeks. We did not identify any PASI data for the comparison of calcipotriol against clobetasol propionate then calcipotriol. Overall, vitamin D plus corticosteroid appeared to be more effective than vitamin D alone: The SMD for the PASI was 0.47 (95% CI 0.34 to 0.59; I^2 statistic = 82.3%). However, there was considerable variation between the findings of the intervention-comparator contrasts. In light of the observed heterogeneity, we only pooled subtotals (Higgins 2011).

In six of the intervention-comparator contrasts, the analysis of the PASI measure found no significant difference between the treatments. This was the case for twice-daily calcipotriol compared with the following:

- a regimen with calcipotriol applied in the morning and the night-time application of betamethasone valerate (Kragballe 1998b; Ruzicka 1998);
- clobetasone butyrate (Kragballe 1998b); or
- diflucortolone valerate (Salmhofer 2000).

Once-daily calcipotriol was no more effective than combined treatment with fluocinonide acetonide (Wozel 2001) or combined with hydrocortisone (Ortonne 2010). Lastly, no significant difference was found between twice-daily calcitriol and combined treatment with diflucortolone valerate (mornings) and calcitriol (night time) (Lee 2007).

In contrast, combined treatment with calcipotriol and betamethasone dipropionate was significantly more effective than twice-daily calcipotriol alone. This finding held for regimens involving night-time applications of betamethasone dipropionate (SMD 0.46; 95% CI 0.10 to 0.82; I^2 statistic = NA) and for treatment with a combined product, whether applied once daily (SMD 0.52; 95% CI 0.38 to 0.67; I^2 statistic = 32.3%) or twice daily (SMD 0.64; 95% CI 0.46 to 0.83; I^2 statistic = 73.6%). Once-daily treatment with the combined calcipotriol/betamethasone dipropionate product was also significantly more effective than once-daily calcipotriol (SMD 0.67; 95% CI 0.23 to 1.11; I^2 statistic = 87.4%) as well as once-daily tacalcitol (SMD 0.47; 95% CI 0.25 to 0.69; I^2 statistic = NA).

Analysis 13: Vitamin D alone or in combination versus other treatments: complex regimens

This comparison summarises findings on complex regimens for body psoriasis, defined here as treatment sequences that do not consist of a simple head-to-head comparison between two active treatments (see Analysis 13.3 and Table 16). PASI data were available for 11 of the 12 intervention-comparator contrasts identified. Data from 2991 participants contributed to the PASI analysis, based on findings from 8 between-patient trials. Trial duration varied between 2 and 12 weeks. Because the interventions and comparators were highly variable and two trials each contributed three pair-wise contrasts, we did not pool the data.

Six intervention-comparator contrasts for which PASI data were available found a significant difference between regimens. A six-week course of calcipotriol was compared with two different complex regimens. Monotherapy with calcipotriol was significantly less effective than two weeks of treatment with calcipotriol and fluocinonide acetonide followed by four weeks of calcipotriol (SMD 0.66; 95% CI 0.01 to 1.32) (Wozel 2001). Calcipotriol monotherapy was also less effective than treatment with calcipotriol to which halometasone was added (SMD 1.13; 95% CI 0.64 to 1.62) (Yang 2009). Monotherapy with tacalcitol (8 weeks) was less effective than sequential treatment with a combined calcipotriol and betamethasone dipropionate product (4 weeks) followed by calcipotriol monotherapy for a further 4 weeks (SMD 0.49; 95% CI 0.31 to 0.67) (Ortonne 2004). White 2006 (P) compared three regimens, all of which included an initial phase in which participants applied combination treatment with calcipotriol and betamethasone dipropionate once a day for four weeks. The subsequent eight-week maintenance phase using placebo ointment was significantly less effective than maintenance with either twice-daily calcipotriol (SMD 0.25; 95% CI 0.10 to 0.39), or maintenance with calcipotriol on weekdays and combination treatment at weekends (SMD 0.59; 95% CI 0.45 to 0.74). When the two active maintenance regimens were compared directly, the alternating (weekday/weekend) regimen was significantly more efficacious (SMD 0.30; 95% CI 0.16 to 0.45) (White 2006 (H)).

In the remaining four intervention-comparator contrasts, we did not detect any significant difference in the PASI assessments (see Analysis 13.3). PASI assessments in the study by Kragballe 2004 found the difference between two complex regimens not to be significant (SMD 0.15; 95% CI -0.01 to 0.30). This result was on the borderline of significance and contrasted with the IAGI assessment in the same study, which was statistically significant in favour of the complex regimen (see Analysis 13.1).

Analysis 14: Vitamin D alone or in combination versus other treatment: long-term studies (> 24 weeks)

We did not identify any relevant study that provided PASI data for this analysis.

Analysis 15: Vitamin D analogues versus other treatment

This comparison incorporated all other vitamin D head-to-head comparisons of treatments for psoriasis of the body (excluding inverse psoriasis) that had not already been included (see Analysis 15.3 and Table 18). We included 12 intervention-comparator contrasts, with PASI data available for 6 of these contrasts. There were six between-patient trials and three within-patient trials, with data for 1228 participants. Trial duration ranged between 4 and 12 weeks. In light of the pharmacological diversity of the comparators, we only pooled data within subgroups (Higgins 2011).

According to the PASI assessment, twice-daily calcipotriol was significantly more effective than coal tar polytherapy (SMD -0.63; 95% CI -1.06 to -0.20; I^2 statistic = NA) as well as propylthiouracil cream (SMD -2.24; 95% CI -3.23 to -1.25; I^2 statistic = NA). Twice-daily calcipotriol was not significantly more effective than coal tar (SMD -0.10; 95% CI -1.54 to 1.35; I^2 statistic = 92.8%), betamethasone dipropionate and salicylic acid (SMD -0.05; 95% CI -0.36 to 0.26; I^2 statistic = NA), or vitamin B12 cream (SMD -0.01; 95% CI -0.78 to 0.75; I^2 statistic = NA). The high level of heterogeneity observed in the pooled analysis of calcipotriol versus coal tar reflects contradictory findings from two studies, one finding in favour of calcipotriol (Tham 1994) and the other in favour of coal tar (Alora-Palli 2010).

When compared with once-daily dosing, twice-daily vitamin D was borderline in demonstrating a significantly better effect (SMD -0.12; 95% CI -0.25 to 0.00; I^2 statistic = 0%). The subgroups contributing

to this result were dosing comparisons of calcipotriol (SMD -0.12; 95% CI -0.28 to 0.03; I^2 statistic = 0%) and combination treatment with calcipotriol and betamethasone dipropionate (SMD -0.12; 95% CI -0.32 to 0.09; I^2 statistic = NA).

Analysis 16: Flexural/facial psoriasis: placebo-controlled trials

This comparison included placebo-controlled trials of topical treatments for inverse or facial psoriasis (see Analysis 16.3 and Table 19). We found evidence on four treatments in this comparison: the potent steroid betamethasone valerate; the vitamin D analogue calcipotriol; and two topical calcineurin inhibitors, pimecrolimus and tacrolimus. We only identified one placebo-controlled trial evaluating tacrolimus ointment (Lebwohl 2004), but the study did not report any effectiveness data suitable for this review. However, the study did contribute data on adverse events and withdrawal rates.

PASI data were available for 3 of the 4 topical treatments for inverse psoriasis, all reported by 1 4-week between-patient study with 75 participants (Kreuter 2006 (P)). In this study, participants applied all treatments once daily. The SMD for the PASI found a statistically significant difference in favour of betamethasone valerate 0.1% (SMD -2.83; 95% CI -3.79 to -1.88) as well as calcipotriol ointment (SMD -1.08; 95% CI -1.77 to -0.40). However, PASI data on once-daily pimecrolimus cream indicated the difference relative to vehicle was not statistically significant (SMD -0.62; 95% CI -1.27 to 0.02).

Analysis 17: Flexural/facial psoriasis: vitamin D alone or in combination versus other treatment

This comparison included head-to-head trials of treatments for inverse psoriasis, where vitamin D was compared with an active control (see Analysis 17.3 and Table 20). We identified five intervention-comparator contrasts. We compared four treatments with calcipotriol: once-daily betamethasone valerate, combined treatment with calcipotriol and hydrocortisone, calcitriol, and pimecrolimus. Calcitriol was compared with tacrolimus.

Two between-patient studies contributed PASI data from 464 study participants on 3 of the 5 intervention-comparator contrasts. Kreuter 2006 (H) found that calcipotriol was significantly less effective than betamethasone valerate (SMD 2.02; 95% CI 1.20 to 2.84), but not significantly different in effect to pimecrolimus (SMD -0.53; 95% CI -1.17 to 0.11). Participants in the Kreuter 2006 (H) trial applied all treatments once daily. When assessed using the PASI, Ortonne 2010 found that calcipotriol was significantly less effective on inverse psoriasis than combined treatment with calcipotriol and hydrocortisone (SMD 0.32; 95% CI 0.12 to 0.51). This finding was consistent with the IAGI assessment in the same trial (see Analysis 17.1).

Analysis 18: Scalp psoriasis: placebo-controlled trials

No PASI data were available for this comparison.

Analysis 19: Scalp psoriasis: vitamin D alone or in combination versus other treatment

No PASI data were available for this comparison.

(d) Patient Assessment of overall Global Improvement (PAGI)/ Patient Global Assessment of Disease Severity (PGA)

Analysis 1: Vitamin D analogues versus placebo

Our review included eight vitamin D analogues for body psoriasis in this comparison, with PAGI data available for three treatments (see Analysis 1.4 and Table 5). Five studies reported PAGI data, all of which were between-patient design, and 1467 participants contributed data. In all six studies, treatment duration was eight weeks. The pooled effect across the 3 studies reporting PAGI data was SMD -0.54; 95% CI -0.72 to -0.36; I^2 statistic = 55.5%.

Analysis 2: Corticosteroid (potent) versus placebo

Our review did not identify any study that compared potent corticosteroids against placebo and reported PAGI data.

Analysis 3: Corticosteroid (very potent) versus placebo

We included three very potent corticosteroids for body psoriasis in this comparison for this outcome (see Analysis 3.4 and Table 7). Three studies reported PAGI data for 283 participants on 2 of these 3 treatments. There was one between-patient trial (Lebwohl 2002) and two within-patient studies. In all three studies, treatment duration was two weeks. The pooled effect across both treatments for PAGI was (SMD -1.22; 95% CI -1.42 to -1.02; I^2 statistic = 0%). Both treatments performed statistically significantly better than placebo. PAGI data on the use of very potent steroids on the scalp are reported in Analysis 18.4.

Analysis 4: Dithranol versus placebo

Our review did not identify any study comparing dithranol against placebo and that reported PAGI data.

Analysis 5: Vitamin D combination products versus placebo

This comparison included treatment with combined calcipotriol and betamethasone dipropionate used either once or twice daily on the body (see Analysis 5.4 and Table 8). None of the studies of twice-daily treatment reported PAGI data, but one parallel-group study with 235 participants contributed data on once-daily treatment (Langley 2011 (P)). Treatment duration was eight weeks. The PAGI SMD was -0.69 (95% CI -0.98 to -0.40; I^2 statistic = NA). Placebo-controlled trials of combination vitamin D/steroid treatments for scalp psoriasis are reported in Analysis 18.4.

Analysis 6: Other treatment versus placebo

This comparison comprised all other treatments for body psoriasis that we did not include in the first five comparisons; therefore, we removed pooling. None of the studies assessed the same treatment, which means that findings should be interpreted with caution.

In total, we included 26 treatments in this analysis (see Analysis 6.4 and Table 9). Two studies with 105 participants reported PAGI data on 2 of these 26 treatments. Both trials were between-patient studies. Treatment duration ranged from 3 to 12 weeks. According to participants' assessments (PAGI), betamethasone 17-valerate 21 acetate plus tretinoin plus salicylic acid performed significantly better than placebo (SMD -0.80; 95% CI -1.26 to -0.35), whilst kukui nut oil was no more effective than placebo (SMD 0.00; 95% CI -0.80 to 0.80). These findings were very similar to the investigators' assessments (see Analysis 6.1).

Analysis 7: Vitamin D analogues versus corticosteroid (potent)

Our review identified eight vitamin D analogue-potent corticosteroid comparisons for body psoriasis (see Analysis 7.4 and Table 10). Two studies with 738 participants reported PAGI data for 1 of these 8 comparisons. One trial was a parallel-group study (Cunliffe 1992), and one was a within-patient study (Kragballe 1991a), both with a treatment duration of six weeks. The PAGI SMD indicated that the vitamin D analogue calcipotriol was significantly more effective than betamethasone valerate (SMD -0.26; 95% CI -0.38 to -0.14; I^2 statistic = 0%).

Analysis 8: Vitamin D analogues versus corticosteroid (very potent)

This comparison included one vitamin D analogue and a very potent corticosteroid contrast, calcipotriol ointment versus clobetasol propionate foam for body psoriasis (see Table 11 and Analysis 8.4). One study with 42 participants reported PAGI data. Koo 2006 was a between-patient study with a treatment duration of two weeks. Findings for the participant-reported assessment (SMD 0.42; 95% CI -0.20 to 1.03) were similar, the investigators' assessment from the same study (SMD 0.19; 95% CI -0.42 to 0.80; see Analysis 8.1).

Analysis 9: Vitamin D combined with corticosteroid versus corticosteroid

We found one study comparing a vitamin D analogue-steroid combination against corticosteroids for body psoriasis that reported PAGI/PGA data (see Table 12 and Analysis 9.4). This two-week between-patient study reported PAGI data for 65 participants (Koo 2006), comparing combined treatment with calcipotriol and clobetasol propionate against the very potent corticosteroid alone. According to the participants' assessment (PAGI), there was no statistically significant difference between the treatment options (SMD -0.28; 95% CI -0.80 to 0.24). This finding contrasts with the investigators' assessment (IAGI), which found in favour of combination treatment (SMD -0.69; 95% CI -1.22 to -0.15) (see Analysis 9.1).

Analysis 10: Vitamin D alone or in combination versus dithranol

This comparison considered vitamin D analogues against dithranol (see Analysis 10.4 and Table 13). We identified three intervention-comparator contrasts: calcipotriol versus dithranol, calcitriol versus dithranol, and tacalcitol versus dithranol. PAGI data were available only for the intervention-comparator contrast of calcipotriol versus dithranol. Two between-patient trials reported PAGI data for 544 participants (Berth Jones 1992b; Van de Kerkhof 2006). Treatment duration ranged from 8 to 12 weeks. The SMD for the PAGI was -0.05 (95% CI -0.90 to 0.80; I^2 statistic = 92.5%), indicating no statistically significant advantage for calcipotriol or dithranol according to the participants' assessment.

Analysis 11: Vitamin D alone or in combination versus other vitamin D analogue

Our review identified three intervention-comparator contrasts for body psoriasis in this comparison: calcipotriol versus calcitriol, calcipotriol versus tacalcitol, and calcipotriol versus maxacalcitol (see Analysis 11.4 and Table 14). One between-patient trial involving 250 participants contributed PAGI data for the comparison of calcipotriol and calcitriol (Ji 2008). Treatment duration was 12 weeks. The SMD for the PAGI indicated that there was no statistically significant difference between calcipotriol and calcitriol (SMD 0.04; 95% CI -0.21 to 0.29; I^2 statistic = NA). This study used three measures to assess the effects of calcipotriol and calcitriol. The investigators' assessment supported the participant assessment (no difference) (see Analysis 11.1), but the TSS found a significant difference in favour of calcipotriol (Analysis 11.2).

Analysis 12: Vitamin D alone or in combination versus vitamin D + corticosteroid

Our review identified 12 intervention-comparator contrasts for body psoriasis, involving 3 vitamin D analogues, 2 combination products, and 7 different corticosteroids (see Analysis 12.4 and Table 15). Two parallel-group trials contributed PAGI data from 399 participants for 2 of these 12 intervention-comparator contrasts. Treatment duration ranged between two and eight weeks. According to the participant assessment, twice-daily calcipotriol was significantly less effective than twice-daily treatment with calcipotriol and clobetasol propionate (SMD 0.70; 95% CI 0.16 to 1.23). Treatment with tacalcitol was also less effective than treatment with a combined product containing calcipotriol and betamethasone dipropionate, when both treatments were applied once daily (SMD 0.46; 95% CI 0.24 to 0.68). The pooled SMD for these two trials (0.49; 95% CI 0.29 to 0.69; I^2 statistic = 0%) gave greater weight to the comparison with tacalcitol, since this was the larger trial (334 participants; Langley 2011 (H)).

Analysis 13: Vitamin D alone or in combination versus other treatments: complex regimens

This comparison summarises findings on complex regimens for body psoriasis, defined here as treatment sequences that do not consist of a simple head-to-head comparison between two active treatments (see Analysis 13.4 and Table 16). We identified 12 intervention-comparator contrasts and data from the Patient Assessment of Global Improvement (PAGI) or Patient Global Assessment of Disease Severity (PGA) were available for 7 of these. Data from 2508 participants contributed to the PAGI analysis, based on findings from 4 between-patient trials. Trial duration varied between 8 and 12 weeks. Because the interventions and comparators were highly variable and two trials each contributed three pair-wise contrasts, we did not pool the data.

Four intervention-comparator contrasts for which PAGI data were available found a significant difference between regimens. Ortonne 2004 found that four weeks of treatment with a combination product of calcipotriol and betamethasone dipropionate, followed by monotherapy with calcipotriol for four weeks, was significantly more effective than monotherapy with tacalcitol (SMD 0.54; 95% CI 0.36 to 0.72). Findings from the patient-reported outcome were identical to the investigators' assessment (Analysis 13.1). The trial by White 2006 (H)/White 2006 (P) compared three regimens. All included an initial phase in which participants applied once-daily combination treatment with calcipotriol and betamethasone dipropionate for four weeks, but differed in their subsequent eight-week maintenance phase. According to the participants' assessment, maintenance therapy with twice-daily placebo ointment was significantly less effective than maintenance with either calcipotriol ointment (SMD 0.28; 95% CI 0.13 to 0.42) or maintenance with calcipotriol on weekdays and combination treatment at weekends (SMD 0.71; 95% CI 0.56 to 0.85). We compared the 2 regimens with active maintenance options directly; the alternating (weekday/weekend) approach was significantly more effective (SMD 0.44; 95% CI 0.29 to 0.58). These findings, based on the participants' assessment of severity, were aligned with those

of both the investigators' assessment (Analysis 13.1) and the PASI assessment (Analysis 13.3).

A head-to-head comparison of two complex regimens found a significant difference (Kragballe 2004). Once-daily combination treatment (calcipotriol/betamethasone dipropionate) for 8 weeks followed by once-daily calcipotriol for 4 weeks was significantly less effective than a regimen consisting of combined treatment for 4 weeks, followed by 8 weeks of once-daily therapy with calcipotriol on weekdays and combined therapy at weekends (SMD 0.23; 95% CI 0.07 to 0.39).

In three of the seven intervention-comparator contrasts, no significant difference was found. Kragballe 2004 also compared 12 weeks of calcipotriol monotherapy with the 2 complex regimens described in the paragraph above. Compared with monotherapy, participants who applied once-daily combination treatment (calcipotriol/betamethasone dipropionate) for 8 weeks followed by once-daily calcipotriol for 4 weeks did not experience a significantly greater improvement in their psoriasis (SMD -0.14; 95% CI -0.30 to 0.02). Similarly, the psoriasis of participants on monotherapy with twice-daily calcipotriol did not improve significantly differently compared to those who applied once-daily combination treatment (calcipotriol/betamethasone dipropionate) for 4 weeks, followed by 8 weeks using calcipotriol once daily (weekdays) and combination therapy (weekends) (SMD 0.10; 95% CI -0.06 to 0.26).

Analysis 14: Vitamin D alone or in combination versus other treatment: long-term studies (> 24 weeks)

We did not identify any relevant study that provided PAGI data for this analysis.

Analysis 15: Vitamin D analogues versus other treatment

This comparison incorporated all other vitamin D head-to-head comparisons of treatments for psoriasis of the body (excluding inverse psoriasis) that we had not already included (see Analysis 15.4 and Table 18). We included 12 intervention-comparator contrasts, with PAGI data available for 6 of these contrasts: 3 between-patient trials and 3 within-patient trials data for 456 participants. Trial duration ranged between 4 and 12 weeks. In light of the pharmacological diversity of the comparators, we only pooled data within subgroups.

According to the participants' assessment, twice-daily calcipotriol was significantly more effective than three comparators, with evidence on each based on a single trial. Calcipotriol was more effective than coal tar both as monotherapy (SMD -1.51; 95% CI -2.12 to -0.90; Tham 1994) and as polytherapy (SMD -0.56; 95% CI -0.99 to -0.13; Van de Kerkhof 2002a), and more effective than betamethasone dipropionate and salicylic acid (SMD -0.49; 95% CI -0.79 to -0.20; Scarpa 1994). No significant difference was evident when calcipotriol was compared to tacrolimus ointment (Ortonne 2006), tazarotene (Tzung 2005), or vitamin B12 cream (Stuecker 2001).

Analysis 16: Flexural/facial psoriasis: placebo-controlled trials

This comparison included placebo-controlled trials of topical treatments for inverse or facial psoriasis (see Analysis 16.4 and Table 19). We found evidence on four treatments in this comparison: the potent steroid betamethasone valerate; the vitamin D analogue calcipotriol; and two topical calcineurin inhibitors, pimecrolimus and tacrolimus. We identified only one placebo-controlled trial evaluating tacrolimus ointment (Lebwohl 2004), but the study did not report any effectiveness data suitable for this review. However, the study did contribute data on adverse events and withdrawal rates.

PAGI (patient-assessment) data were available for one of the four topical treatments for inverse psoriasis. One 8-week between-patient study (Gribetz 2004) reported data from 47 participants. Relative to placebo, the SMD for the PAGI found a statistically significant difference in favour of twice-daily pimecrolimus cream (SMD -0.65; 95% CI -1.24 to -0.06).

Analysis 17: Flexural/facial psoriasis: vitamin D alone or in combination versus other treatment

We did not identify any relevant study that provided PAGI data for this analysis.

Analysis 18: Scalp psoriasis: placebo-controlled trials

This comparison included placebo-controlled trials of treatments for scalp psoriasis (see Analysis 18.4 and Table 21). We included evidence on 11 treatments in this comparison, with PAGI data available for 5 treatments. Five between-patient trials contributed data from 1875 participants. Trial duration ranged between three and eight weeks.

Four of the five treatments for scalp psoriasis that were evaluated using the Patient Global Assessment Scale were significantly more effective than placebo. The least effective treatment was calcipotriol (SMD -0.66; 95% CI -1.28 to -0.05; I^2 statistic = 74.5%), and the most effective was betamethasone dipropionate (SMD -1.23; 95% CI -1.43 to -1.03; I^2 statistic = NA). Effects for the very potent steroid amcinonide (SMD -0.97; 95% CI -1.33 to -0.61 I^2 statistic = NA) and combination treatment with calcipotriol and betamethasone dipropionate (SMD -1.00; 95% CI -1.79 to -0.22; I^2 statistic = 93.2%) fell between these two extremes. There were no data suitable for pooling across subcategories.

Only for ciclopirox olamine shampoo was the difference relative to placebo found to be non-significant: SMD -0.11 (95% CI -0.86 to 0.64; I^2 statistic = NA).

Analysis 19: Scalp psoriasis: vitamin D alone or in combination versus other treatment

This comparison included head-to-head trials of treatments for scalp psoriasis in which one of the interventions was a vitamin D product (used either as monotherapy or in combination with another product) (see Analysis 19.4 and Table 22).

We identified six intervention-comparator contrasts, and PAGI data were available for four of these contrasts (there were no participant-assessed outcomes data for the comparison of calcipotriol against either clobetasol propionate or against coal tar polytherapy). All studies were parallel-group in design (between-patient). Six studies contributed PAGI data from 3742 participants, and trial duration ranged from 4 to 8 weeks.

Based on the participant assessment scores, calcipotriol was significantly less effective than betamethasone dipropionate (SMD 0.56; 95% CI 0.31 to 0.81; I^2 statistic = 82.8%), betamethasone valerate (SMD 0.41; 95% CI 0.22 to 0.59; I^2 statistic = NA), and combination treatment with calcipotriol and betamethasone dipropionate (SMD 0.84; 95% CI 0.61 to 1.08; I^2 statistic

= 81.5%). Combination treatment (calcipotriol/betamethasone dipropionate) was significantly more effective than betamethasone dipropionate alone (SMD -0.17; 95% CI -0.25 to -0.09; I^2 statistic = 0%).

(e) Combined end point (IAGI/TSS/PASI/PAGI)

Analysis 1: Vitamin D analogues versus placebo

Our review included eight vitamin D analogues for body psoriasis in this comparison (see Analysis 1.5 and Table 5). Thirty studies, involving 4986 participants, contributed data. Eighteen trials were between-patient design, and 12 were within-patient studies. Treatment duration ranged from 3 to 12 weeks. Six studies had adequately concealed treatment allocation. The pooled effect across all 30 studies was -0.90 (95% CI -1.07 to -0.72; I^2 statistic = 87.5%), which equates to 1.03 on a 6-point IAGI scale. However, the summary statistic conceals considerable variation between treatments. In two treatments, the effect was not statistically significantly different to placebo (twice-daily calcipotriol plus occlusion for 2 weeks followed by 4 weeks with no treatment, and once-daily becocalcidiol). In treatments that were significantly more effective than placebo, the effect ranged from -0.67 (twice-daily becocalcidiol) to -1.66 (once-daily paricalcitol); on a 6-point IAGI scale, these effects translate into 0.80 and 1.91 points, respectively. However, given the high level of heterogeneity found in the meta-analysis, it may be more informative to look at individual products within the class, rather than treating this class as a single group. We removed the pooling across the class, so that we only pooled subtotals.

We reported placebo-controlled trials of vitamin D products for scalp psoriasis (Analysis 18.5) and inverse psoriasis (Analysis 16.5) elsewhere.

Sensitivity analyses

We explored differences in within-patient and between-patient designs using one-way sensitivity analysis (Table 5). The SMD for the 12 within-patient studies (600 participants) was -1.11 (95% CI -1.58 to -0.64; I^2 statistic = 91.5%). This translates into a change of 1.27 on a 6-point IAGI scale, slightly larger than the effect size for all studies. The SMD for the 18 between-patient studies (4386 participants) was -0.80 (95% CI -0.96 to -0.63; I^2 statistic = 83.2%). This translates into a change of 0.91 on a 6-point IAGI scale, slightly smaller than the effect size for the within-patient studies.

We also used sensitivity analysis to explore the impact of varying the correlation coefficient (rho) for the 12 within-patient studies. As no trial in the review reported this statistic, we tested values of 0, 0.25, 0.50, and 0.75. Varying the value of rho for the within-patient studies had no significant effect on the findings: The pooled SMD ranged from -0.85 (95% CI -1.00 to -0.71; I^2 statistic = 87.8%; 30 studies), when we assumed the correlation to be zero, to -0.91 (95% CI -1.07 to -0.75; I^2 statistic = 93.2%; 30 studies), when we assumed the correlation to be 0.75.

The study by Perez 1996 comparing calcitriol and placebo reported large and statistically significant differences for both TSS and IAGI outcomes. In both outcomes, the magnitude of the effect was the largest across all comparisons and treatments. Perez 1996 was a 10-week within-patient study involving 84 participants. The study included people with severe disease (mean TSS at baseline: 7.6 on a 10-point scale, with at least 10% of body surface area affected) who had previously had an unsatisfactory response to at least 1 previous treatment including topical steroids, UVB, PUVA, and methotrexate. The dramatic improvement observed in the intervention group is difficult to interpret in the context of findings from other trials, and we explored the impact of removing this study in a sensitivity analysis. When we removed Perez 1996 from the pooled analysis for calcitriol, the effect size was smaller but still statistically significantly different from placebo: SMD with Perez 1996 was -0.92 (95% CI -1.54 to -0.29; I^2 statistic = 94.9%; 7 studies), and SMD without Perez 1996 was -0.60 (95% CI -0.78 to -0.41; I^2 statistic = 30%; 6 studies). On a 6-point IAGI scale, these effect sizes equate to 1.05 and 0.68, respectively (Table 5).

The trials of calcipotriol varied by dose, treatment duration, and dosing frequency; where trials reported more than one dose (Kragballe 1988b) or type of vehicle (Harrington 1996a), we estimated the weighted mean and standard deviation across the trial. The effect size for twice-daily regimens was -1.02 (95% CI -1.23 to -0.82 I^2 statistic = 73.5%; 13 studies); this equates to 1.18 on a 6-point IAGI scale. For once-daily calcipotriol, the corresponding figures were -0.76 (95% CI -1.13 to -0.40; I^2 statistic = 82.3%; 4 studies) and 0.87 on a 6-point IAGI scale. Therefore, both dosing frequencies were more effective than placebo, but once-daily applications had a smaller effect (Table 5).

Analysis 2: Corticosteroid (potent) versus placebo

Our review identified 10 potent corticosteroids for body psoriasis in this comparison (see Analysis 2.5 and Table 6). The treatments included three betamethasone dipropionate regimens, but we identified no effectiveness evidence for budesonide and no study reporting PAGI data. Therefore, 13 studies involving 2216 participants contributed data on 9 of the 10 treatments. Eleven trials were between-patient design, and two were within-patient studies. Treatment allocation was adequately concealed in four studies. Treatment duration ranged from 2 to 12 weeks. Participant numbers for individual studies ranged from 9 (Wortzel 1975 (2)) to 633 (Kaufmann 2002 (P)). The pooled effect across all 13 studies was -0.89 (95% CI -1.06 to -0.72; I^2 statistic = 65.1%). This equates to 1.02 on a 6-point IAGI scale. With the exception of diflorasone diacetate (Lane 1983), all potent corticosteroids were significantly more effective than placebo at the 5% level of significance. We reported elsewhere placebo-controlled trials of potent corticosteroid products for scalp psoriasis (Analysis 18.5) and inverse psoriasis (Analysis 16.5).

Sensitivity analyses

We explored differences in within-patient and between-patient designs using one-way sensitivity analysis (Table 6). The SMD for the 2 within-patient studies was -1.33 (95% CI -1.78 to -0.89; I^2 statistic = 0%). This translates into a change of 1.53 on a 6-point IAGI scale, which is larger than the effect for all studies. However, as just 48 participants contributed data to this analysis, robust inferences cannot be drawn. The SMD for the 11 between-patient studies (2168 participants) was -0.85 (95% CI -1.03 to -0.67; I^2 statistic = 66.7%). This translates into a change of 0.98 on a 6-point IAGI scale, slightly smaller than the effect for all studies.

We also used sensitivity analysis to explore the impact of varying the correlation coefficient (rho) for the 2 within-patient studies. As no trial in the review reported this statistic, we tested values of 0, 0.25, 0.50, and 0.75. Varying the value of rho for the within-patient studies had no significant effect on the findings: the pooled SMD

ranged from -0.89 (95% CI -1.06 to -0.72; I^2 statistic = 77.7%; 14 studies), when we assumed the correlation was to be zero, to -0.91 (95% CI -1.08 to -0.74; I^2 statistic = 80.2%; 13 studies), when we assumed the correlation to be 0.75.

Analysis 3: Corticosteroid (very potent) versus placebo

Our review identified three very potent corticosteroids for body psoriasis in this comparison (see Analysis 3.5 and Table 7), but effectiveness data were not available for one of these treatments (halcinonide). Ten studies reported data for 1264 participants. There were seven between-patient trials and three within-patient studies. Treatment duration ranged from two to four weeks. In no study was treatment allocation adequately concealed. The SMD across the 2 treatments was -1.56 (95% CI -1.87 to -1.26; I^2 statistic = 81.7%; 10 studies). This equates to 1.80 points on a 6-point IAGI scale. Both clobetasol propionate (SMD -1.65; 95% CI -2.10 to -1.20; I^2 statistic = 86.3%; 7 studies) and halobetasol (SMD -1.36; 95% CI -1.65 to -1.07 I^2 statistic = 47.1%; 3 studies) performed significantly better than placebo.

We reported elsewhere placebo-controlled trials of very potent corticosteroid products for scalp psoriasis (Analysis 18.5).

Sensitivity analyses

We explored differences in within-patient and between-patient designs using one-way sensitivity analysis (Table 7). The SMD for the 3 within-patient studies (229 participants) was -1.52 (95% CI -2.02 to -1.02; I^2 statistic = 79.3%). This translates into a change of 1.74 on a 6-point IAGI scale. The SMD for the 7 between-patient studies (1035 participants) was -1.58 (95% CI -1.99 to -1.17; I^2 statistic = 84.4%). This translates into a change of 1.81 on a 6-point IAGI scale.

We also used sensitivity analysis to explore the impact of varying the correlation coefficient (rho) for the 3 within-patient studies. As no trial in the review reported this statistic, we tested values of 0, 0.25, 0.50, and 0.75. Varying the value of rho for the within-patient studies had no significant effect on the findings: The pooled SMD ranged from -1.52 (95% CI -1.80 to -1.24; I^2 statistic = 81.6%; 10 studies), when we assumed the correlation to be zero, to -1.55 (95% CI -1.80 to -1.29; I^2 statistic = 85.9%; 10 studies), when we assumed the correlation to be 0.75.

Analysis 4: Dithranol versus placebo

This comparison considered dithranol against placebo (see Analysis 4.5 and Table 23). Three within-patient trials reported data for 47 participants. The only outcome reported by these trials was the TSS, so results for the combined end point are identical to the TSS results section. The types of treatment comprised the following: dithranol 0.1% in a carbamide (17% urea) base twice daily (Buckley 1978), dithranol in aqueous gel (dose titration 0.1% to 2.0%) twice daily (Grattan 1997 (P)), and dithranol 2% ointment 'one minute therapy' once daily (Jekler 1992).

Treatment duration ranged from three to eight weeks. In all three studies, the adequacy of the concealment of treatment allocation was unclear. The SMD for the combined end point was -1.06 (95% CI -1.66 to -0.46; I^2 statistic = 37.4%; 3 studies), which equates to 1.22 on a 6-point IAGI scale. All three trials found a statistically significant effect in favour of dithranol.

Sensitivity analysis

We used sensitivity analysis to explore the impact of varying the correlation coefficient (rho) for the 3 within-patient studies. As no trial in the review reported this statistic, we tested values of 0, 0.25, 0.50, and 0.75. Varying the value of rho for the within-patient studies had no significant effect on the findings: The pooled SMD ranged from -0.98 (95% CI -1.56 to -0.41; I^2 statistic = 13.9%; 3 studies), when we assumed the correlation to be zero, to -1.17 (95% CI -1.81 to -0.52; I^2 statistic = 78.5%), when we assumed the correlation to be 0.75.

Analysis 5: Vitamin D combination products versus placebo

This comparison included treatment with combined calcipotriol and betamethasone dipropionate used either once or twice daily on the body (see Analysis 5.5 and Table 8). As all five studies reported IAGI data, results for the combined end point are identical to those in Analysis 5.1. Five parallel-group studies with 2058 participants contributed data. Treatment duration ranged from four to eight weeks. Three trials adequately concealed treatment allocation. The SMD for the combined end point across treatments was -1.44 (95% CI -1.76 to -1.12; I^2 statistic = 89.4%; 5 studies), with twice-daily combination treatment (SMD -1.90; 95% CI -2.09 to -1.71; 2 studies) achieving a significantly larger effect than once-daily treatment (SMD -1.21; 95% CI -1.50 to -0.91; 3 studies). On a 6-point IAGI scale, these equate to improvements of 2.18 and 1.39 points, respectively.

However, the PASI assessments differed from the IAGI: although twice-daily combination treatment achieved a larger effect than once-daily treatment (SMD -1.41 and -1.14, respectively), the difference was not statistically significant (see Analysis 5.3).

In Analysis 18.5, we reported placebo-controlled trials of combination vitamin D/steroid treatments for scalp psoriasis.

Analysis 6: Other treatment versus placebo

This comparison comprised all other treatments for psoriasis of the body that we did not include in the first five comparisons; therefore, we removed pooling. None of the studies assessed the same treatment, which means that findings should be interpreted with caution.

In total, we included 26 treatments in this analysis (see Analysis 6.5 and Table 9). Twenty-six studies, with 1450 participants, reported data on 25 of these 26 treatments. The study of omega-3-polyunsaturated fatty acids ointment (Henneicke-v. Z. 1993) did not report usable effectiveness data, but did contribute data to the analysis of withdrawals. Twelve trials were between-patient design, and 14 were within-patient studies. Treatment duration ranged from 2 to 12 weeks. Two studies adequately concealed treatment allocation (Levine 2010 (P); Stutz 1996).

As assessed by the combined end point, just over half the treatments (13/25) performed statistically significantly better than placebo: aloe vera cream, anti-IL-8 monoclonal antibody cream, betamethasone 17-valerate 21-acetate plus tretinoin plus salicylic acid, combined treatment with calcipotriene and nicotinamide, fish oil plus occlusion, herbal skin care products, indigo naturalise 1.4% ointment, *Mahonia aquifolium*, methotrexate gel, mycophenolic acid ointment, PTH (1-34) in Novasome cream®, tazarotene, and theophylline 1% ointment. The effect size (SMD) for the combined end point ranged from -0.48 (Levine 2010 (P); calcipotriene

combined with nicotinamide) to -2.96 (Maier 2004; herbal skin care products), or 0.55 to 3.40, respectively, on a 6-point IAGI scale.

The trial of herbal skin care products enrolled just 34 participants, of which 24 contributed data (Maier 2004), so this study is classed as having a high risk of attrition bias (Figure 3; see Risk of bias in included studies). The results of this study were published as an abstract, and our searches failed to locate a full publication. Therefore, findings should be treated with caution.

In the remaining 12 treatments, the difference relative to placebo using the combined end point was not statistically significant. These included topical caffeine, Dead Sea salts emollient lotion, hexafluoro-1,25-dihydroxyvitamin D3, kukui nut oil, NG-monomethyl-L-arginine (L-NMMA) cream, nicotinamide 1.4%, oleum horwathiensis, platelet aggregation activating factor (PAF), polymyxin B cream, topical sirolimus, topical tacrolimus, and tar.

In two treatments, findings by different outcomes were inconsistent. When assessed by the TSS, hexafluoro-1,25-dihydroxyvitamin D3 was significantly more effective than placebo (-1.13; 95% CI -1.91 to -0.35) (Analysis 6.2), whereas the difference assessed by the IAGI was non-significant (-0.62; 95% CI -1.35 to 0.12) (Analysis 6.1). We based these findings on a single trial (Durakovic 2001). Similarly, the difference for oleum horwathiensis was statistically significant using the TSS (-0.77; 95% CI -1.40 to -0.14) (Analysis 6.2) whereas the difference assessed by the IAGI was not (-0.02; 95% CI -0.63 to 0.58) (Analysis 6.1). We also based findings for this treatment on a single trial (Lassus 1991).

We reported elsewhere placebo-controlled trials of other treatments for scalp psoriasis (Analysis 18.5) and inverse psoriasis (Analysis 16.5).

Analysis 7: Vitamin D analogues versus corticosteroid (potent)

Our review identified eight vitamin D analogue-potent corticosteroid comparisons for body psoriasis for this comparison (see Analysis 7.5 and Table 10). Fourteen studies with 3542 participants reported data for these 8 intervention-comparator contrasts. Nine trials were between-patient design, and five were within-patient studies. Treatment duration ranged from three to eight weeks. One study adequately concealed treatment allocation (Papp 2003 (H)).

The combined end point SMD indicated that, overall, there was no statistically significant difference between vitamin D and potent corticosteroids: SMD 0.11 (95% CI -0.07 to 0.30; I^2 statistic = 85.6%; 14 studies). There was however substantial heterogeneity and variation in effect underlying this summary statistic. Therefore, we only pooled subtotals.

The difference between the vitamin D analogue and the potent corticosteroid was not statistically significant for four intervention-comparator contrasts (calcipotriol versus betamethasone valerate, calcipotriol versus desoxymetasone, calcitriol versus betamethasone dipropionate, calcitriol versus betamethasone valerate). In the comparison of calcipotriol and betamethasone valerate, the non-significant result was borderline (SMD -0.12; 95% CI -0.26 to 0.02; I^2 statistic = 41.6%; 4 studies). When assessed using the TSS (one study), PASI (four studies), and PAGI (two studies), calcipotriol was significantly more effective than betamethasone valerate (see Analysis 7.2, Analysis 7.3, and Analysis 7.4). There were similar inconsistencies between the outcome assessments for the comparison of calcitriol with betamethasone dipropionate, all of which we based on a single study (Camarasa 2003). According to the TSS and PASI, calcitriol was significantly less effective than betamethasone dipropionate, but the IAGI indicated that the difference was not significant (see Analysis 7.1).

In one intervention-comparator contrast (calcipotriol versus fluocinonide), the vitamin D analogue was significantly more effective than potent corticosteroid: SMD -0.58 (95% CI: -0.99 to -0.18; I^2 statistic = NA). This effect is equivalent to a gain of approximately two-thirds of a point (0.64) on a 6-point IAGI scale. In three intervention-comparator contrasts, the potent corticosteroid was significantly more effective than the vitamin D analogue (calcipotriol versus betamethasone dipropionate, calcipotriol versus diflorasone diacetate, tacalcitol versus betamethasone valerate). The SMD effect sizes for these were 0.43, 0.27, and 0.41, respectively, equivalent to improvements of 0.47, 0.30, and 0.45 on a 6-point IAGI scale.

We reported elsewhere trials comparing vitamin D and potent corticosteroids for scalp psoriasis (Analysis 19.5) and inverse psoriasis (Analysis 17.5).

Sensitivity analyses

We explored differences in within-patient and between-patient designs using one-way sensitivity analysis (Table 10). In both types of design, the difference between vitamin D and potent corticosteroid was not statistically significant, but we associated the pooled results with substantial levels of heterogeneity (Higgins 2011). The SMD for the 5 within-patient studies (554 participants) was 0.17 (95% CI -0.20 to 0.54; I^2 statistic = 81.9%). The SMD for the 9 between-patient studies (2988 participants) was 0.10 (95% CI -0.11 to 0.31; I^2 statistic = 84.9%).

We also used sensitivity analysis to explore the impact of varying the correlation coefficient (rho) for the 5 within-patient studies. As no trial in the review reported this statistic, we tested values of 0, 0.25, 0.50, and 0.75. Varying the value of rho for the within-patient studies had no significant effect on the findings: The pooled SMD ranged from 0.10 (95% CI -0.08 to 0.28; I^2 statistic = 90.5%; 14 studies), when we assumed the correlation to be zero, to 0.12 (95% CI -0.06 to 0.30; I^2 statistic = 94.3%), when we assumed the correlation to be 0.75.

Analysis 8: Vitamin D analogues versus corticosteroid (very potent)

This comparison considered vitamin D analogues against very potent corticosteroids for body psoriasis (see Analysis 8.5 and Table 11). We found data on one intervention-comparator contrast: calcipotriol versus clobetasol propionate. Two between-patient trials reported data for 82 participants. Treatment duration ranged between two and six weeks. The adequacy of treatment allocation was unclear in both studies. The SMD for the combined end point indicated that there was no statistically significant difference between the vitamin D analogue and the very potent corticosteroid: -0.06 (95% CI -0.57 to 0.44; I^2 statistic = 25.7%; 2 studies).

We reported elsewhere trials comparing vitamin D and very potent corticosteroids for scalp psoriasis (Analysis 19.5).

Analysis 9: Vitamin D combined with corticosteroid versus corticosteroid

This comparison considered combined treatment with vitamin D analogues and corticosteroids against potent or very potent corticosteroid for body psoriasis (see Analysis 9.5 and Table 12). Five parallel-group studies, ranging in treatment duration from 2 to 8 weeks, provided data on 2113 participants. The adequacy of the concealment of treatment allocation was unclear in all five trials.

Effectiveness data were available for three contrasts:

- calcipotriol plus betamethasone dipropionate versus betamethasone dipropionate;
- calcipotriol plus betamethasone dipropionate versus clobetasol propionate; and
- calcipotriol plus clobetasol propionate versus clobetasol propionate.

Overall, combination treatment was more effective than monotherapy with corticosteroids: SMD -0.26 (95% CI -0.52 to -0.00; I^2 statistic = 84.4%; 5 studies). This effect is equivalent to a change of 0.29 on a 6-point IAGI scale. However, the pooled finding masks important diversity between the three intervention-comparator contrasts. When we compared combination treatment with calcipotriol and betamethasone dipropionate with a potent steroid (betamethasone dipropionate alone), combination treatment was more effective (SMD -0.40; 95% CI -0.52 to -0.27; I^2 statistic = 41.8%; 3 studies). However, the same combination treatment was significantly less effective than monotherapy with a very potent steroid (clobetasol propionate) (SMD 0.45; 95% CI 0.09 to 0.81; I^2 statistic = NA). Calcipotriol in combination with clobetasol propionate however was more effective than the very potent steroid used alone (SMD -0.69; 95% CI -1.22 to -0.15; I^2 statistic = NA). Therefore, we removed pooling for this analysis, but the findings demonstrate that combination treatment with vitamin D analogue and a corticosteroid is more effective than the same steroid used as a monotherapy.

We reported elsewhere trials comparing combination therapy (with vitamin D and potent corticosteroids) against potent steroids for scalp psoriasis (Analysis 19.5).

Analysis 10: Vitamin D alone or in combination versus dithranol

This comparison considered vitamin D analogues against dithranol for body psoriasis (see Analysis 10.5 and Table 13). We identified three intervention-comparator contrasts: calcipotriol versus dithranol, calcitriol versus dithranol, and tacalcitol versus dithranol. Seven between-patient trials and one within-patient trial (Grattan 1997 (H)) reported data for 1284 participants. We considered concealment of treatment allocation to be adequate in one trial (Van de Kerkhof 2006). Treatment duration ranged from 4 weeks to 12 weeks. In addition, there was some variation in the dithranol regimens employed by trials and in the baseline severity of trial participants. These factors may explain the high level of heterogeneity found in the pooled results.

The SMD for the combined end point was 0.09 (95% CI -0.44 to 0.63; I^2 statistic = 94.9%; 8 studies), indicating that there was no evidence of a statistically significant difference in effect between vitamin D analogues and dithranol. The pooled findings for calcipotriol against dithranol (SMD 0.07; 95% CI -0.57 to 0.71; I^2 statistic = 95.7%; 6 studies) and tacalcitol versus dithranol (SMD -0.18; 95% CI -0.60 to 0.25; I^2 statistic = NA) were aligned with, and drove, this result. However, the high levels of heterogeneity mean that findings merit closer scrutiny. Six studies contributed data from 1086 participants to the comparison of calcipotriol and dithranol. In three of these studies, calcipotriol performed significantly better than dithranol; two trials found significant differences in favour of dithranol; and one study found no significant difference between the treatments (see Analysis 10.5). A single study of 114 participants compared calcitriol against dithranol (Hutchinson 2000) and found a statistically significant difference in favour of dithranol (SMD 0.51; 95% CI 0.14 to 0.88; I^2 statistic = NA). This equates to just over half a point (0.56 of a point) improvement on a 6-point IAGI scale. However, the same study found no significant difference between the treatments in the assessment using the TSS (Analysis 10.2) or the PASI (Analysis 10.3).

In light of the considerable level of observed variation within and between studies (Higgins 2011), we removed pooling from this comparison.

Analysis 11: Vitamin D alone or in combination versus other vitamin D analogue

Our review identified three intervention-comparator contrasts for body psoriasis in this comparison: calcipotriol versus calcitriol, calcipotriol versus tacalcitol, and calcipotriol versus maxacalcitol (see Analysis 11.5 and Table 14). Four trials involving 513 participants contributed data. One trial was within-patient (Barker 1999 (H)); three were between-patient in design; and no trials demonstrated the concealment of treatment allocation to be adequate. Treatment duration ranged from 8 to 12 weeks.

The SMD for the combined end point indicated that there was no statistically significant difference between the treatments: -0.17 (95% CI -0.62 to 0.27; I^2 statistic = 78.5%; 4 studies). When we considered individual intervention-comparator contrasts using the combined end point, calcipotriol was more effective than tacalcitol (SMD -0.47; 95% CI -0.73 to -0.21; I^2 statistic = NA), which equates to an improvement of 0.52 on a 6-point IAGI scale. However, there was no statistically significant difference between calcipotriol and calcitriol (SMD -0.41; 95% CI -1.46 to 0.64; I^2 statistic = 72.3%; 2 studies) or between calcipotriol and maxacalcitol (SMD 0.43; 95% CI -0.12 to 0.98; I^2 statistic = NA). Participants in all trials applied treatments twice daily, with the exception of tacalcitol, which was applied once daily (Veien 1997).

Sensitivity analysis

The trial by Ji 2008 used three outcome measures to assess the effects of calcipotriol and calcitriol. Both the investigators' assessment (Analysis 11.1) and the participants' assessment found no difference between the two vitamin D products (Analysis 11.4), but the TSS found a statistically significant difference in favour of calcipotriol (Analysis 11.2). As findings for Ji 2008 varied depending on the outcome measure used, we tested the impact of using TSS data for the combined end point instead of IAGI data. The sensitivity analysis demonstrated that findings were robust, both for the SMD for the combined end point for all treatments (SMD -0.28; 95% CI -0.66 to 0.10; I^2 statistic = 70.6%; 4 studies) and for the comparison of calcipotriol and calcitriol (SMD -0.52; 95% CI -1.19 to 0.15; I^2 statistic = 44.9%; 2 studies).

Analysis 12: Vitamin D alone or in combination versus vitamin D + corticosteroid

Our review identified 12 intervention-comparator contrasts for body psoriasis, involving 3 vitamin D analogues, 2 combination products, and 7 different corticosteroids (see Analysis 12.5 and Table 15). Seventeen trials involving 5856 participants contributed data. Sixteen trials were between-patient, and 1 was within-patient in design (Salmhofer 2000). Treatment duration ranged from 2 to 12 weeks. Four trials adequately concealed treatment allocation, but concealment was inadequate in one trial (in the other trials, insufficient data were reported to allow an assessment of adequacy).

Overall, vitamin D plus corticosteroid was more effective than vitamin D alone: The SMD for the combined end point was 0.46 (95% CI 0.33 to 0.59; I^2 statistic = 83.3%; 17 studies), which translates into half of 1 point (0.50) on a 6-point IAGI scale. The substantial level of heterogeneity reflects not only different dosing schedules of the intervention and comparator products, but also the different potency of the corticosteroids and the different vitamin D analogues evaluated; we therefore removed pooling (Higgins 2011).

Twice-daily calcipotriol was significantly less effective than combination treatment with betamethasone dipropionate. This finding held whether participants applied the corticosteroid separately at night time (SMD 0.56; equivalent to 0.61 on a 6-point IAGI scale) or as a combined product used once daily or twice daily (SMD 0.43 and 0.66, respectively, translating into improvements of 0.48 and 0.73 points on a 6-point IAGI scale). Twice-daily calcipotriol was also significantly less effective than combination treatment with clobetasone butyrate (SMD 0.27; 95% CI 0.05 to 0.48; I^2 statistic = NA; 0.29 of a point on a 6-point IAGI) or clobetasol propionate (SMD 0.88; 95% CI 0.34 to 1.42; I^2 statistic = NA; 0.97 of a point on a 6-point IAGI scale). Once-daily combination treatment with calcipotriol and betamethasone dipropionate was significantly more effective than once-daily treatment with either calcipotriol (SMD 0.66; 95% CI 0.31 to 1.02; I^2 statistic = 80.9%; 2 studies) or tacalcitol (SMD 0.48; 95% CI 0.26 to 0.70; I^2 statistic = NA).

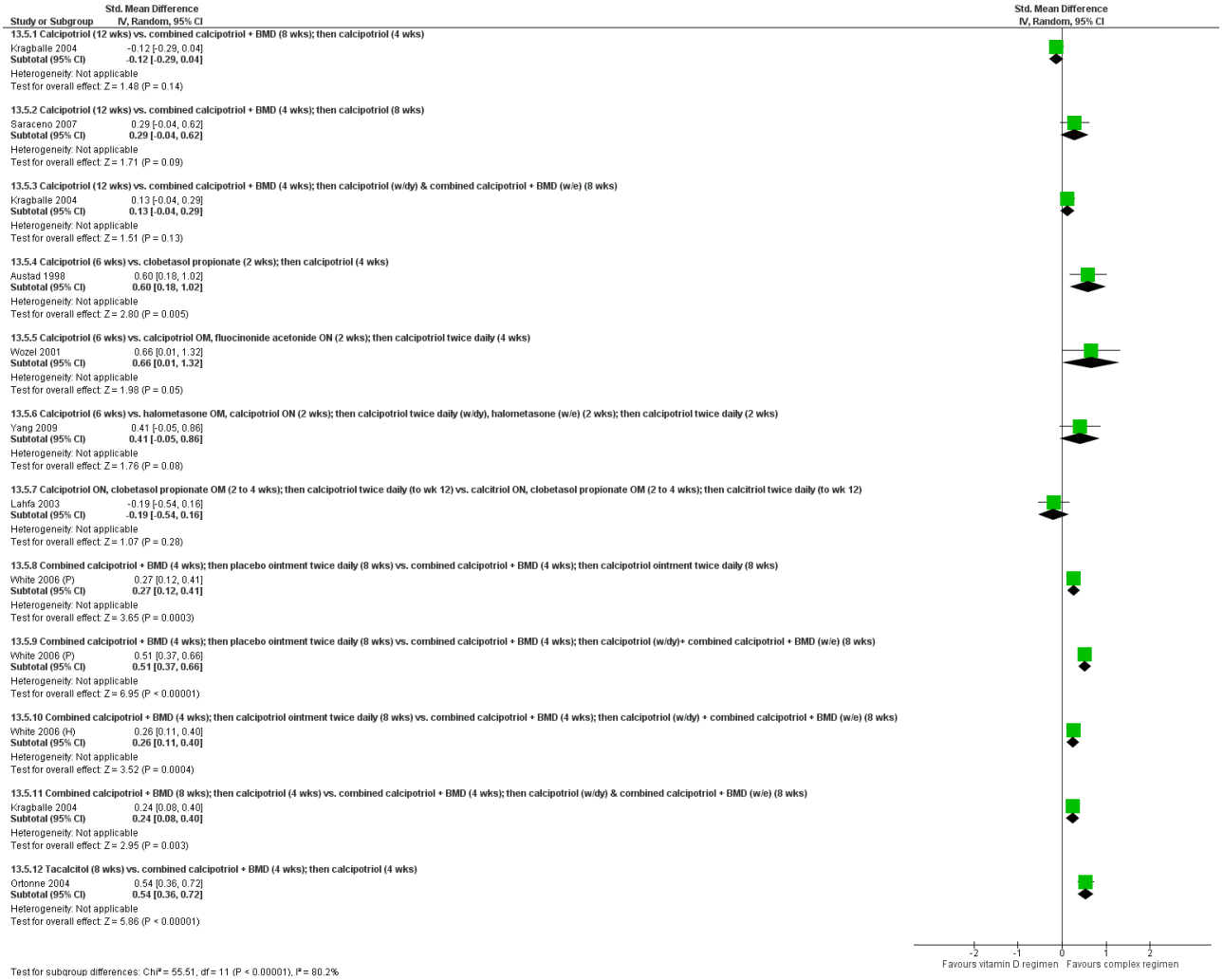
In none of the 12 intervention-comparator contrasts was the vitamin D analogue significantly more effective than combined vitamin D plus corticosteroid. However, in five instances, there was no significant difference between vitamin D and the comparator (combination treatment). These included twice-daily calcipotriol against combination treatment with betamethasone valerate or diflucortolone valerate, once-daily calcipotriol against combination treatment with fluocinonide acetonide or hydrocortisone, and twice-daily calcitriol against combination treatment with diflucortolone valerate.

We reported elsewhere trials comparing vitamin D and combination therapy with vitamin D/potent corticosteroids for scalp psoriasis (Analysis 19.5).

Analysis 13: Vitamin D alone or in combination versus other treatments: complex regimens

This comparison summarises complex regimens for body psoriasis, defined here as treatment sequences that do not consist of a simple head-to-head comparison between two active treatments (see Analysis 13.5 and Table 16). Using the combined end point, data were available for all 12 intervention-comparator contrasts (Figure 4). Data were available from 2936 participants from 8 between-patient trials and 1 within-patient trial (Austad 1998). Trial duration varied between 2 and 12 weeks. One trial adequately concealed treatment allocation. As the interventions and comparators were highly variable and because two trials each contributed three pair-wise contrasts, we did not pool the data.

Figure 4. Forest plot of comparison: 13 Vitamin D alone or in combination vs. other treatments: complex regimens, outcome: 13.5 Combined end point (IAGI/TSS/PASI/PAGI).



Seven intervention-comparator contrasts found a significant difference between regimens. Six weeks' monotherapy with twice-daily calcipotriol was less effective than clobetasol propionate (2 weeks) followed by 4 weeks' monotherapy with calcipotriol (SMD 0.60; 95% CI 0.18 to 1.02) (Austad 1998). A similar effect was evident when calcipotriol monotherapy (once daily for two weeks, then twice daily for four weeks) was compared with two weeks of treatment with calcipotriol (mornings) and fluocinonide acetonide (evenings), followed by 4 weeks' monotherapy with calcipotriol (SMD 0.66; 95% CI 0.01 to 1.32) (Wozel 2001). These benefits translated into improvements of 0.66 and 0.72 (i.e. around two-thirds of a point) on a 6-point IAGI scale.

The 12-week trial by White 2006 (H)/White 2006 (P) compared 3 regimens; all included an initial phase in which participants applied once-daily combination treatment with calcipotriol and betamethasone dipropionate for 4 weeks, but differed in their subsequent 8-week maintenance phase. Maintenance therapy with twice-daily placebo ointment was significantly less effective than maintenance with either calcipotriol ointment (SMD 0.27; 95% CI 0.12 to 0.41) or maintenance with calcipotriol on weekdays and combination treatment at weekends (SMD 0.51; 95% CI 0.37 to 0.66). When we directly compared the two regimens with active maintenance options, the alternating (weekday/weekend) approach was significantly more effective (SMD 0.26; 95% CI 0.11 to 0.40). The benefits of these 3 regimens equate to an improvement of 0.29, 0.56, and 0.28 of a point, respectively, on a 6-point IAGI scale. These findings, based on the investigators' assessment of severity, were aligned with those of both the PASI assessment (Analysis 13.3) and the participants' assessment (PAGI) (Analysis 13.4).

Ortonne 2004 demonstrated that four weeks of treatment with a combination product of calcipotriol and betamethasone dipropionate followed by monotherapy with calcipotriol for four weeks was significantly more effective than monotherapy with tacalcitol (SMD 0.54; 95% CI 0.36 to 0.72) (0.59 on a 6-point IAGI scale). Findings from the investigators' assessment (Analysis 13.1) were aligned with the PASI assessment (Analysis 13.3) and the participants' assessment (Analysis 13.4).

Kragballe 2004 compared 12 weeks of calcipotriol monotherapy with 2 complex regimens, both of which involved different sequences of combination therapy (calcipotriol/betamethasone dipropionate) and calcipotriol. When we directly compared these

two complex regimens, 8 weeks of combination therapy followed by 4 weeks of once-daily calcipotriol was significantly less effective than a routine involving 4 weeks of combination therapy followed by 8 weeks of once-daily calcipotriol on weekdays and combination therapy at the weekend (SMD 0.24; 95% CI 0.08 to 0.40, equivalent to 0.27 (¼ of 1 point) on a 6-point IAGI scale). This finding was based on the investigators' assessment (IAGI), which was very similar to the participants' (PAGI) assessment (Analysis 13.4). However, the PASI found a non-significant trend in favour of the weekday/weekend regimen (Analysis 13.3).

In five intervention-comparator contrasts, we found no significant difference. A single study reported two of the non-significant intervention-comparator contrasts: Kragballe 2004 compared 12 weeks of calcipotriol monotherapy with each of the 2 complex regimens described in the paragraph above. Compared with monotherapy, participants who applied once-daily combination treatment (calcipotriol/betamethasone dipropionate) for 8 weeks followed by once-daily calcipotriol for 4 weeks did not experience a significantly greater improvement (SMD -0.12; 95% CI -0.29 to 0.04). Similarly, the psoriasis of participants on monotherapy with twice-daily calcipotriol did not improve significantly more or less than the disease in participants who applied once-daily combination treatment (calcipotriol/betamethasone dipropionate) for 4 weeks followed by 8 weeks using once-daily calcipotriol (weekdays) and once-daily combination therapy (weekends) (SMD 0.13; 95% CI -0.04 to 0.29). These findings were based on the investigators' assessment (IAGI), which were consistent with those of the participants (Analysis 13.4) and with the PASI assessment (Analysis 13.3).

Similarly to Kragballe 2004, Saraceno 2007 compared 12 weeks of calcipotriol monotherapy with 4 weeks of combined therapy followed by 8 weeks of twice-daily calcipotriol. The SMD for the combined end point (0.29; 95% CI -0.04 to 0.62) showed a non-significant trend in favour of the complex regimen. Yang 2009 also explored how monotherapy with calcipotriol compared with combined vitamin D/corticosteroid treatment. A 6-week course of monotherapy with calcipotriol was not significantly different to a sequential regimen involving halometasone (SMD 0.41; 95% CI -0.05 to 0.86). Lahfa 2003 found that the effect of clobetasol propionate combined with calcipotriol was similar to the effect of a regimen where the same corticosteroid was used in conjunction with calcitriol: SMD -0.19 (95% CI -0.54 to 0.16).

Analysis 14: Vitamin D alone or in combination versus other treatment: long-term studies (> 24 weeks)

This comparison included active-controlled studies of psoriasis of the body that were at least 24 weeks in duration (see Analysis 14.5 and Table 17). One longer-term placebo-controlled trial of the body (Katz 1991a) and two long-term scalp trials (Luger 2008; Poulin 2010) did not meet the inclusion criteria for this comparison, so we evaluated them elsewhere (Analyses 2, 19, and 18, respectively).

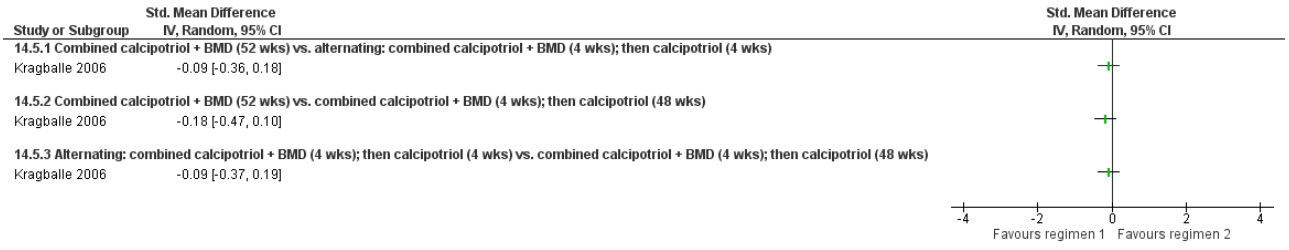
This comparison included one trial, Kragballe 2006, which was a between-patient trial that compared 3 52-week regimens with all treatments used once daily:

- first, combination treatment with calcipotriol and betamethasone dipropionate;
- second, alternating treatment with combination therapy for 4 weeks, then calcipotriol for 4 weeks; and
- third, combination therapy for 4 weeks, then calcipotriol for 48 weeks.

In total, 297 participants contributed data to the analysis. The only outcome measure from the trial that could be included in our review was the Investigator's Global Assessment of Disease Severity (scored from 0, absent, to 5, severe); therefore, results from this section are identical to those in Analysis 14.1. Data were unsuitable for pooling because the same participants contributed to more than one analysis. The adequacy of the concealment of treatment allocation was unclear in this trial.

Data from the combined end point showed there was no significant difference between the three long-term regimens (Figure 5). One year's combination therapy was not significantly better than either the alternating regimen (SMD -0.09; 95% CI -0.36 to 0.18) or the regimen of treatment with 4 weeks of combination therapy followed by 48 weeks of calcipotriol (SMD -0.18; 95% CI -0.47 to 0.10). In both these comparisons, combination therapy achieved a larger absolute benefit, but the difference was not statistically significant. When we compared the alternating therapy with the regimen of 4 weeks' combination therapy followed by 48 weeks of calcipotriol, the SMD for the IAGI also indicated the 2 regimens were not statistically significantly different: -0.09 (95% CI -0.37 to 0.19).

Figure 5. Forest plot of comparison: 14 Vitamin D alone or in combination vs. other treatment: long term studies (>24wks), outcome: 14.5 Combined end point (IAGI/TSS/PASI/PAGI).



Findings were based on unpublished data supplied by the trial sponsor. Although these data were described as 'intention-to treat', just 47% of the enrolled participants contributed data to the 52-week assessment. The reasons why participants withdrew are summarised in Analysis 14.6, Analysis 14.7, and Analysis 14.8.

Analysis 15: Vitamin D analogues versus other treatment

This comparison incorporated all other vitamin D head-to-head comparisons of treatments for psoriasis of the body (excluding inverse psoriasis) that we had not already included (see Analysis 15.5 and Table 18). We included 12 intervention-comparator contrasts, with data using the combined end point available for 11 of these contrasts. No effectiveness data were available for the comparison of calcipotriol and combined treatment with tazarotene gel plus mometasone furoate cream (Guenther 2000), but the trial did report data on withdrawal and adverse events. Thirteen between-patient trials and 6 within-patient trials provided data for the combined end point from 2364 participants. Trial duration ranged between 4 and 12 weeks. Three studies adequately concealed treatment allocation. In light of the pharmacological diversity of the comparators, we only pooled data within subgroups.

In three intervention-comparator contrasts, vitamin D was significantly more effective than the comparator. Specifically, twice-daily calcipotriol was more effective than coal tar polytherapy (SMD -0.59; 95% CI -0.87 to -0.31; I^2 statistic = 0%; 2 studies) and propylthiouracil cream (SMD -2.24; 95% CI -3.23 to -1.25; I^2 statistic = NA). On a 6-point IAGI scale, these equate to improvements of 0.65 of a point and 2.46 points, respectively. Twice-daily vitamin D was significantly more effective than once-daily treatment (SMD -0.20; 95% CI -0.32 to -0.07; I^2 statistic = 0%; 3 studies), achieving an additional improvement of around 0.22 of a point on a 6-point IAGI scale. This finding was based on dosing assessments of 2 vitamin D products: calcipotriol (SMD -0.19; 95% CI -0.37 to -0.02; I^2 statistic = 12%; 2 studies) and combination treatment with calcipotriol and betamethasone dipropionate (SMD -0.20; 95% CI -0.41 to 0.00; I^2 statistic = NA).

In the remaining eight intervention-comparator contrasts, we found no significant difference between twice-daily calcipotriol and the comparators. This finding held for the comparison against the following products: coal tar monotherapy (SMD -0.53; 95% CI -1.74 to 0.68; I^2 statistic = 91.1%; 3 studies); nicotinamide, either alone (SMD -0.09; 95% CI -0.49 to 0.31; I^2 statistic: NA) or in combination with calcipotriol (SMD 0.19; 95% CI -0.14 to 0.52; I^2 statistic = NA); betamethasone dipropionate ointment and salicylic acid (SMD -0.05; 95% CI -0.26 to 0.15; I^2 statistic = NA); tacrolimus ointment (SMD -0.55; 95% CI -1.28 to 0.17; I^2 statistic = 75.9%; 2 studies); tazarotene (SMD -0.10; 95% CI -0.35 to 0.16; I^2 statistic = 0%; 2 studies); and vitamin B12 cream (SMD -0.55; 95% CI -1.33 to 0.24; I^2 statistic = NA). The addition of occlusion to calcipotriol did not significantly improve the drug's effectiveness (SMD -0.18; 95% CI -2.04 to 1.68; I^2 statistic = 96.2%; 2 studies).

Two of the three trials comparing calcipotriol with coal tar monotherapy found a significant difference in favour of calcipotriol (De Simone 1993; Tham 1994); the other trial found a significant difference in favour of coal tar (Alora-Palli 2010). This apparent contradiction may reflect different formulations of coal tar, treatment durations, or different baseline disease severity. Alora-Palli 2010 also assessed effectiveness and quality of life over the six-week post-treatment period, finding that the coal tar group maintained their improvement significantly better than those treated with calcipotriol (see section (c) Quality of life measures).

The two occlusion trials used very different regimens and may be better considered separately. Hindsén 2006 (H) compared calcipotriol with occlusion (applied once weekly for 2 weeks) followed by 4 weeks off treatment against 6 weeks of calcipotriol monotherapy. This trial does not provide a simple assessment of occlusion, since, additionally, treatment is withdrawn. This parallel-group trial contributed data from 209 participants with moderately severe disease and found monotherapy was significantly more effective at the 6-week end point (SMD -1.11; 95% CI -1.40 to -0.81). In the other trial, 19 participants were treated for 8 weeks with twice-daily calcipotriol on both sides of the body, and one side was randomised to receive overnight occlusion with polythene. Bourke 1993b found a significant difference in favour of occlusion (SMD 0.79; 95% CI 0.13 to 1.45); the trial did not explicitly state the severity of participants.

We reported elsewhere trials comparing vitamin D and other treatments for scalp psoriasis (Analysis 19.5) and inverse psoriasis (Analysis 17.5).

Analysis 16: Flexural/facial psoriasis: placebo-controlled trials

This comparison included placebo-controlled trials of topical treatments for inverse or facial psoriasis (see Analysis 16.5 and Table 19). We found evidence on four treatments in this comparison: the potent steroid betamethasone valerate; the vitamin D analogue calcipotriol; and two topical calcineurin inhibitors, pimecrolimus and tacrolimus. We identified only one placebo-controlled trial evaluating tacrolimus ointment (Lebwohl 2004), but the study did not report any effectiveness data suitable for this review. However, the study did contribute data on adverse events and withdrawal rates. We pooled only subtotals in this comparison.

Using the combined end point, data were available for three of the four topical treatments for inverse psoriasis. Two between-patient trials contributed data from 122 participants. Gribetz 2004 was a eight-week study that evaluated twice-daily pimecrolimus cream. The four-week trial by Kreuter 2006 (P) compared betamethasone valerate, calcipotriol, and pimecrolimus against placebo; all treatments were applied once daily. Treatment allocation was adequately concealed in one trial (Gribetz 2004). Therefore, we based the findings for each treatment on a single study.

The SMD for the combined end point found a statistically significant difference in favour of betamethasone valerate (SMD -2.83; 95% CI -3.79 to -1.88) and calcipotriol ointment (SMD -1.08; 95% CI -1.77 to -0.40). These equate to improvements of 3.25 points and 1.24 points on a 6-point IAGI scale. Pimecrolimus cream was also significantly more effective than vehicle (SMD -0.86; 95% CI -1.30 to -0.41; I^2 statistic = 0%), equivalent to almost 1 point on a 6-point IAGI. This result pooled data on twice-daily applications for 8 weeks (SMD -1.07; 95% CI -1.69 to -0.45) and once-daily pimecrolimus cream for 4 weeks (SMD -0.62; 95% CI -1.27 to 0.02). These findings suggest that different dosing schedules may influence efficacy.

Analysis 17: Flexural/facial psoriasis: vitamin D alone or in combination versus other treatment

This comparison included head-to-head trials of treatments for inverse psoriasis, where we compared vitamin D with an active control (see Analysis 17.5 and Table 20). We identified five intervention-comparator contrasts. Four treatments were compared with calcipotriol: once-daily betamethasone valerate, combined treatment with calcipotriol and hydrocortisone,

calcitriol, and pimecrolimus. Calcitriol was compared with tacrolimus.

Using the combined end point, data were available for all five intervention-comparator contrasts. Four trials, varying in duration from 4 to 8 weeks, contributed data from 588 participants. Three studies were between-patient trials, and one was a within-patient study (Ortonne 2003). The adequacy of concealment of treatment allocation was unclear in all four trials.

When applied to sensitive areas of the body, calcipotriol was significantly less effective than three of the comparators. These included betamethasone valerate (SMD 2.02; 95% CI 1.20 to 2.84) (Kreuter 2006 (H)), combination treatment with calcipotriol and hydrocortisone (SMD 0.30; 95% CI 0.11 to 0.50) (Ortonne 2010), and calcitriol (SMD 0.61; 95% CI 0.28 to 0.94) (Ortonne 2003). On a 6-point IAGI scale, the additional benefit equates to 2.22 points for betamethasone valerate, ⅓ of a point for combination treatment with hydrocortisone, and ⅔ of a point for calcitriol.

There was no significant difference between vitamin D and the topical calcineurin inhibitors (calcipotriol versus pimecrolimus: SMD -0.53 (95% CI -1.17 to 0.11; I^2 statistic = NA); calcitriol versus tacrolimus: SMD 0.42 (95% CI -0.15 to 0.98; I^2 statistic = NA)).

Analysis 18: Scalp psoriasis: placebo-controlled trials

This comparison included placebo-controlled trials of treatments for scalp psoriasis (see Analysis 18.5, Figure 6, and Table 21). We included evidence on 11 treatments in this comparison, with data from the combined end point available for all 11 treatments. Thirteen between-patient trials and 1 within-patient trial (Lepaw 1978) contributed data from 3011 participants. Trial duration ranged between two and eight weeks. Concealment of treatment allocation was adequate in one trial.

Figure 6. Forest plot of comparison: 18 Scalp psoriasis: placebo-controlled trials, outcome: 18.5 Combined end point (IAGI/TSS/PASI/PAGI).

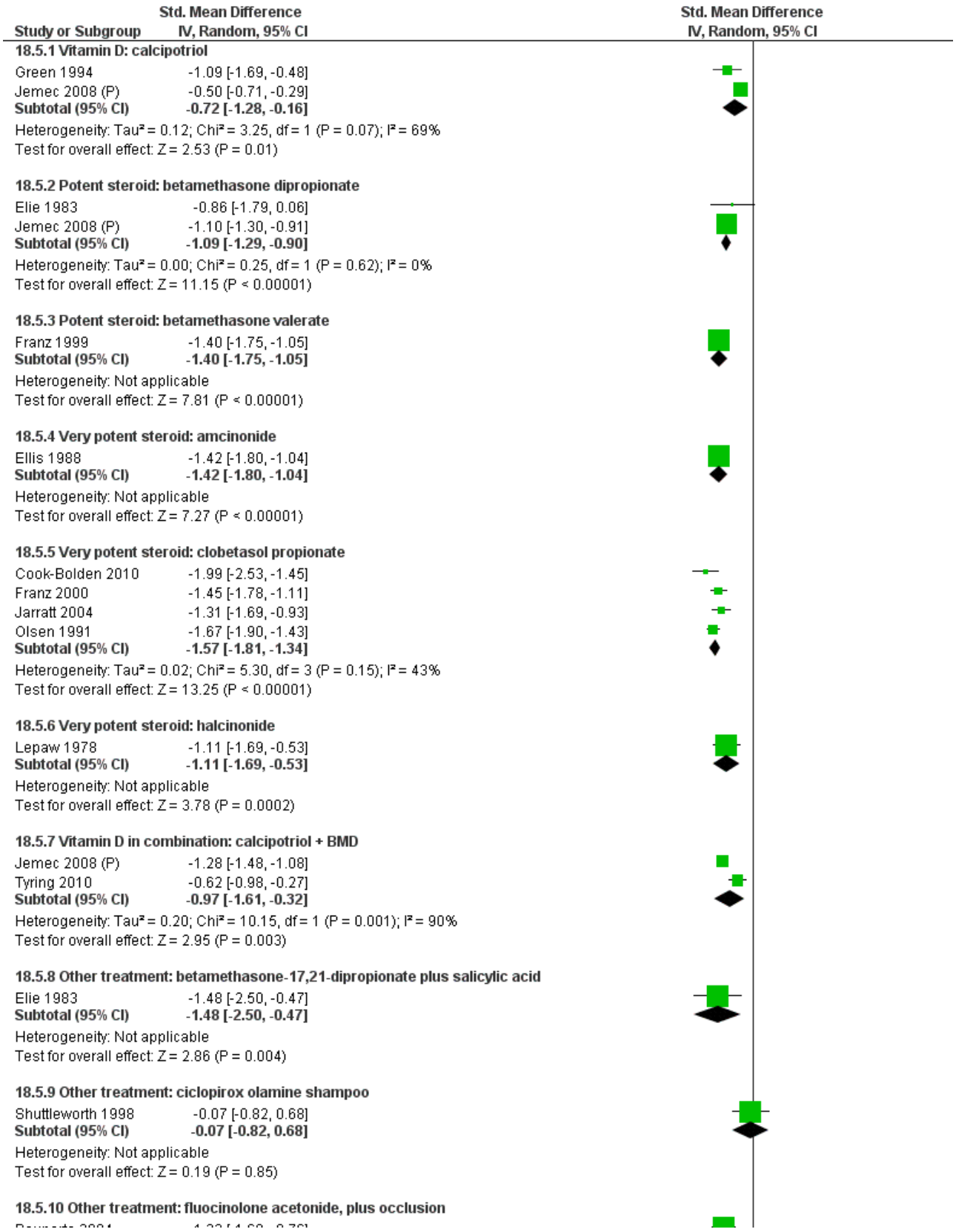
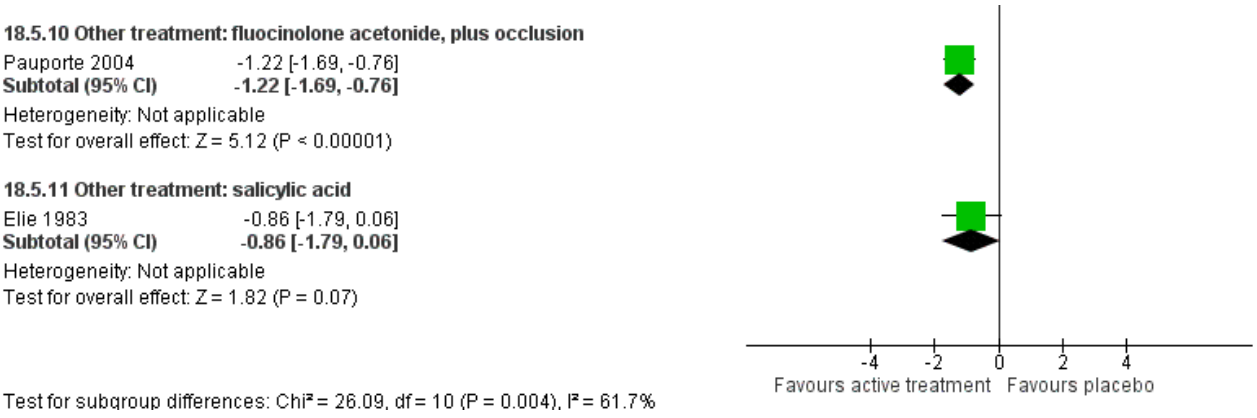


Figure 6. (Continued)



Two treatments were not significantly more effective than placebo. These were ciclopirox olamine shampoo (SMD -0.07; 95% CI -0.82 to 0.68; I^2 statistic = NA) and salicylic acid (SMD -0.86; 95% CI -1.79 to 0.06; I^2 statistic = NA). Of the nine treatments demonstrated to be significantly more effective than placebo, corticosteroids achieved the largest effects. Two very potent corticosteroids, amcinonide (SMD -1.42; 95% CI -1.80 to -1.04; I^2 statistic = NA) and clobetasol propionate (SMD -1.57; 95% CI -1.81 to -1.34; I^2 statistic = 43.3%; 4 studies), delivered benefits equating to almost 2 points (1.70 and 1.88 points, respectively) on a 6-point IAGI (Investigator's Assessment of Global Improvement) scale. Betamethasone dipropionate combined with salicylic acid achieved a similar effect (SMD -1.48; 95% CI -2.50 to -0.47; I^2 statistic = NA), translating into 1.77 point improvement on the 6-point IAGI over and above placebo.

When used as monotherapy, the 2 potent corticosteroids evaluated were both more effective than placebo: Betamethasone dipropionate (SMD -1.09; 95% CI -1.29 to -0.90; I^2 statistic = 0%; 2 studies) had a smaller effect than betamethasone valerate (SMD -1.40; 95% CI -1.75 to -1.05; I^2 statistic = NA), although the difference was not statistically significant. Calcipotriol had the smallest observed benefit (SMD -0.72; 95% CI -1.28 to -0.16; I^2 statistic = 69.2%; 2 studies). When calcipotriol was combined with betamethasone dipropionate, the pooled effect was larger than for calcipotriol used alone (SMD -0.97; 95% CI -1.61 to -0.32; I^2 statistic = 90.2%; 2 studies), or 1.16 points on a 6-point improvement scale. Figure 6 shows that both trials found combination therapy to be significantly more effective, but Jemec 2008 (P) found a significantly larger effect (SMD -1.28; 95% CI -1.48 to -1.08) than Tyring 2010 (SMD -0.62; 95% CI -0.98 to -0.27). Participants in the two trials contributing data to the analysis of combination therapy differed in their ethnicity: Tyring 2010 recruited 177 people of Hispanic, Latino, Black, and African American ethnicity; in the trial by Jemec 2008 (P), over 96% of the 1505 enrollees were white. In addition, the trial by Jemec 2008 (P) included a larger proportion of people with severe or very severe disease (37% versus 20%). These factors may help explain the considerable level of heterogeneity (Higgins 2011) observed in the pooled effect for combination therapy.

Sensitivity analysis

We pooled data for the two potent corticosteroids, betamethasone dipropionate and betamethasone valerate. The SMD for the combined end point was -1.18 (95% CI -1.40 to -0.96; I^2 statistic = 19.9%; 3 studies), equating to 1.41 points on a 6-point IAGI scale. For the 3 very potent corticosteroids, the SMD was -1.51 (95% CI -1.70 to -1.31; I^2 statistic = 37.5%; 6 studies), translating as a 1.80 point improvement over placebo on the IAGI.

Analysis 19: Scalp psoriasis: vitamin D alone or in combination versus other treatment

This comparison included head-to-head trials of treatments for scalp psoriasis in which one of the interventions was a vitamin D product (used either as monotherapy or in combination with another product) (see Analysis 19.5 and Table 22).

We identified six intervention-comparator contrasts, and data on the combined end point were available for all these contrasts. All studies were parallel-group in design (between-patient). Twelve studies contributed data from 5413 participants. Trial duration ranged from 4 to 8 weeks in 11 studies, but duration was 52 weeks in one trial (Luger 2008). The adequacy of the concealment of treatment allocation was unclear in all 12 trials.

Based on the combined end point scores, monotherapy with vitamin D was consistently less effective than monotherapy with potent or very potent corticosteroids, and it was also significantly less effective than combination therapy with vitamin D and a potent steroid. Specifically, calcipotriol was significantly less effective than betamethasone dipropionate (SMD 0.48; 95% CI 0.32 to 0.64; I^2 statistic = 60.4%; 2 studies), betamethasone valerate (SMD 0.37; 95% CI 0.20 to 0.55; I^2 statistic = 0%; 2 studies), and clobetasol propionate (SMD 0.37; 95% CI 0.05 to 0.69; I^2 statistic = NA). On a 6-point investigators' global assessment of improvement (IAGI) scale, these SMDs translate into 0.62, 0.48, and 0.48 points, respectively.

Combination treatment achieved a significantly greater benefit than either calcipotriol alone or betamethasone dipropionate alone. Calcipotriol was significantly less effective than combination treatment (SMD 0.64; 95% CI 0.44 to 0.84; I^2 statistic = 82.3%; 4 studies), with combined therapy delivering a benefit equivalent to 0.83 of a point on a 6-point IAGI. Combination treatment was significantly more effective than monotherapy with betamethasone dipropionate (SMD -0.18; 95% CI -0.26 to -0.10; I^2 statistic = 0%; 3 studies), translating into a net benefit of 0.24 of a point on a 6-point IAGI scale.

Compared with coal tar polytherapy, calcipotriol achieved a larger benefit, though this was not statistically significant at the 5% level (SMD -0.45; 95% CI -0.92 to 0.02; I^2 statistic = 89.8%; 3 studies).

(2) Secondary outcome measures

(a) Withdrawal rates (total rate; withdrawal due to adverse events; withdrawal due to treatment failure)

Analysis 1: Vitamin D analogues versus placebo

We pooled withdrawal data from seven of the eight vitamin D analogues using a random-effects risk difference (RD) metric (see Analysis 1.6, Analysis 1.7, and Analysis 1.8). There were no withdrawal data for the comparison of calcipotriol plus occlusion versus placebo.

There was no significant difference in the pooled rate of withdrawals from the trials for any reason (total withdrawals) (RD: -0.02; (95% CI -0.05 to 0.00; I^2 statistic = 51.4%). Rates of withdrawals due to adverse events were not statistically significantly different (RD -0.00; 95% CI -0.02 to 0.01; I^2 statistic = 36.4%), and neither were withdrawals due to treatment failure (RD -0.03; 95% CI -0.05 to 0.00; I^2 statistic = 81.7%). Individually, none of the eight vitamin D analogues were significantly different to placebo in any of the three withdrawal rates.

Analysis 2: Corticosteroid (potent) versus placebo

This comparison included 10 potent corticosteroids. No withdrawal data were available for diflorasone diacetate, and some withdrawal data were missing for fluticasone propionate, mometasone furoate, and betamethasone dipropionate. Where available, we pooled data using a random-effects risk difference metric (see Analysis 2.6, Analysis 2.7, and Analysis 2.8). There was a small but statistically significant difference in favour of potent corticosteroids for withdrawals from the trials for any reason (total withdrawals): RD -0.14 (-0.22 to -0.05; I^2 statistic = 81.5%). This finding was driven by two large trials of once-daily betamethasone dipropionate (Fleming 2010 (P); Kaufmann 2002 (P)) and two small trials of betamethasone dipropionate used as maintenance (weekend pulse therapy) (Katz 1987a; Katz 1991a). In the other corticosteroids, the RD showed no statistically significant difference.

There was no significant difference in the pooled rate of withdrawals due to adverse events (RD -0.01; 95% CI -0.05 to 0.02; I^2 statistic = 60.9%). However, betamethasone dipropionate once daily was associated with statistically significantly lower rates of withdrawal due to adverse events than placebo (RD -0.07; 95% CI -0.11 to -0.02; I^2 statistic = NA).

For the rate of withdrawals due to treatment failure (Analysis 2.8), findings differed by treatment duration; therefore, we only pooled subgroup data. For short-term treatments, there was no difference relative to placebo (RD 0.00; 95% CI -0.02 to 0.02; I^2 statistic = 0.0%). This is the pooled effect for the placebo comparisons with betamethasone valerate, budesonide, desonide, and hydrocortisone buteprate (data on withdrawals due to treatment failure for once-daily and twice-daily betamethasone dipropionate were not available). For maintenance treatment with betamethasone dipropionate, there was a statistically significant difference in favour of maintenance treatment when compared with placebo: RD -0.46; 95% CI -0.61 to -0.31; I^2 statistic = 0.0% (Katz 1987a; Katz 1991a).

Analysis 3: Corticosteroid (very potent) versus placebo

We identified withdrawal data for two of the three very potent corticosteroids in this comparison and pooled data using a random-effects risk difference metric (see Analysis 3.6, Analysis 3.7, and Analysis 3.8). There were no withdrawal data available for halcinonide. There were no statistically significant differences between very potent corticosteroids and placebo for any type of withdrawal or for any individual treatment. For total withdrawals, the risk difference was -0.05 (95% CI -0.10 to 0.01; I^2 statistic = 83.7%). Differences in withdrawals due to adverse events (RD -0.00; 95% CI -0.01 to 0.01; I^2 statistic = 0.0%) and withdrawals due to treatment failure (RD -0.00; 95% CI -0.02 to 0.01); I^2 statistic = 13.5%) were also small and non-significant.

Analysis 4: Dithranol versus placebo

We pooled withdrawal data on dithranol versus placebo using a random-effects risk difference metric (see Analysis 4.6, Analysis 4.7, and Analysis 4.8). There were no statistically significant differences between dithranol and placebo for any type of withdrawal. For total withdrawals, the risk difference was 0.00 (95% CI -0.09 to 0.09; I^2 statistic = 0%). Differences in withdrawals due to adverse events (RD 0.00; 95% CI -0.05 to 0.05; I^2 statistic = 0%) and withdrawals due to treatment failure (RD 0.00; 95% CI -0.11 to 0.11; I^2 statistic = 0%) were also small and non-significant.

Analysis 5: Vitamin D combination products versus placebo

We pooled data from trials of vitamin D combination products using a random-effects risk difference (RD) metric (see Analysis 5.6, Analysis 5.7, and Analysis 5.8). In all three withdrawal measures, combined treatment - whether used once or twice daily - was significantly less likely to lead to withdrawal from the trial. This finding held for total withdrawals (RD -0.12; 95% CI -0.17 to -0.07; I^2 statistic = 59.3%), withdrawals due to adverse events (RD -0.07; 95% CI -0.11 to -0.04; I^2 statistic = 55.0%), and withdrawals due to treatment failure (RD -0.09; 95% CI -0.12 to -0.06; I^2 statistic = 0%).

Analysis 6: Other treatment versus placebo

We report findings separately for 22 of the 26 treatments considered; no withdrawal data were available for four placebo comparisons: those involving a herbal skin care product, topical sirolimus, topical tacrolimus, or coal tar. Data on total withdrawals were available for 22 treatments; for withdrawals due to adverse events or treatment failure, data were available for 18 treatments (see Analysis 6.6, Analysis 6.7, and Analysis 6.8).

We assessed withdrawal data using a random-effects risk difference metric. Relative to placebo, tazarotene was associated with a significantly higher rate of withdrawal due to adverse events (RD 0.07; 95% CI 0.05 to 0.10) and *Mahonia aquifolium* was associated with a significantly lower rate of total withdrawal (i.e. withdrawal from the trial for any reason) (RD -0.23; 95% CI -0.32 to -0.14). No other treatment was significantly different from placebo on any of the three withdrawal measures assessed.

Aloe vera extract 0.5% hydrophilic cream, three times per day

Sixty participants contributed data (Syed 1996). The comparison with placebo found no statistically significant difference for aloe vera extract, for total withdrawals, withdrawals due to adverse events, or withdrawals due to treatment failure.

Anti-IL-8 monoclonal antibody cream

Ninety-six participants contributed data (Jin 2001). For total withdrawals, the comparison with placebo found no statistically significant difference for anti-IL-8 monoclonal antibody cream. The study did not report data on withdrawals due to adverse events or treatment failure.

Betamethasone 17-valerate 21-acetate plus tretinoin plus salicylic acid

Eighty-five participants contributed data (Santoianni 2001). The comparison with placebo found no statistically significant difference for betamethasone 17-valerate 21-acetate plus tretinoin plus salicylic acid for total withdrawals, withdrawals due to adverse events, or withdrawals due to treatment failure.

Caffeine (topical) 10%, three times per day

Thirty-nine participants contributed data (Vali 2005). The comparison with placebo found no statistically significant difference for topical caffeine for total withdrawals, withdrawals due to adverse events, or withdrawals due to treatment failure.

Calcipotriene 0.005% ointment + nicotinamide 0.05% or 0.1% or 0.7% or 1.4%, twice daily

One hundred and sixty participants contributed data (Levine 2010 (P)). The comparison with placebo found no statistically significant difference for combination therapy with calcipotriol and nicotinamide for total withdrawals, withdrawals due to adverse events, or withdrawals due to treatment failure.

Dead Sea salts emollient lotion

Twenty-four participants contributed data (Cheesbrough 1992). The comparison with placebo found no statistically significant difference for Dead Sea salts emollient lotion for total withdrawals, withdrawals due to adverse events, or withdrawals due to treatment failure.

Fish oil plus occlusion

Twenty-five participants contributed data (Escobar 1992). The comparison with placebo found no statistically significant difference for fish oil plus occlusion for total withdrawals, withdrawals due to adverse events, or withdrawals due to treatment failure.

Herbal skin care (Dr Michaels® cleansing gel, ointment, and skin conditioner), twice daily

No withdrawal data were available for this comparison.

Hexafluoro-1,25-dihydroxyvitamin D3

Fifteen participants contributed data (Durakovic 2001). The comparison with placebo found no statistically significant difference for hexafluoro-1,25-dihydroxyvitamin D3 for total withdrawals, withdrawals due to adverse events, or withdrawals due to treatment failure.

Indigo naturalise 1.4% ointment

Fifty-six participants contributed data from two within-patient trials (Lin 2007; Lin 2008). The comparison with placebo found no statistically significant difference for indigo naturalise ointment for total withdrawals, withdrawals due to adverse events, or withdrawals due to treatment failure.

Kukui nut oil, three times per day

Thirty participants contributed data (Brown 2005). The comparison with placebo found no statistically significant difference for kukui nut oil for total withdrawals, withdrawals due to adverse events, or withdrawals due to treatment failure.

***Mahonia aquifolium* (Reliéva™), twice daily**

Two hundred participants contributed data (Bernstein 2006). For total withdrawals, the comparison with placebo found a statistically significant difference for *Mahonia aquifolium* (RD -0.23; 95% CI -0.32 to -0.14). The trial did not report data on withdrawals due to adverse events or treatment failure.

Methotrexate gel

Sixty participants contributed data (Syed 2001b). The study by Sutton 2001 on methotrexate gel did not report withdrawal data. The comparison with placebo found no statistically significant difference for methotrexate gel for total withdrawals, withdrawals due to adverse events, or withdrawals due to treatment failure.

Mycophenolic acid ointment

Seven participants contributed data (Geilen 2000). The comparison with placebo found no statistically significant difference for mycophenolic acid ointment for total withdrawals, withdrawals due to adverse events, or withdrawals due to treatment failure.

NG-monomethyl-L-arginine (L-NMMA) cream

Seventeen participants contributed data (Ormerod 2000). The comparison with placebo found no statistically significant difference for NG-monomethyl-L-arginine (L-NMMA) cream for total withdrawals, withdrawals due to adverse events, or withdrawals due to treatment failure.

Nicotinamide 1.4%, twice daily

Eighty-eight participants contributed data (Levine 2010 (P)). The comparison with placebo found no statistically significant difference for nicotinamide for total withdrawals, withdrawals due to adverse events, or withdrawals due to treatment failure.

Oleum horwathiensis

Fifty participants contributed data (Lassus 1991). The comparison with placebo found no statistically significant difference for oleum horwathiensis for total withdrawals, withdrawals due to adverse events, or withdrawals due to treatment failure.

Omega-3 polyunsaturated fatty acids ointment

Seventy-three participants contributed data (Henneicke-v. Z. 1993). The comparison with placebo found no statistically significant difference for omega-3 polyunsaturated fatty acids ointment for total withdrawals, withdrawals due to adverse events, or withdrawals due to treatment failure.

Platelet aggregation activating factor (PAF) (Ro 24-0238)

Fifty-two participants contributed data (Wolska 1995). The comparison with placebo found no statistically significant difference for platelet aggregation activating factor for total withdrawals. The trial did not report data on withdrawals due to adverse events or treatment failure.

Polymyxin B cream, 200,000 U/g

Fifteen participants contributed data (Stutz 1996). The comparison with placebo found no statistically significant difference for polymyxin B cream for total withdrawals. The trial did not report data on withdrawals due to adverse events or treatment failure.

PTH (1-34) in Novasome A® liposomal cream, twice daily

Fifteen participants contributed data (Holick 2003). The comparison with placebo found no statistically significant difference for PTH (1-34) in Novasome A® liposomal cream for total withdrawals, withdrawals due to adverse events, or withdrawals due to treatment failure.

Sirolimus (topical)

No withdrawal data were available for this comparison.

Tacrolimus ointment

No withdrawal data were available for this comparison.

Tar

No withdrawal data were available for this comparison.

Tazarotene

Two studies, with 1627 participants, contributed data (Weinstein 1996; Weinstein 2003). The comparison with placebo found no statistically significant difference for tazarotene for total withdrawals or withdrawals due to treatment failure. However, tazarotene was significantly more likely to lead to withdrawal from the trial due to adverse events (RD 0.07; 95% CI 0.05 to 0.10; I^2 statistic = 0%).

Theophylline 1% ointment, twice daily

Twenty-two participants contributed data (Papakostantinou 2005). The comparison with placebo found no statistically significant difference for theophylline ointment for total withdrawals, withdrawals due to adverse events, or withdrawals due to treatment failure.

Analysis 7: Vitamin D analogues versus corticosteroid (potent)

Seven of the eight vitamin D analogues that were compared with potent corticosteroids reported withdrawal data (withdrawal data on calcipotriol versus desoxymetasone were not available) (see Analysis 7.6, Analysis 7.7, and Analysis 7.8). We pooled withdrawal data on these seven treatment comparison pairs using a random-effects risk difference (RD) metric.

Relative to potent corticosteroid, there was a statistically significant difference in total withdrawals in favour of corticosteroids: RD 0.02 (95% CI 0.00 to 0.03; I^2 statistic = 0%). Pooled rates of withdrawals due to adverse events or treatment failure were not statistically significantly different. Regarding individual vitamin D analogues, the only statistically significant differences in withdrawals relative to corticosteroid were for the comparison of calcipotriol against betamethasone dipropionate (total withdrawals: RD 0.03 (95% CI 0.01 to 0.06; I^2 statistic = 0%); withdrawals due to adverse events: RD 0.02 (95% CI 0.00 to 0.04; I^2 statistic = NA)).

Analysis 8: Vitamin D analogues versus corticosteroid (very potent)

We pooled withdrawal data on calcipotriol against clobetasol propionate using a random-effects risk difference (RD) metric (see Analysis 8.6, Analysis 8.7, and Analysis 8.8). Relative to the very potent corticosteroid, we found no statistically significant difference for calcipotriol on any of the withdrawal assessments: total withdrawals, withdrawals due to adverse events, or withdrawals due to treatment failure.

Analysis 9: Vitamin D combined with corticosteroid versus corticosteroid

We pooled withdrawal data on combination treatment (vitamin D and a corticosteroid) against monotherapy with a corticosteroid using a random-effects risk difference (RD) metric (see Analysis 9.6, Analysis 9.7, and Analysis 9.8).

Relative to the corticosteroid, we found no statistically significant difference for combination treatment on total withdrawals, withdrawals due to adverse events, or withdrawals due to treatment failure. There were no data on the rate of withdrawals due to treatment failure for the comparison of combined treatment with calcipotriol and betamethasone dipropionate versus betamethasone dipropionate monotherapy.

Analysis 10: vitamin D alone or in combination versus dithranol

Withdrawal data were available for three intervention-comparator pairs: calcipotriol versus dithranol, calcitriol versus dithranol, and tacalcitol versus dithranol. We pooled these data using a random-effects risk difference (RD) metric (see Analysis 10.6, Analysis 10.7, and Analysis 10.8). For the comparison of tacalcitol versus dithranol, there were no data available on withdrawals due to adverse events or treatment failure.

There was no statistically significant difference for total withdrawals, either for individual intervention-comparator pairs or for the pooled effect (RD -0.02; 95% CI -0.06 to 0.01; I^2 statistic = 0%). The pooled risk difference showed a significant difference in favour of vitamin D for withdrawals due to adverse events (RD -0.03; 95% CI -0.06 to -0.00; I^2 statistic = 26.3%), but no significant difference in the rate of withdrawals due to treatment failure (RD -0.00; 95% CI -0.02 to 0.02; I^2 statistic = 0%).

Analysis 11: Vitamin D alone or in combination versus other vitamin D analogue

Two of the three vitamin D analogues head-to-head comparisons reported withdrawal data (withdrawal data on calcipotriol versus tacalcitol were not available). We pooled withdrawal data on calcipotriol versus calcitriol, and calcipotriol versus maxacalcitol, using a random-effects risk difference (RD) metric (see Analysis 11.6, Analysis 11.7, and Analysis 11.8). We found no statistically significant difference on any of the withdrawal assessments: total withdrawals, withdrawals due to adverse events, or withdrawals due to treatment failure. There was also no significant difference in the withdrawal rates for the individual contrasts, calcipotriol versus calcitriol, and calcipotriol versus maxacalcitol.

Analysis 12: Vitamin D alone or in combination versus vitamin D + corticosteroid

To simplify the analysis, we summarised withdrawal data by grouping the first 10 intervention-comparator pairs in a single category: calcipotriol versus calcipotriol and corticosteroid. The remaining comparisons were calcitriol versus calcitriol and corticosteroid, and tacalcitol versus calcipotriol and corticosteroid. We pooled withdrawal data using a random-effects risk difference (RD) metric (see Analysis 12.6, Analysis 12.7, and Analysis 12.8).

There were no data on withdrawals due to treatment failure for the comparisons of combined therapy versus calcitriol or combined therapy versus tacalcitol.

In the comparison of calcipotriol against calcipotriol plus corticosteroid, total withdrawals were statistically significantly different in favour of polytherapy: RD 0.03 (95% CI 0.01 to 0.05; I^2 statistic = 13.3%). We based this on findings from 4922 participants in 13 trials. Similarly, a significant difference in favour of polytherapy was evident from the data on withdrawals due to adverse events: RD 0.02 (95% CI 0.01 to 0.03; I^2 statistic = 32.9%). However, we found no statistically significant difference for withdrawals due to treatment failure (RD 0.01; 95% CI -0.00 to 0.02; I^2 statistic = 0%). When either calcitriol or tacalcitol was compared with combination therapy, differences in total withdrawals and in withdrawals due to adverse events were not statistically significant.

Analysis 13: Vitamin D alone or in combination versus other treatments: complex regimens

This comparison covers complex regimens, defined here as treatment sequences that do not consist of a simple head-to-head comparison between two active treatments. We summarised withdrawals rates on twelve intervention-comparator contrasts (see Analysis 13.6, Analysis 13.7, and Analysis 13.8). There were data on total withdrawal rates for all 12 contrasts, but data on withdrawals due to adverse events were missing for 3 contrasts, and there were no data on withdrawals due to treatment failure for 6 contrasts.

In the analysis of total withdrawals (Analysis 13.6), there was a significant difference in favour of the complex regimen for four contrasts:

- Participants were significantly more likely to withdraw from the trial after 12 weeks of calcipotriol than participants who received combination therapy (8 weeks) followed by calcipotriol (4 weeks) (RD 0.05; 95% CI 0.00 to 0.10).
- Trial withdrawal rates were also significantly higher in participants receiving 12 weeks of monotherapy with calcipotriol than those treated with combination therapy (4 weeks) followed by alternating calcipotriol on weekdays and combination therapy at the weekend (8 weeks) (RD 0.08; 95% CI 0.03 to 0.13).
- After an initial 4-week phase with combination ointment, participants who received 8 weeks' maintenance with calcipotriol (RD 0.08; 95% CI 0.03 to 0.14) or 8 weeks' maintenance with an alternating calcipotriol/combined therapy routine (RD 0.11; 95% CI 0.06 to 0.17) were significantly less likely to withdraw than participants who used vehicle ointment for maintenance.

In the analysis of withdrawals due to adverse events (Analysis 13.7), there were no significant differences between vitamin D and any of the complex regimens.

In the analysis of withdrawals due to treatment failure (Analysis 13.8), there were significant differences in two of the six contrasts for which we had reported data. After 12 weeks of calcipotriol, participants were significantly more likely to withdraw from the trial because of treatment failure than those who received combination therapy followed by calcipotriol (RD 0.21; 95% CI 0.10 to 0.33). Withdrawals due to treatment failure were more likely in participants who received 8 weeks' monotherapy with tacalcitol than those who received combination therapy followed by calcipotriol (RD 0.05; 95% CI 0.02 to 0.08).

Analysis 14: Vitamin D alone or in combination versus other treatment: long-term studies (> 24 weeks)

This comparison included active-controlled trials of psoriasis of the body that were at least 24 weeks in duration (see Analysis 14.6, Analysis 14.7, and Analysis 14.8). There were three intervention-comparator contrasts, all 52 weeks in duration and all reported by a single study (Kragballe 2006).

Participants received one of three long-term treatments:

- once-daily combined calcipotriol and betamethasone dipropionate;
- combination therapy (4 weeks) followed by calcipotriol (for 4 weeks), rotated over 52 weeks; or
- combination therapy for 4 weeks followed by calcipotriol for 48 weeks.

There were no significant differences between these three regimens in any of the withdrawal assessments: total withdrawals, withdrawals due to adverse events, or withdrawals due to treatment failure.

Analysis 15: Vitamin D analogues versus other treatment

This comparison compared vitamin D analogue with 12 other treatments. We assessed the results from the analyses of withdrawal data using a random-effects risk difference (RD) metric, and we report these separately (see Analysis 15.6, Analysis 15.7, and Analysis 15.8). Withdrawal data were missing only in the head-to-head comparison of vitamin D (alone or in combination) versus calcipotriol with occlusion.

Of the remaining 11 intervention-comparator contrasts, we found only 1 statistically significant difference in withdrawal rates: The rate of total withdrawals was significantly lower for calcipotriol than for tacrolimus (RD -0.13; 95% CI -0.25 to -0.01).

Calcipotriol versus coal tar

In the comparison of calcipotriol and coal tar, we found no statistically significant difference on any of the withdrawal assessments: total withdrawals, withdrawals due to adverse events, or withdrawals due to treatment failure.

Calcipotriol versus coal tar polytherapy

In the comparison of calcipotriol and coal tar polytherapy, we found no statistically significant difference on any of the withdrawal assessments: total withdrawals, withdrawals due to adverse events, or withdrawals due to treatment failure.

Calcipotriol versus nicotinamide 1.4%, twice daily

We found no statistically significant difference on any of the withdrawal assessments: total withdrawals, withdrawals due to adverse events, or withdrawals due to treatment failure.

Calcipotriol versus calcipotriol + nicotinamide (0.05%, 0.1%, 0.7%, or 1.4%), twice daily

We found no statistically significant difference on any of the withdrawal assessments: total withdrawals, withdrawals due to adverse events, or withdrawals due to treatment failure.

Calcipotriol versus corticosteroid + salicylic acid

We found no statistically significant difference on any of the withdrawal assessments: total withdrawals, withdrawals due to adverse events, or withdrawals due to treatment failure. However, the risk difference for the withdrawal rate for adverse events was almost statistically significant in favour of combined therapy (RD 0.05; 95% CI -0.00 to 0.10).

Calcipotriol versus propylthiouracil cream

We found no statistically significant difference on any of the withdrawal assessments: total withdrawals, withdrawals due to adverse events, or withdrawals due to treatment failure.

Calcipotriol versus tacrolimus ointment

We found no statistically significant difference in withdrawals due to adverse events or withdrawals due to treatment failure. However, the rate of total withdrawals was significantly lower for calcipotriol than for tacrolimus (RD -0.13; 95% CI -0.25 to -0.01) (Ortonne 2006).

Calcipotriol versus tazarotene

We found no statistically significant difference on any of the withdrawal assessments: total withdrawals, withdrawals due to adverse events, or withdrawals due to treatment failure.

Calcipotriol versus tazarotene gel plus mometasone furoate cream

We found no statistically significant difference on any of the withdrawal assessments: total withdrawals, withdrawals due to adverse events, or withdrawals due to treatment failure.

Calcipotriol versus vitamin B12 cream

We found no statistically significant difference on any of the withdrawal assessments: total withdrawals, withdrawals due to adverse events, or withdrawals due to treatment failure.

Head-to-head vitamin D alone or in combination: dosing

We found no statistically significant difference on any of the withdrawal assessments: total withdrawals, withdrawals due to adverse events, or withdrawals due to treatment failure.

Head-to-head vitamin D alone or in combination: occlusion

We found no usable withdrawal data reported for this comparison.

Analysis 16: Flexural/facial psoriasis: placebo-controlled trials

This comparison included placebo-controlled trials of four topical treatments for inverse or facial psoriasis. Data on three withdrawal rates were available for all four treatments: the potent steroid betamethasone valerate; the vitamin D analogue calcipotriol; and two topical calcineurin inhibitors, pimecrolimus and tacrolimus (see Analysis 16.6, Analysis 16.7, and Analysis 16.8).

Relative to placebo, participants receiving topical tacrolimus were significantly less likely to withdraw from treatment for any reason (RD -0.17; 95% CI -0.30 to -0.03) or because of treatment failure (RD -0.11; 95% CI -0.19 to -0.02). No other treatment was significantly different from placebo on any of the three withdrawal measures assessed.

Analysis 17: Flexural/facial psoriasis: vitamin D alone or in combination versus other treatment

This comparison included head-to-head trials of treatments for flexural or facial psoriasis, where we compared vitamin D with an active control (see Analysis 17.6, Analysis 17.7, and Analysis 17.8). We identified five intervention-comparator contrasts, and no withdrawal data were missing. Four treatments were compared with calcipotriol: once-daily betamethasone valerate, combined treatment with calcipotriol and hydrocortisone, calcitriol, and pimecrolimus. Calcitriol was compared with tacrolimus.

The rate of withdrawals due to adverse events was significantly higher in people treated with calcipotriol compared to those receiving combination therapy with calcipotriol and hydrocortisone for facial psoriasis (RD 0.06; 95% CI 0.02 to 0.11) and compared to those receiving calcitriol (RD 0.09; 95% CI 0.01 to 0.18). We found no other significant differences in withdrawal rates.

Analysis 18: Scalp psoriasis: placebo-controlled trial

This comparison included placebo-controlled trials of 11 topical treatments for scalp psoriasis (see Analysis 18.6, Analysis 18.7, and Analysis 18.8). All treatments had data on at least one withdrawal measure, which we assessed using a risk difference (RD) metric.

Relative to placebo, participants treated with betamethasone dipropionate were significantly less likely to withdraw from the trial for any reason (total withdrawals) (RD -0.14; 95% CI -0.21 to -0.06), because of adverse events (RD -0.04; 95% CI -0.08 to -0.00), or because of treatment failure (RD -0.10; 95% CI -0.16 to -0.05). Participants receiving combination therapy with calcipotriol and betamethasone dipropionate were significantly less likely to withdraw from the trial for any reason (total withdrawals) (RD -0.09; 95% CI -0.16 to -0.03) or because of treatment failure (RD -0.11; 95% CI -0.17 to -0.06). We found no other significant differences in withdrawal rates.

Analysis 19: Scalp psoriasis: vitamin D alone or in combination versus other treatment

This comparison included head-to-head trials of treatments for scalp psoriasis in which one of the interventions was a vitamin D product (used either as monotherapy or in combination with another product) (see Analysis 19.6, Analysis 19.7, and Analysis 19.8). We identified six intervention-comparator contrasts. There were no data for withdrawal due to treatment failure for one of these contrasts (calcipotriol versus coal tar polytherapy). No other withdrawal data were missing.

Relative to combination treatment with calcipotriol and betamethasone dipropionate, calcipotriol monotherapy was associated with a significantly higher rate of total withdrawals (RD 0.11; 95% CI 0.05 to 0.18; I^2 statistic = 78.5%), withdrawals due to adverse events (RD 0.06; 95% CI 0.02 to 0.09; I^2 statistic = 78.9%) and withdrawals due to treatment failure (RD 0.05; 95% CI 0.01 to 0.10; I^2 statistic = 88.2%). Compared with betamethasone dipropionate, combination therapy was also significantly less likely to result in participant withdrawal due to treatment failure (RD -0.01; 95% CI -0.02 to -0.00; I^2 statistic = 0%).

Study participants treated with calcipotriol were significantly more likely to withdraw because of adverse events than participants receiving betamethasone valerate (RD 0.03; 95% CI 0.01 to 0.06; I^2 statistic = 0%) or coal tar polytherapy (RD 0.08; 95% CI 0.02 to 0.14; I^2 statistic = NA).

(b) Adverse events (local (cutaneous) and systemic)

(i) Findings from the main review

Analysis 1: Vitamin D analogues versus placebo

We pooled data on adverse events using a random-effects risk difference metric (see Analysis 1.9 and Analysis 1.10). There were no adverse events data for the comparison of calcipotriol plus occlusion versus placebo. Therefore, data were available for seven of the eight vitamin D analogues evaluated against placebo

Of the seven vitamin D analogues evaluated against placebo, we found only one statistically significantly difference. Twice-daily becocalcidiol was significantly more likely to cause local adverse events than placebo (RD 0.10; 95% CI 0.00 to 0.19). There were no significant differences for the pooled risk difference for either local adverse events (RD 0.00; 95% CI -0.01 to 0.02; I^2 statistic = 0%) or systemic adverse events (RD 0.00; 95% CI -0.01 to 0.01; I^2 statistic = 0%).

Analysis 2: Corticosteroid (potent) versus placebo

We pooled data on adverse events using a random-effects risk difference metric (see Analysis 2.9 and Analysis 2.10). Data on local adverse events were available for 7 of the 10 corticosteroids; data on systemic adverse events were available only for betamethasone dipropionate twice daily, betamethasone dipropionate (maintenance), and mometasone furoate.

The pooled analysis of local adverse events found a significant difference in favour of corticosteroids (RD -0.04; 95% CI -0.08 to -0.00; I^2 statistic = 56.2%). Among the individual potent corticosteroids evaluated against placebo, we found only one statistically significantly difference. Once-daily betamethasone dipropionate was less likely than placebo to be associated with local adverse events: RD -0.10 (95% CI -0.15 to -0.04; I^2 statistic = 2.5%). We found no significant difference in the pooled analyses of systemic adverse events data.

Analysis 3: Corticosteroid (very potent) versus placebo

We pooled data on adverse events using a random-effects risk difference metric (see Analysis 3.9 and Analysis 3.10). The comparison with placebo found no statistically significant difference for any of the three very potent corticosteroids considered for either local adverse events or systemic adverse events.

Analysis 4: Dithranol versus placebo

We pooled data on adverse events using a random-effects risk difference metric (see Analysis 4.9 and Analysis 4.10). The comparison with placebo found no statistically significant difference for pooled findings on local adverse events or systemic adverse events. In one study, a significant difference in favour of placebo was evident: RD 0.40 (95% CI 0.08 to 0.72; I^2 statistic = NA) (Volden 1992).

Analysis 5: Vitamin D combination products versus placebo

We pooled data on adverse events using a random-effects risk difference metric (see Analysis 5.9 and Analysis 5.10). The rate of local adverse events was significantly lower for combination therapy compared with placebo (RD -0.05; 95% CI -0.08 to -0.02; I^2 statistic = 10.0%). There was no significant difference in the rate of systemic adverse events.

Analysis 6: Other treatment versus placebo

Our review reports findings separately for 22 of the 26 comparisons considered (see Analysis 6.9 and Analysis 6.10). No data on adverse events were available for placebo comparisons involving polymyxin B cream, topical sirolimus, topical tacrolimus, coal tar, or tazarotene. Data on local adverse events were available for 22 comparisons, but data on systemic adverse events were reported for just 9 of the 26 comparisons. We assessed data on adverse events using a random-effects risk difference metric. The comparison with placebo found no statistically significant difference in the rate of either local or systemic adverse events for any treatment.

Analysis 7: Vitamin D analogues versus corticosteroid (potent)

Of the eight vitamin D analogues that were compared with potent corticosteroids, data on local adverse events were available for five comparisons, and data on systemic events were available for four comparisons (see Analysis 7.9 and Analysis 7.10). There were no data on adverse events for calcipotriol versus desoxymetasone, calcipotriol versus diflorasone diacetate, and calcitriol versus betamethasone valerate. In addition, systemic adverse events data were unavailable for calcipotriol versus fluocinonide. We pooled data on adverse effects using a random-effects risk difference metric.

In the comparison of individual vitamin D analogues and potent corticosteroids, our review found one statistically significant difference in favour of potent corticosteroids. Pooled data from 3 trials with 1739 participants indicated that the rate of local adverse events was significantly higher in the calcipotriol group than in the group receiving betamethasone dipropionate (RD 0.07; 95% CI 0.04 to 0.09; I^2 statistic = 0%). This finding drove the pooled (class) result for local adverse events (RD 0.07; 95% CI 0.02 to 0.11; I^2 statistic = 82.4%). Our review found no other statistically significant differences for local or systemic adverse events in this comparison.

Analysis 8: Vitamin D analogues versus corticosteroid (very potent)

We pooled withdrawal data on adverse effects using a random-effects risk difference metric (see Analysis 8.9 and Analysis 8.10). There was no statistically significantly difference between calcipotriol and clobetasol propionate, either for local adverse events (RD -0.05; 95% CI -0.18 to 0.08) or systemic events (RD -0.05; 95% CI -0.18 to 0.08).

Analysis 9: Vitamin D combined with corticosteroid versus corticosteroid

We pooled withdrawal data on combination treatment (vitamin D and a corticosteroid) against monotherapy with a corticosteroid using a random-effects risk difference metric (see Analysis 9.9 and Analysis 9.10). No adverse events data were available for the comparison of combination (calcipotriol/clobetasol propionate) therapy and clobetasol propionate.

The pooled analysis found no statistically significant difference in adverse event rates between combination (calcipotriol/betamethasone dipropionate) therapy and betamethasone dipropionate. There was no significant difference in local adverse events for combination (calcipotriol/betamethasone) therapy and clobetasol propionate, and there were no data on systemic adverse events for this comparison.

Analysis 10: Vitamin D alone or in combination versus dithranol

Adverse events data were available for three intervention-comparator pairs: calcipotriol versus dithranol, calcitriol versus dithranol, and tacalcitol versus dithranol. We pooled these data using a random-effects risk difference metric (see Analysis 10.9 and Analysis 10.10).

Vitamin D was statistically significantly less likely to cause local adverse events (RD -0.32; 95% CI -0.43 to -0.20; I^2 statistic = 84.5%), although substantial heterogeneity was evident in the pooled statistic (Higgins 2011). This finding also held for each of the three intervention-comparator pairs, with the effect size ranging from -0.25 (calcipotriol versus dithranol) to -0.67 (calcitriol versus dithranol). However, the analysis of systemic adverse events found no statistically significant differences.

Analysis 11: Vitamin D alone or in combination versus other vitamin D analogue

We reported local adverse events data on two of the vitamin D analogues head-to-head comparisons (see Analysis 11.9 and Analysis 11.10). Systemic adverse events data were not available for any of the three comparisons. We pooled data on adverse effects using a random-effects risk difference metric. Overall, our review found no statistically significant difference on either local or systemic adverse events when comparing pooled vitamin D analogues head-to-head. However, in the comparison of calcipotriol against calcitriol, the rate of local adverse events was significantly lower for calcitriol: RD 0.07 (95% CI 0.01 to 0.14; I^2 statistic = NA).

Analysis 12: Vitamin D alone or in combination versus vitamin D + corticosteroid

To simplify the comparison, we summarised adverse events data by grouping the first 10 intervention-comparator pairs in a single category: calcipotriol versus calcipotriol and corticosteroid. The remaining comparisons were 1) calcitriol versus calcitriol and 2) corticosteroid and tacalcitol versus calcipotriol and corticosteroid. There were no data on systemic adverse events for the comparison of tacalcitol against calcipotriol and corticosteroid.

We pooled data on adverse effects using a random-effects risk difference (RD) metric (see Analysis 12.9 and Analysis 12.10). In the local adverse events comparison of vitamin D against vitamin D plus corticosteroid, our review found a statistically significantly difference in favour of combination therapy: RD 0.06 (95% CI 0.05 to 0.08; I^2 statistic = 4.1%). This finding also held for each individual intervention-comparator pair. Our analysis found no statistically significantly difference in the rates of systemic adverse events.

Analysis 13: Vitamin D alone or in combination versus other treatments: complex regimens

This comparison included 12 intervention-comparator contrasts (see Analysis 13.9 and Analysis 13.10). Data on local adverse events were available for 11 contrasts, but there were no data on the comparison of calcipotriol (12 weeks) versus combination therapy (4 weeks) followed by calcipotriol (8 weeks). No trial in this comparison reported data on systemic adverse events.

In 4 of the 11 contrasts for which data were available, the complex regimen was associated with a significantly lower rate of local adverse events than when the vitamin D analogue was used alone. Twelve weeks of calcipotriol monotherapy was associated with significantly higher rates of local adverse events than two complex regimen comparators. Specifically, the rate of local adverse events was higher for calcipotriol monotherapy than for a regimen consisting of 8 weeks of combination therapy followed by 4 weeks of once-daily calcipotriol (RD 0.11; 95% CI 0.06 to 0.17). Calcipotriol monotherapy was also more likely to be associated with local adverse events than 4 weeks of combination therapy followed by 8 weeks of once-daily calcipotriol on weekdays and combination therapy at the weekend (RD 0.11; 95% CI 0.05 to 0.17) (Kragballe 2004). When we compared the two complex regimens directly, the rates of cutaneous adverse events were not significantly different.

Relative to calcipotriol, combination therapy with halometasone and calcipotriol had a significantly lower rate of adverse events of the skin (RD 0.26; 95% CI 0.07 to 0.45). An 8-week course of tacalcitol had significantly higher rates of adverse events than a routine of 4 weeks' combined (calcipotriol/betamethasone dipropionate) therapy followed by 4 weeks' monotherapy with calcipotriol (RD 0.06; 95% CI 0.01 to 0.11).

There was no significant difference in the rate of local adverse events in any of the remaining seven intervention-comparator contrasts.

Analysis 14: Vitamin D alone or in combination versus other treatment: long-term studies (> 24 weeks)

This comparison included active-controlled studies of psoriasis of the body that were at least 24 weeks in duration (see Analysis 14.9 and Analysis 14.10). No data on systemic adverse events were reported. We included one trial in this comparison: Kragballe 2006 compared 3 52-week regimens with all treatments used once daily.

Combination therapy with calcipotriol and betamethasone dipropionate was associated with significantly lower rates of adverse events than either of the two 'complex' long-term regimens:

- alternating treatment with combination therapy for 4 weeks, then calcipotriol for 4 weeks (RD -0.08; 95% CI -0.17 to -0.00); and
- combination therapy for 4 weeks, then calcipotriol for 48 weeks (RD -0.16; 95% CI -0.25 to -0.08).

The difference between the two 'complex' regimens was not statistically significant at the 5% level (RD -0.08; 95% CI -0.17 to 0.01), although there was a trend in favour of alternating therapy.

Analysis 15: vitamin D analogues versus other treatment

A vitamin D analogue was compared with 12 other treatments (see Analysis 15.9 and Analysis 15.10). Data on local adverse events were available for 10 intervention-comparator contrasts, and systemic adverse events data were available for 8 intervention-comparator contrasts.

We assessed results from the analyses of adverse events data using a random-effects risk difference metric and report these separately.

For local adverse events, three intervention-comparator contrasts were significantly different. These were the comparison of calcipotriol against calcipotriol + nicotinamide (RD -0.17; 95% CI -0.30 to -0.03), calcipotriol versus corticosteroid + salicylic acid (RD 0.09; 95% CI 0.02 to 0.15), and calcipotriol versus tacrolimus ointment (RD -0.19; 95% CI -0.37 to -0.01). No trial that reported the rate of systemic adverse events found a significant difference in this outcome.

Calcipotriol versus coal tar

Our review found no statistically significant difference for local or systemic adverse events.

Calcipotriol versus coal tar polytherapy

Our review found no statistically significant difference for local or systemic adverse events.

Calcipotriol versus nicotinamide 1.4%, twice daily

Systemic adverse events data were not reported for this analysis. There was no significant difference between the local adverse event rates, although there was a trend in favour of calcipotriol (RD -0.15; 95% CI -0.32 to 0.03; I^2 statistic = NA).

Calcipotriol versus calcipotriol + nicotinamide (0.05%, 0.1%, 0.7%, or 1.4%), twice daily

Systemic adverse events data were not reported for this analysis. Monotherapy with calcipotriol was significantly less likely to cause local adverse events than combined therapy with nicotinamide (RD -0.17; 95% CI -0.30 to -0.03; I^2 statistic = NA).

Calcipotriol versus corticosteroid + salicylic acid

Relative to calcipotriol alone, combination therapy with betamethasone dipropionate and salicylic acid was significantly less likely to be associated with local adverse events (RD 0.09; 95% CI 0.02 to 0.15). There was no significant difference in the rate of systemic adverse events.

Calcipotriol versus propylthiouracil cream

Our review found no statistically significant difference for local or systemic adverse events.

Calcipotriol versus tacrolimus ointment

Relative to calcipotriol, tacrolimus was associated with a significantly higher rate of local adverse events (RD -0.19; 95% CI -0.37 to -0.01). There was no significant difference in the rate of systemic adverse events.

Calcipotriol versus tazarotene

Our review found no statistically significant difference for local or systemic adverse events.

Calcipotriol versus tazarotene gel plus mometasone furoate cream

Adverse events data were not reported for this analysis.

Calcipotriol versus vitamin B12 cream

Our review found no statistically significant difference in the rates of local adverse events. Data on systemic adverse events were not reported.

Head-to-head vitamin D alone or in combination: dosing

Our review found no statistically significant difference for local or systemic adverse events.

Head-to-head vitamin D alone or in combination: occlusion

Local adverse events data were not reported for this analysis. Our review found no statistically significant difference in the rate of systemic adverse events.

Analysis 16: Flexural/facial psoriasis: placebo-controlled trials

This comparison included placebo-controlled trials of four topical treatments for inverse or facial psoriasis. Data on local adverse events were available for all four treatments, but data on systemic events were reported only for one treatment, i.e. the comparison of tacrolimus against placebo (see Analysis 16.9 and Analysis 16.10).

Relative to placebo, participants receiving topical tacrolimus were significantly less likely to report local adverse events (RD -0.17; 95% CI -0.30 to -0.03), but there was no significant difference in the rate of systemic events. No other treatment was significantly different from placebo.

Analysis 17: Flexural/facial psoriasis: vitamin D alone or in combination versus other treatment

This comparison included head-to-head trials of treatments for flexural or facial psoriasis, where vitamin D was compared with an active control. We identified five intervention-comparator contrasts (see Analysis 17.9 and Analysis 17.10). Local adverse events data were missing for the comparison of calcitriol and tacrolimus. There were no data on systemic events for any of the five contrasts.

In people treated with calcipotriol, the rate of local adverse events was significantly higher compared to those receiving combination therapy with calcipotriol and hydrocortisone for facial psoriasis (RD 0.15; 95% CI 0.08 to 0.23) and also compared to those receiving calcitriol (RD 0.09; 95% CI 0.02 to 0.17). These findings aligned with the withdrawal rates for adverse events (Analysis 17.7). We found no other significant differences in adverse events rates.

Analysis 18: Scalp psoriasis: placebo-controlled trials

This comparison included placebo-controlled trials of 11 topical treatments for scalp psoriasis (see Analysis 18.9 and Analysis 18.10). There were no adverse events data for two treatments, betamethasone valerate and amcinonide. Data on systemic events were available for four treatments.

Relative to placebo, participants treated with betamethasone dipropionate were significantly less likely to suffer local adverse events (RD -0.07; 95% CI -0.13 to -0.01; I^2 statistic = 0%). These findings aligned with the withdrawal rates for adverse events (Analysis 18.7). We found no other significant differences in adverse events rates.

Analysis 19: Scalp psoriasis: vitamin D alone or in combination versus other treatment

This comparison included head-to-head trials of treatments for scalp psoriasis in which one of the interventions was a vitamin D product (used either as monotherapy or in combination with another product) (see Analysis 19.9 and Analysis 19.10). We identified six intervention-comparator contrasts, and there were no adverse events data.

Calcipotriol monotherapy was associated with a significantly higher rate of local adverse events than five of the comparator treatments; these included betamethasone dipropionate (RD 0.07; 95% CI 0.04 to 0.11; I^2 statistic = 0%), betamethasone valerate (RD 0.17; 95% CI 0.01 to 0.33; I^2 statistic = 76.5%), and clobetasol propionate (RD 0.19; 95% CI 0.10 to 0.28; I^2 statistic = 0%). Relative to calcipotriol, combined therapy with calcipotriol and betamethasone dipropionate (RD 0.09; 95% CI 0.06 to 0.12; I^2 statistic = 28.1%), and coal tar polytherapy (RD 0.24; 95% CI 0.15 to 0.33; I^2 statistic = NA), were also associated with significantly lower rates of adverse events. Compared with betamethasone dipropionate monotherapy, the rate of adverse events for combined therapy with calcipotriol and betamethasone dipropionate was not significantly different (RD -0.00; 95% CI -0.02 to 0.01; I^2 statistic = NA). There were no significant differences in the rates of systemic adverse events.

(ii) Findings from the separate search for additional studies of adverse events

In addition to findings on adverse events from the main review, we undertook a separate search for additional safety and tolerability studies. The update searches in 2011 identified 3 new literature reviews and 12 potentially relevant records. Eight studies (reported in seven references) met the inclusion criteria, and we excluded five studies from the review (Breneman 2007; Carboni 2005; Feldman 2007a; Hong 2010; and Hong 2011; Jacobi 2008) in addition to the 13 trials excluded in the previous edition of this review (Aste 2004; Bos 2002; Floden 1975; Franssen 1999; Kang 1998; Lebwohl 1996; Park 2002; Senter 1983; Singh 2000; Stevanovic 1977; Traulsen 2003; Uhoda 2003; Vissers 2004). Table 24 details the characteristics and key findings of the included studies, and Table 25 lists the excluded studies. Langner 1996 and van de Kerkhof 1996c also reported the study by Gerritsen 2001. Two papers reported two studies (Berth-Jones 1993; Kimball 2008), which we analysed separately. Kimball 2008 was a review reporting findings from phase II and phase III trials of clobetasol foam (we did not locate any other reports of these studies). The study by van de Kerkhof 2002c reported a two-phase open study of tacalcitol, where 'responders' to part 1 were eligible for part 2. Full results for part 2 were not reported separately (e.g. incidence of local adverse events was reported only for all trial participants). The study by Lambert 2002 appeared very similar to the second phase of the study reported by van de Kerkhof 2002c, but as there was no explicit evidence of an association, we analysed it as a separate trial.

Of the 29 included adverse events studies, 20 were uncontrolled (Barnes 2000; Berth-Jones 1992c; Berth-Jones 1993; Bleiker 1998; Brodell 2011b; Cullen 1996; Gerritsen 2001 and Langner 1996; Kimball 2008 (phase II trial); Kragballe 1991b; Lambert 2002; Menter 2007; Miyachi 2002; Poyner 1993; Ramsay 1994; Roelofzen 2010; van de Kerkhof 1997b; van de Kerkhof 2002c; Vazquez-Lopez 2004; Veraldi 2006; Wishart 1994), 8 were randomised trials (Andres 2006; Corbett 1976; Guzzo 1996; Katz 1987b; Katz 1989; Kimball 2008 (phase III trial); Lebwohl 1998b; Lebwohl 2001), 1 was a retrospective controlled study (Heng 1990), and 1 reported a control group of people using treatment other than calcipotriol (Berth-Jones 1993).

We did not include any of the eight RCTs in the main review. Six RCTs did not meet the inclusion criteria for the main review, because they did not address comparisons of interest (Andres 2006; Corbett 1976; Katz 1987b; Katz 1989; Lebwohl 1998b) or effectiveness (Guzzo 1996). We excluded one RCT from the main review because it did not report the numbers of participants in each arm of the trial (Lebwohl 2001). In all eight RCTs, the adequacy of concealment of treatment allocation was unclear, the method of randomisation was unclear, and all were double-blind (participant/investigator) trials. Five of the eight trials reported baseline comparability, with two studies demonstrating between-group comparability in both clinical and demographic characteristics (Katz 1987b; Katz 1989), two reporting differences in baseline severity (Guzzo 1996; Lebwohl 1998b), and one with some significant differences in demographics and clinical severity (Andres 2006). Four of the eight RCTs were placebo-controlled and six included active controls.

Of the nine controlled studies, two were within-patient designs (Corbett 1976; Katz 1989), and the remainder were between-patient (parallel-group) designs.

Trials ranged in size from 10 to over 4000 participants. Treatment duration ranged from 2 weeks to 18 months. Loss to follow up averaged 9.5% (range = 0% to 63%). The mean age of participants was 48 (range = 15 to 85), and participants were more likely to be men (mean: 55%; range = 40 to 82%). In 12 studies, the baseline severity of participants was unclear. Remaining studies recruited participants with mild to moderate disease (N = 4), mild to severe disease (N = 4), moderate to severe disease (N = 6), and severe disease (N = 3).

Study treatments included vitamin D products (18/29), topical corticosteroids (12/29), coal tar (1/29), and tazarotene (2/29). Some comprised of combination regimens, such as vitamin D and corticosteroid (Lebwohl 1996; Lebwohl 1998b; Vazquez-Lopez 2004) or tazarotene and corticosteroid (Lebwohl 2001). No study of dithranol met the inclusion criteria for the review. Twenty-one of the studies assessed local adverse events, 18 assessed systemic effects, and 11 studies assessed both types. Although six RCTs reported some data on cutaneous adverse events (Andres 2006; Corbett 1976; Katz 1987b; Katz 1989; Lebwohl 1998b), these were neither suitable nor adequate for pooling.

Vitamin D products (N = 18)

Eleven studies evaluated local (N = 7) or systemic (N = 8) adverse effects associated with calcipotriol, or both. The rate of withdrawals due to local adverse events ranged from 4% to 14% and the rate of adverse events ranged between 20% and 41%; larger trials reported higher rates (weighted mean: 36%). In the 52-week trial by Barnes 2000, facial irritation affected 30% of participants in the early stages of the trial, but the incidence declined over time. The incidence of systemic effects was less common: 5/8 studies found no significant effects. Bleiker 1998's study of inpatients with severe disease found 5/28 developed hypercalcaemia after receiving a dose greater than 5 g/kg. The study by Berth-Jones 1993, in which 10 trial participants received a weekly dose of 100 g of calcipotriol for 4 weeks, found that urinary calcium increased significantly from baseline levels.

Four studies evaluated both local and systemic adverse effects associated with tacalcitol. The rate of withdrawals due to local adverse events ranged from 0% to 6%, and the rate of adverse events ranged between 10% and 21%. Three studies found no systemic effects. The study by van de Kerkhof 2002c found that over half of study participants with psoriasis affecting 10% to 20% of their body surface area exceeded the recommended daily dose of 5 g/day (up to 13 g daily), but there was no effect on calcium

homeostasis. Systemic effects were identified in over half enrolled participants in the trial by Miyachi 2002, but only 6/155 events were considered to be treatment-related in this uncontrolled study.

Three studies looked at adverse events associated with calcitriol (Brodell 2011b; Gerritsen 2001; Wishart 1994). One study examined the tolerability and systemic effects of calcitriol used as monotherapy (3 mcg/g ointment applied twice daily, as per licence) (Gerritsen 2001). Three per cent of participants withdrew due to adverse events, and 15% reported local adverse events. The withdrawal rate due to systemic effects was low (0.4%), but 4 cases of hypercalcaemia were reported (N = 253). Mean daily use of calcitriol in this trial was 6 g (range = 1 to 24 g). In Brodell 2011b, participants who had responded to treatment with clobetasol spray then received 8 weeks of maintenance treatment with calcitriol 3 mcg/g ointment twice-daily. Around 15% (35/235) of participants reported burning or stinging at the end of treatment. Wishart 1994 tested the effects of high-dose calcitriol (15 mcg/g once-daily) on 3 groups of participants, with the quantity used proportional to the area affected The trial recruited participants with psoriasis affecting up to 30% of the body surface area. Mean daily drug use ranged from 74 to 306 mcg. The study did not observe any systemic adverse events, skin irritation, or 'clinically relevant' changes in vital signs, haematology, biochemistry, urine, or electrocardiograms.

Corticosteroids (N = 12)

The 12 studies of adverse events associated with steroids adopted a range of different study designs. Four studies had no comparator group (Brodell 2011b; Kimball 2008 (Phase II); Menter 2007; Vazquez-Lopez 2004). Seven studies were randomised trials (Andres 2006; Corbett 1976; Katz 1987b; Katz 1989; Kimball 2008 (Phase III); Lebwohl 1998b; Lebwohl 2001), of which six used active treatment controls and three were placebo-controlled. The remaining study retrospectively compared 13 participants who had used topical corticosteroids for between 6 months and 12 years with a 'no steroid' group (N = 15).

Eight of the 12 corticosteroid studies assessed atrophy or preatrophy in people with psoriasis who were treated with topical steroids. Three studies explicitly described the methods used to assess atrophy, and some studies did not clearly state the numbers of participants affected by atrophy or its extent.

The retrospective study by Heng 1990 compared 13 participants who had used topical corticosteroids for between 6 months and 12 years with a 'no steroid' group: These 15 individuals had previously used tar, UVB, or were untreated. Light microscopy revealed no between-group differences. However, electron microscopy revealed multi-layered, fragmented, and disorganised basal laminae (the lining of the outer surface of the cell membrane) in the steroid group; this appeared to be correlated with duration of treatment. Fragmentation was not observed in the control group.

The 4-week study by Katz 1989 identified preatrophy in 20% of involved plaques, using a hand-held magnifying lens. Two long-term (26-week) studies of combination maintenance therapy with steroids (Lebwohl 1998b; Lebwohl 2001) did not observe cutaneous atrophy, but neither study reported the assessment method. A 4-week trial of clobetasol propionate for scalp psoriasis assessed atrophy using an ultrasound probe (20 MHz) (Andres 2006). No case of cutaneous atrophy was detected in either the gel (which was left in) or shampoo formulations (which was rinsed out after 15 minutes). However, there was a significantly greater reduction in skin thickness in participants treated with the gel, compared to the shampoo group (Andres 2006).

An uncontrolled study of clobetasol spray (Brodell 2011b) detected atrophy in 7/285 participants after 4 weeks of treatment, though the study did not describe the assessment method. A randomised trial compared 2 weeks of treatment with clobetasol propionate foam (N = 253), clobetasol propionate ointment (N = 121), or placebo foam (N = 123) (Kimball 2008, Phase III). The paper did not describe the assessment method. The trial found five cases of skin atrophy in the clobetasol foam group and one case in the placebo group, but the paper did not report the number of atrophy cases in the clobetasol ointment group. COBRA (Clobex Spray Community-Based Research Assessment) was an open-label 4-week study where 1421 people with psoriasis used clobetasol spray 0.05% twice daily as monotherapy (Menter 2007). Cases of telangiectasia, skin atrophy, or folliculitis each occurred in less than 1% of participants (the study did not report the numbers affected or the assessment method).

Four studies examined systemic effects associated with corticosteroids. The study by Corbett 1976 compared betamethasone valerate with clobetasol propionate. Quantities used by study participants were small (mean: 7 g/wk), and the study observed no pituitary-adrenal suppression. Katz 1987b compared two 'superpotent' corticosteroids and identified temporary and reversible adrenal suppression in 20% (8/40) of study participants. In the study by Andres 2006, none of the 14 participants assigned to clobetasol propionate shampoo experienced hypothalamic-pituitary-adrenal (HPA) axis suppression. Conversely, 2 of the 12 participants in the gel group experienced HPA axis suppression. Neither formulation had an impact on ocular safety. In a phase II study (Kimball 2008), higher levels of clobetasol were found in the plasma tests in ointment group than in the shampoo group, though the difference was not statistically significant.

Tazarotene (N = 2)

The study by Lebwohl 2001 compared three types of maintenance therapy: tazarotene plus steroid, tazarotene plus placebo, and placebo alone. In this 6-month trial, there were no withdrawals due to adverse events, but 24% of participants in the tazarotene/steroid group and 29% of participants in the tazarotene/placebo group experienced adverse events. There were no adverse events in the placebo group, and the study did not assess systemic effects. Veraldi 2006 evaluated short-contact treatment with tazarotene gel in 43 participants. The study drug was applied once daily, left for 20 minutes, and then rinsed off with water. The number of participants reporting pruritis and burning decreased over the 45-day study period, with 14/43 participants reporting mild pruritis at the end of treatment, and the same number reporting mild burning. The study did not assess systemic effects.

(c) Quality of life measures

Eight of the 177 studies included in the main review formally assessed quality of life (QoL) (Alora-Palli 2010; Bernstein 2006; Cook-Bolden 2010; Guenther 2002 (H) and Guenther 2002 (P); Hutchinson 2000; Saraceno 2007; Van de Kerkhof 2006; Wall 1998).

The trials used different QoL measures. Alora-Palli 2010 used the Dermatology Quality of Life Index (DLQI), and Bernstein 2006 used the Quality of Life Index. In both measures, higher scores indicate

poorer QoL. The trial by Guenther (2002) measured quality of life using the Psoriasis Disability Index (PDI) and the EuroQOL (EQ-5D and EQ-VAS), reporting it in a separate publication (van de Kerkhof 2004). Hutchinson 2000 and Wall 1998 also assessed quality of life using the Psoriasis Disability Index; Wall 1998 also used the Sickness Impact Profile (SIP). Although four studies used the PDI to measure quality of life, they did not report data in sufficient detail to allow pooling, so we reported findings narratively. Four trials included participants with mild to moderate disease; the other three trials included participants with at least moderately severe disease. The number of participants ranged from 60 (Alora-Palli 2010) to 828 (Guenther 2002 (P)), although PDI scores were obtained for only 51% of participants in this trial (van de Kerkhof 2004). Saraceno 2007 and Van de Kerkhof 2006 used the Skindex-29, with Van de Kerkhof 2006 also employing the SF-36. One trial used a QoL instrument designed specifically for the scalp, the Scalpdex (Cook-Bolden 2010).

Dermatology Quality of Life Index (DLQI) (N = 1)

The Dermatology Quality of Life Index (DLQI) is scored from 0 to 30, where higher scores indicate poorer QoL. Alora-Palli 2010 used the DLQI to compare calcipotriol and liquid carbonis distillate (LCD) 15% solution. Both treatments improved QoL relative to baseline, but there was no significant difference between the groups at the end of the 12-week treatment period. Participants were followed up for 6 weeks post-treatment; in the LCD group, quality of life continued to improve, but it deteriorated in the calcipotriol group. There was a significant between-group difference in the DLQI scores at the 18-week follow-up assessment. This QoL effect reflected the PASI and physician global assessments, which demonstrated significantly lower recurrence rates in the LCD group at 18 weeks.

EuroQOL (EQ-5D and EQ-VAS) (N = 1)

The EQ5D is a generic quality of life measure. van de Kerkhof 2004 reported quality of life data from the trial by Guenther 2002. The study presented the EQ5D scores in a non-standard method, making their interpretation problematic. EQ-VAS (scored from 1 to 100) supported findings from the PDI assessments, with all groups improving quality of life scores relative to baseline. However, the EQ-VAS score for the once-daily combined calcipotriol/betamethasone dipropionate (plus placebo) group was higher (with a better quality of life) than the corresponding score in the twice-daily group. Relative to baseline, improvements in mean quality of life scores were statistically significant in all treatment groups, but the significance of between-group differences was not reported.

Psoriasis Disability Index (PDI) (N = 4)

In all four trials reporting this measure, there was an improvement in mean quality of life scores for participants in every group. The trial by Guenther 2002 found the greatest improvement (reduction in PDI from baseline, i.e. improvement in QoL) for twice-daily combination treatment with calcipotriol and betamethasone (50%). Corresponding figures were as follows: once-daily combination treatment with calcipotriol and betamethasone (plus placebo): 41%, calcipotriol twice daily: 31%, and placebo twice daily: 9%. In terms of absolute scores, the group using twice-daily combination treatment with calcipotriol and betamethasone had the best (lowest) quality of life score, followed by the once-daily combined treatment group, calcipotriol group, and placebo group. Relative to baseline, improvements in mean quality of life scores were statistically significant in all treatment groups, but the statistical significance of between-group differences was not reported. In the study by Hutchinson 2000, quality of life improved from baseline significantly more in the group treated with calcitriol relative to the dithranol group. The comparison of dithranol and calcipotriol by Wall 1998 found that the magnitude of the difference was greater in the calcipotriol group, but the difference was not statistically significant at the 5% level.

Quality of Life Index (N = 1)

Bernstein 2006 used the Quality of Life Index to compare *Mahonia aquifolium* with placebo in participants with mild to moderate psoriasis. The index ranges from 0 to 120, with higher scores indicating poorer quality of life. *Mahonia aquifolium* was significantly more effective than placebo, and this was also reflected in the QoL index.

Scalpdex (N = 1)

Cook-Bolden 2010 used the Scalpdex, a scalp dermatitis-specific quality of life instrument comprising 23 questions, each scored 0 (never) to 100 (all the time). Relative to baseline scores, the study found a significant improvement in QoL for participants in the clobetasol spray arm of the trial and no significant improvement in the placebo spray arm.

SF-36 (N = 1)

The SF-36 is a generic short-form health survey with 36 questions covering physical and mental health. The study by Van de Kerkhof 2006 compared calcipotriol and dithranol administered in a day-care setting. The study found no significant difference in quality of life, either for the Skindex-29 or for the SF-36.

Sickness Impact Profile (SIP) (N = 1)

The SIP is a generic quality of life measure. Wall 1998 assessed participants using the SIP, which has a maximum score of 136. As with the PDI, the SIP found a statistically significant improvement from baseline in both groups, but the between-group difference was not statistically significant.

Skindex-29 (N = 2)

The Skindex-29 is a dermatology-specific QoL index that includes three domains: emotions, symptoms, and functioning. Two trials used the Skindex-29, both enrolling participants with mild to moderate disease. Saraceno 2007 compared a 12-week course of calcipotriol against 4 weeks of combination therapy (calcipotriol/betamethasone dipropionate) followed by maintenance with calcipotriol for 8 weeks. Quality of life improved in both groups relative to baseline. Van de Kerkhof 2006's study in a day-care treatment setting found no significant difference between calcipotriol and dithranol, either for the Skindex-29 or for the SF-36.

(d) Economic outcomes

(THIS SECTION HAS NOT BEEN UPDATED)

A number of studies have looked at economic aspects of topical treatment for psoriasis. These include cost-of-illness studies (Feldman 1997; Jenner 2002; Poyner 1999), quality-of-life studies (Leu 1985; Lundberg 1999; Ortonne 2000; Schiffner 2003; Zachariae 2002; Zug 1995), methodological issues (Lambert 1996; Lambert 1999), willingness to pay analyses (Lundberg 1999; Poyner 2000; Schiffner 2003), cost analysis (Feldman 2000),

and cost-effectiveness analyses (Ashcroft 2000; de Tiedra 1997; Harrington 1995; Köse 1997; Marchetti 1998; Oh 1997; Owen 1993; Parodi 1991; Schwicker 1992; Sorensen 2002; Stern 1988). These analyses involve a range of modelling approaches and assumptions and have not been formally reviewed here, although they were part of our original review (Mason 2002a). Our updated review revealed no substantial variations in tolerability or effectiveness for most treatment comparisons, and no trials provided robust resource data on the consequences of managing treatment failure. Consequently, any economic models extrapolating beyond the duration of the trials may be largely speculative and uninformative. In the light of available data, a 'cost and consequences' approach, in which costs and outcomes are reported separately, may be most informative to clinical decision-makers. The relative short-term clinical performance of topical antipsoriatic treatments can be set against their reimbursed costs. While it is accepted that long-term sequelae in participants not responding to treatment may be very important when considering overall costs and benefits, there are no good comparative data on these costs with which to distinguish between treatments (Mason 2002a).

(e) Concordance or adherence with treatment

(THIS SECTION HAS NOT BEEN UPDATED)

The separate search for studies of concordance/adherence identified 246 potentially relevant studies for screening. Of these, we retrieved 18 papers, and we included in the review 12 papers reporting on 11 studies (see Table 26) (Balkrishnan 2003; Carroll 2004a; Carroll 2004b; Feldman 2007; Ferrandiz 1998; Fouere 2005; Gokdemir 2008; Richards 1999; van de Kerkhof 1998c; van de Kerkhof 2000; van de Kerkhof 2001; Zaghloul 2004). Some studies were pilots (e.g. Balkrishnan 2003; van de Kerkhof 1998c) for other studies (i.e. Carroll 2004a; van de Kerkhof 2000). We listed studies that did not meet the inclusion criteria in Table 27 (Atkinson 2004; Chu 2000; Gupta 2007; Lee 2006; Osborne 2002; Richards 2006; Szeimies 2004). We identified three reviews and bibliographies were checked for further potentially relevant studies (Gupta 2007; Lee 2006; Richards 2006). Of the 11 studies included in the review, 2 were randomised controlled trials (Carroll 2004a; Ferrandiz 1998) and 4 were questionnaire surveys Fouere 2005; Richards 1999; van de Kerkhof 1998; van de Kerkhof 2000). The remaining five studies were prospective experiments, of which one included a control group (van de Kerkhof 2001). The number of participants included in the adherence studies ranged from 10 to 1281, and the study duration ranged from 1 to 16 weeks. In total, 11 studies enrolled 5541 participants, of which 39% were men and the mean age was 47.0 (range = 4 to 91). Study size ranged from 10 to 1281 participants, with the questionnaire surveys reporting the largest sample sizes. Studies covered four main issues. First, some reported methodological issues on the measurement of adherence (Balkrishnan 2003; Carroll 2004a; Fouere 2005; Zaghloul 2004). Second, some studies reported adherence rates (Balkrishnan 2003; Carroll 2004a; Fouere 2005; Richards 1999; van de Kerkhof 2000; van de Kerkhof 2001; Zaghloul 2004). Third, seven studies considered reasons for non-adherence (Carroll 2004a; Gokdemir 2008; Fouere 2005; Richards 1999; van de Kerkhof 1998c; van de Kerkhof 2000; Zaghloul 2004). Fourth, three studies assessed interventions to improve adherence (Feldman 2007; Ferrandiz 1998; van de Kerkhof 2001).

Methodological issues relating to adherence measurement and adherence rates

Some studies used self-reported adherence rates (Gokdemir 2008; Richards 1999; van de Kerkhof 2000; van de Kerkhof 2001; Zaghloul 2004). In these studies, which included short-term prospective trials and cross-sectional questionnaire surveys, rates varied between 61% and 72%. However, other studies adopted more objective assessment methods. The study by Fouere used a semistructured participant questionnaire: The PMAQ-3w scale (Patient Medication Adherence Questionnaire) asked about strict adherence to prescribed regimen over the previous three days and previous weekend. Using this method, the study (Fouere 2005) deemed just 27% of participants as 'compliant'. Some studies adopted a single-blind approach to assess electronic bottle caps (i.e. participants were unaware that bottles were fitted with electronic measuring devices) (Balkrishnan 2003; Carroll 2004a; Feldman 2007). Known as a 'MEMS cap' (Medication Event Monitoring System), the medication bottle cap was fitted with a microprocessor to record the time/date of every opening of the bottle. When compared with participant logs, electronic methods suggested that adherence was considerably lower than rates reported by participants. For example, Balkrishnan's 1-week pilot study of 10 participants found that the adherence rate was 67% by electronic assessment compared with a self-reported rate of 92%. Carroll and colleagues took this pilot study forward using an 8-week trial of 30 participants (Carroll 2004a). Adherence rates fell over time and averaged 55% over the study period when assessed using the MEMS cap. Twice-daily dosing was achieved on 39% of the treatment days.

Reasons for non-adherence

Reasons for non-adherence comprised therapy characteristics (real or perceived), participants' clinical characteristics, and participants' demographic characteristics. Regarding therapy characteristics, the included studies identified the following as influences on adherence: efficacy (Fouere 2005; van de Kerkhof 1998c; van de Kerkhof 2000), side-effects (Fouere 2005; Richards 1999; Zaghloul 2004), time for application (Fouere 2005; Gokdemir 2008; van de Kerkhof 2000), and 'messiness' (Fouere 2005; Richards 1999; van de Kerkhof 1998c). Adherence was higher for topical therapy compared with systemic treatment (Zaghloul 2004), but adherence rates also varied by type of topical treatment (Fouere 2005). Disease severity was inversely related to adherence (Carroll 2004a; Richards 1999), although the direction of causality is unclear. Higher adherence rates were variously associated with female gender (Carroll 2004a; Zaghloul 2004), older age (Carroll 2004a; Richards 1999), higher educational achievement (Gokdemir 2008), and older age of disease onset (Richards 1999), but findings on marital status were mixed (Gokdemir 2008; Zaghloul 2004).

Methods to improve adherence

Office visits to clinicians were found to temporarily increase adherence rates (Carroll 2004a; Feldman 2007). An educational programme designed to improve adherence had no impact on the effectiveness of treatment (Ferrandiz 1998). Van de Kerkhof's study comparing ointment/cream regimen with ointment-only treatment found no clear impact, with 51% of participants reporting better adherence with the cream/ointment option (van de Kerkhof 2001).

DISCUSSION

Summary of main results

Effectiveness

This review analysed evidence from 177 studies that included 34,808 participants. We reported results separately for treatments of the body, inverse psoriasis, and psoriasis of the scalp.

Treatments for psoriasis of the body

We analysed six placebo-controlled comparisons of treatments for psoriasis of the body. Most treatments were significantly more effective than placebo, with the equivalent pooled effect on a 6-point improvement (IAGI) scale ranging from 1.02 (potent corticosteroid) to 1.80 (very potent corticosteroid). Pooled effects indicated similar improvements for vitamin D analogues (1.03 points), dithranol (1.22 points), and combination therapy with vitamin D and potent corticosteroid (1.65) on a 6-point scale.

Amongst less frequently researched treatments, 13 were significantly more effective than placebo. For these treatments, the equivalent effect on a 6-point IAGI scale ranged from 0.55 (calcipotriol plus nicotinamide) to 3.40 (herbal skin care products). Tazarotene achieved an equivalent improvement of 0.99 on the 6-point IAGI scale. One small within-patient study found that tar was no more effective than placebo (Kanzler 1993). Findings from single studies should be treated with caution and regarded as requiring further evidence before guiding treatment.

We evaluated nine head-to-head comparisons. Findings from the comparisons of vitamin D against potent or very potent corticosteroids were mixed, and they varied depending on which vitamin D and which corticosteroid were analysed. Combination treatment with vitamin D/corticosteroid was usually more effective than monotherapy with the same vitamin D, and it was always more effective than the same corticosteroid used alone.

Twelve complex regimens (i.e. treatment sequences that do not consist of a simple head-to-head comparison between two active treatments) were compared with vitamin D. Seven of the complex regimens were more effective than vitamin D, achieving an additional benefit of between 0.27 points and 0.72 points on an equivalent 6-point IAGI. A comparison of three long-term regimens found no significant difference in effect, but some were better tolerated (see below). These studies were interpreted independently, reflecting the differing management regimens. None of the studies presented have been replicated precisely. Therefore, while supportive evidence for findings can be drawn from similar studies, trial findings for complex regimens should be interpreted with caution when informing clinical decisions.

Treatments for inverse psoriasis

The review included four placebo-controlled comparisons of treatments for psoriasis of the sensitive areas of the body. As there were no effectiveness data for tacrolimus, the review evaluated benefits for three treatments. All three were significantly more effective than placebo, with the pooled effect on a 6-point IAGI scale ranging from 0.98 (pimecrolimus) to 3.25 (betamethasone valerate). Five treatments were compared head-to-head against vitamin D. Betamethasone valerate, combined treatment with calcipotriol and hydrocortisone, and calcitriol were all significantly more effective than calcipotriol alone. On an equivalent 6-point IAGI, these treatments achieved an additional benefit of 2.22, 0.33, and 0.67 points, respectively.

Treatments for psoriasis of the scalp

We compared 11 treatments for scalp psoriasis with placebo. All but two were significantly more effective than vehicle alone; the most effective was the very potent corticosteroid, clobetasol propionate, which delivered a benefit of almost 2 points (1.88) on an equivalent 6-point IAGI scale. When compared head-to-head, vitamin D was significantly less effective than both potent and very potent corticosteroids. On an equivalent 6-point IAGI scale, the additional benefit was between 0.48 and 0.67 points. Combination therapy with calcipotriol and betamethasone dipropionate was significantly more effective than either product used alone.

Adverse effects

Randomised evidence found that vitamin D was significantly more likely than potent corticosteroids to cause local adverse effects (15% versus 8%, P = 0.006), and participants were (borderline) more likely to withdraw for this reason (2% versus 1%, P = 0.059). These findings were supported by indirect comparisons of placebo-controlled trials. Participants tolerated combined treatment with vitamin D/corticosteroid on either the body or the scalp as well as potent corticosteroids and significantly better than vitamin D alone. No comparison of topical agents found a significant difference in systemic adverse effects.

Studies of longer-term adverse events found that up to 40% of those using vitamin D analogues experienced cutaneous effects and that up to 14% of participants stopped using vitamin D analogues for this reason. There was some evidence to suggest that using vitamin D analogues at high doses could cause systemic adverse effects.

Two of the major cutaneous adverse effects of topical corticosteroids are dermal and epidermal atrophy (Hengge 2006; Kragballe 2006). Only 25 of the 78 RCTs of corticosteroids included in the review explicitly assessed cutaneous atrophy, and in these the duration of the trials, skin sites assessed, and methods employed reduced the chance of detection. The studies either did not support the methods used to assess atrophy (14/25 trials), physicians undertook them (10/25), study participants self-reported them (5/25), or a combination of the aforementioned. Where physician assessments were conducted, the methods used were not explicit (for example, whether microscopy or ultrasound was used). Two of the 25 trials featured an independent 'adjudication committee', which assessed whether atrophy was likely to be treatment-related (Kragballe 2006; Poulin 2010). Trial duration of the 25 trials was typically between 4 and 8 weeks, but there were 2 6-month studies (Katz 1991a; Poulin 2010) and 2 52-week studies (Kragballe 2006; Luger 2008).

Two trials that assessed atrophy did not report whether or not any cases of atrophy occurred (Huang 2009; Koo 2006). Ten RCTs reported cases of atrophy, and these were trials of either very potent corticosteroids (Cook-Bolden 2010; Decroix 2004; Lowe 2005; Poulin 2010; Reygagne 2005) or combination treatment with potent corticosteroids (Guenther 2002 (H); Kragballe 2004; Kragballe 2006; Papp 2003 (H) and Papp 2003 (P); Yang 2009). Three of the 10 were trials of scalp psoriasis (Cook-Bolden 2010; Poulin 2010; Reygagne 2005), all of which investigated clobetasol propionate.

Some studies reviewed as part of our search for additional studies of adverse events of longer-term use of topical corticosteroids revealed atrophy and damage to basal laminae, the extent of which appeared to be correlated with dosage and duration of use. Research of very potent steroids on the skin of normal volunteers (Kao 2003). Longer-term use with topical retinoids caused cutaneous effects in around 30% of participants, but systemic effects were not assessed.

Concordance/adherence

Thirty-four of the 177 RCTs assessed adherence ('compliance'), and 26 trials reported findings. Trials used various methods such as self-report by participants, medication weight, and treatment completion. Most of the 26 studies that reported findings on adherence found it to be suboptimal. However, Gupta has argued that the relevant notion is concordance rather than compliance or adherence (Gupta 2007). Whereas adherence implies that people comply with clinicians' prescribed treatment, concordance involves a negotiated doctor-patient agreement about the treatment regimen. Van de Kerkhof's survey of over 800 European people with psoriasis found that some chose not to comply, preferring to apply the 'minimum' dose needed to achieve the effect they wanted (van de Kerkhof 2000). If prescribed regimens reflected the wishes of the person with psoriasis, 'adherence' rates might be expected to rise. Nonetheless, poor adherence to treatment regimens is likely to impair the effectiveness of treatment.

The review identified one study that used an educational programme to improve adherence rates in people with psoriasis (Ferrandiz 1998). This study found no statistically significant difference in outcomes, a finding which contrasts with evidence concerning an educational programme for atopic dermatitis (Cork 2003). However, whereas the programme in the Ferrandiz 1998 study provided education about the disease, the study by Cork involved specialist nurses teaching methods for applying topical treatments. Therefore, the findings from Ferrandiz 1998 may not generalise to reflect the value of other educational programmes.

Sensitivity analysis

In four comparisons, we used sensitivity analysis to explore whether within-patient versus between-patient study designs were associated with different effect sizes. When comparing within-patient and between-patient study designs, our review found no statistically significant difference in treatment effect size. If within-patient studies featured some correlation, due to systemic effects or cross contamination, then one would expect systematically smaller effect sizes from within-patient studies. If there is no correlation, then one would expect the variance to be smaller (as other sources of between-patient variation have been removed) but the effect size to be similar. We found no evidence to support a correlation for within-patient studies, and variances were similar for within and between-patient studies (Table 3), supporting the pooling of these, although it is accepted that within-patient designs are 'underweighted' in meta-analyses.

In the placebo-controlled studies of vitamin D products, there was little difference when comparing within-patient and between-patient study findings. On average, within-patient studies identified a slightly greater effect than between-patient studies (mean difference: 0.36 points on a 6-point IAGI scale). For placebo-controlled potent corticosteroids, there was a more pronounced difference in favour of within-patient studies (mean difference: 0.55 points on a 6-point IAGI scale). In the case of very potent corticosteroids, the mean effect relative to placebo was slightly larger in the between-patient studies (mean difference: 0.07 points on a 6-point IAGI scale), and the analysis of vitamin D against potent corticosteroid was similar in this respect (a small positive difference in favour of between-patient studies). These non-statistically significant differences may be chance findings.

Quality of the evidence

All included trials were randomised, but only 47 studies (27%) clearly reported the method used to randomise participants (Figure 3). Just 15 trials (9%) adequately concealed treatment allocation, but most (74%) masked participants to treatment. Of the 177 studies assessed, 151 reported loss to follow up, and 143 demonstrated that groups were comparable at baseline. Based on the 100 studies that reported assessable data on baseline severity, it was apparent that a wide range of severity was included within and between trials. If the PASI is unreliable for mild-to-moderate disease (PASI scores less than 10) (Brownell 2007), it is possible that some trials may have contributed unreliable PASI data to this review.

Trials varied in their treatment duration and in their outcome measures (see Included studies section for details). One reason for the variation in trial treatment duration is that the time taken for an intervention to be effective differs between treatments. The analyses and forest plots do not provide information on treatment duration, but this is an important consideration for clinical decisions. Trials also used different outcome measures; for example, only 113 studies reported data on the IAGI or IGA, and 65 studies reported PASI data. In order to maximise the number of studies contributing data for a particular treatment comparison, we used a combined end point that incorporated different outcome measures. This approach is not ideal; although all outcome measures essentially assess redness, thickness, and scaling (and sometimes area of psoriatic involvement), they differ in their construct. Therefore, the composite end points should be seen as indicative rather than definitive.

Medical text books commonly document the risk of skin atrophy and tachyphylaxis (diminution of the effects of a drug with continual use) as problems associated with topical corticosteroids (Bos 2008). Randomised evidence reported in this review suggests that maintenance regimens using intermittent dosing are safe and effective, and no RCT included in the review detected a statistically significant difference in systemic effects. However, the RCTs did not clearly report the methods employed (e.g. whether the investigator used ultrasound) and may have reduced the chance of detection. We undertook a separate search for longer-term studies of adverse events, which identified 12 relevant studies of corticosteroids. Studies were heterogeneous in terms of design, assessment methods, comparators considered, and doses used, so we did not pool data (Higgins 2011). Eight studies assessed atrophy, and six found some evidence of basal damage and atrophy. We identified no studies reporting adequate data on tachyphylaxis, despite including this term in our searches.

Potential biases in the review process

There are a number of limitations to this review. First, one author extracted data and a second checked it. Ideally, two authors

should extract data independently (NHSCRD 2001). However, this approach was not feasible for this review because of funding constraints. Second, requests for unpublished data from trialists and sponsors were of variable success; requests were more likely to be successful when made for more recently published studies, products still on patent, or both.

This review included 19 comparisons with 10 potential outcomes, so multiple analyses may be expected to generate occasional chance findings. Thus, greater importance is attached where supportive findings are found from placebo-controlled and head-to-head studies as well as linked therapeutic modalities.

Agreements and disagreements with other studies or reviews

A systematic review by Ashcroft and colleagues focused on head-to-head trials of one vitamin D analogue, calcipotriol (Ashcroft 2000a). Based on data from 37 studies with over 6000 participants, the review found that calcipotriol was at least as effective as potent topical corticosteroids and more effective than calcitriol, tacalcitol, coal tar, and short contact dithranol. Our review generally supported these findings. However, we found no significant difference for the comparison of calcipotriol and calcitriol (SMD -0.41; 95% CI -1.46 to 0.64), a finding based on 2 head-to-head trials with 261 participants. Our review also found that calcitriol is more efficacious than calcipotriol when used for inverse psoriasis, and it is also better tolerated. Our findings on the effectiveness of short-contact dithranol compared with calcipotriol were mixed, but physicians and people with psoriasis may be interested to know that inpatient treatment with dithranol appears more effective than calcipotriol (Monastirli 2000). Our review also supported findings from the review by Ashcroft 2000a that although calcipotriol caused significantly more skin irritation than potent topical corticosteroids, skin irritation rarely led to withdrawal of calcipotriol treatment.

The review by Afifi 2005 concluded that combined treatment with steroids and vitamin D analogues or topical retinoids appeared the most promising current treatment on account of its superior efficacy and favourable side-effects profile. However, longer-term adverse effects were not addressed by this review. In contrast, the review by Bruner 2003a focused on adverse effects. This review supported our findings that there is little robust evidence on longer-term adverse effects; therefore, concluding that since clearance is not a realistic expectation, "reasonable goals" are needed to avoid increasing the risk of cutaneous and systemic side-effects through over use.

AUTHORS' CONCLUSIONS

Implications for practice

Evidence from large numbers of trials indicates that most of the topical treatments tested in the trials reviewed here alleviate the symptoms of psoriasis. However, it was not possible to assess the performance of treatments at different levels of severity of psoriasis.

The evidence suggests that vitamin D products are more effective than emollient alone. Potent and very potent corticosteroids are also effective, and very potent corticosteroids are more effective than either potent corticosteroids or vitamin D products. The effectiveness of dithranol and tazarotene appears to be similar to that of vitamin D products. Although vitamin D and corticosteroids are equally effective for treating psoriasis of the body, corticosteroids appear to be more effective than vitamin D for treating psoriasis of the scalp. Combined treatment of vitamin D with corticosteroid is more effective than either vitamin D alone or corticosteroid alone. Vitamin D is more effective than coal tar, but findings on the relative effectiveness of vitamin D and dithranol were mixed. Occlusion enhances the effectiveness of vitamin D, as does twice-daily rather than once-daily application.

Compared with vitamin D alone, combined therapy that uses two products separately (vitamin D in the morning and corticosteroid at night) can achieve similar effects and be as well tolerated as using a combined product. However, some corticosteroids seem to perform better than others when used separately (see Analysis 12.5 and Analysis 12.9), and disease severity may also affect treatment performance, though poor reporting of baseline severity in trials means that we cannot confirm this. Use of a combined product may also enhance concordance, and there is evidence to suggest that adherence is higher when application time is shorter.

Potent corticosteroids are less likely than vitamin D to cause local adverse events, and treatment with corticosteroids is less likely to result in discontinued use because of these adverse events. Tazarotene is more likely than emollient to cause local adverse events. Our review found no difference between placebo and any other topical treatment in the assessment of systemic adverse events. However, this may reflect an absence of evidence (trials failing to appropriately assess these events over adequate time periods) rather than being evidence of absence.

Although current evidence demonstrates that topical steroids are as effective as and at least as well tolerated as vitamin D analogues, concern remains about the potential safety problems associated with corticosteroids (Bos 2008). Concerns include the risk of rebound (a worsening of disease following treatment discontinuation), skin atrophy (skin thinning), and tachyphylaxis (decreasing response to the drug) after long-term use (Hengge 2006). Methods to assess rebound have been developed and should be used in future research (Carey 2006). Regarding skin thinning, one problem with psoriasis is that the skin is very thick and a goal of therapy is to reduce the thickness of lesional (epidermal) skin. Damage to the surrounding normal skin may occur, and for that reason, people should use topical corticosteroids for limited periods or sparingly in delicate areas, such as the face or folds of the skin.

Although topical corticosteroids have been in use for about 50 years, there is a surprising lack of relevant evidence addressing steroid-associated skin dermal atrophy in people with chronic plaque psoriasis requiring long-term treatment. It is improbable that short-term (less than three weeks) courses of topical corticosteroids cause dermal skin atrophy, except in delicate areas such as the face and flexures (groin, axillae, inframammary). However, treatment may be long-term and continuous for people with more severe chronic psoriasis. Current assessments of cutaneous dermal atrophy within trials have largely been limited to clinical observation or symptom and sign reporting by trial participants (which will only detect severe atrophy of the dermis). More sensitive and reliable methods, such as high frequency ultrasound, are routinely available (Cossmann 2006). Dermal atrophy might be monitored in part if trials routinely

adopted more robust methods, such as high frequency ultrasound, to assess dermal skin atrophy skin-thinning, providing useful information for patients and clinicians.

Excessive use of topical corticosteroids can also cause a substantial thinning of the epidermis (Kao 2003). However, thickening of the epidermis is part of the problem in psoriasis and so thinning of the epidermis (not dermis) that has been caused by topical corticosteroids may be of benefit in psoriasis. Evidence drawn from healthy volunteers or severe long-term cases cannot be generalised. Specifically, evidence is required concerning the frequency and spectrum of atrophy in people with chronic psoriasis requiring long-term treatment.

Topical vitamin D analogues (calcipotriol, tacalcitol) and topical calcineurin inhibitors (tacrolimus and pimecrolimus) do not cause cutaneous atrophy. The issue may become a historical one if newer safer steroids, currently being developed and evaluated for atopic dermatitis, subsequently demonstrate efficacy and safety in chronic plaque psoriasis.

We found no evidence on tachyphylaxis, but if treatment response were to decline, this could lead to over-use, increasing the risk of percutaneous absorption. As the evidence base on longer-term adverse effects in psoriasis is inadequate, the preferences of people with psoriasis and their attitudes to these perceived risks should inform treatment choice. Further research is required to inform approaches to long-term maintenance.

Implications for research

Evidence showing that treatments improve the symptoms of psoriasis has focused mainly on treatments with relatively short duration. Although improving, there is still relatively limited randomised evidence to tell us about the long-term effect of using these treatments; good quality head-to-head evidence is therefore needed to quantify and compare long-term adverse events and to explore the feasibility of long-term treatment. There are important sources of heterogeneity in currently available trial findings, which it is not possible to explore in anything other than a qualitative sense. For example, the properties of the vehicle preparation are known to deliver wide variation in response to treatment. This is important when interpreting the findings of this review. The value of the active ingredient may be worth one point on a six-point (IAGI) scale, but possibly one to two points are also being contributed by the vehicle. However, an analysis of vehicle performance was outside the scope of the review. Trial publications included in this review span 45 years. Reporting standards within these trials are generally suboptimal by today's standards, and it would be useful to ensure that current trials adhere to CONSORT (CONsolidated Standards of Reporting Trials) standards to help future reviews to interpret findings appropriately. For example, where trials enrol participants with a wide range of baseline severity, stratifying the randomisation by baseline severity would be a useful design feature. We are not aware of studies that have adopted this approach. Trialists might usefully consider including more homogeneous participant groups in terms of severity, so that the clinical implications of findings are clearer.

Given the importance of safety to patients and to resolve clinical uncertainties, it would be valuable to obtain reliable data on the safety of corticosteroids used long-term at recommended doses, including step-down or intermittent management. Historically, these uncertainties have been driven by unrepresentative case series of non-standard use of steroids. Given the variety of methods used to assess atrophy and other sequelae, it would be valuable to reach clinical consensus about reliable assessment methods (Cossmann 2006).

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* Indicates the major publication for the study

CHARACTERISTICS OF STUDIES

Characteristics of included studies *[ordered by study ID]*

Agrup 1981

Methods	**DESIGN** Within-patient Participant delivery **ALLOCATION** Random Method of randomisation: unclear

Agrup 1981 *(Continued)*

	Concealment: unclear **BLINDING** Double-blind (participant/investigator) **WITHDRAWAL/DROPOUT** Described
Participants	N: 11 Treatment duration: 3 wks; FU: 3 wks LF: 0 (0%) BC: not reported Age: not reported Gender (per cent men): not reported Severity: not reported **INCLUSION CRITERIA** • Chronic plaque psoriasis • Stable symmetrical lesions of the same morphology • Adult **EXCLUSION CRITERIA** • Pregnancy • Receiving steroid preparations
Interventions	• Budesonide ointment 0.025% BD (B) • Placebo (vehicle) BD (P)
Outcomes	1. Investigator's preference 2. Patient's preference
Notes	The trial did not report sponsorship.

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Unclear risk	The trial reported insufficient details.
Blinding (performance bias and detection bias) All outcomes	Low risk	The trial was double-blind (participant/investigator).
Randomisation method reported	Unclear risk	The trial did not report this.
Loss to follow up	Low risk	0.0%
Baseline assessments	Low risk	These were partially done.
Baseline comparability demonstrated	Unclear risk	The trial did not report this.

Alora-Palli 2010

Methods	**DESIGN** Between-patient Participant delivery **ALLOCATION** Random Method of randomisation: computer-generated list Concealment: unclear **BLINDING** Single-blind (investigator) **WITHDRAWAL/DROPOUT** Described
Participants	N: 60 Treatment duration: 12 wks; FU: 18 wks LF: 5 (8.3%) BC: Yes Age: 48.5 (15.4SD); range = 19 to 77 Gender (per cent men): 56.7% Severity: mPASI = 7.09 (3.14SD); PGA = 3.05 Duration (yrs): 16.5 (13.0SD); range = 1 to 62 **INCLUSION CRITERIA** • People aged > = 18 with moderate plaque psoriasis • BSA: 3% to 15% (excluding head, groin, palms, and soles) **EXCLUSION CRITERIA** • Pregnancy or lactation • Topical or UVB therapy within previous 2 wks • Systemic corticosteroids, PUVA, or laser phototherapy within previous 4 wks • Other systemic therapies or biologicals within previous 12 wks
Interventions	• Calcipotriol cream 0.005% BD (C) • Liquid carbonis distillate (LCD) 15% solution BD (T)

Outcomes	1. Per cent change modified PASI (0 to 64.8)
	2. Physician's Global Assessment (PGA): 6-pt (0 = no disease to 5 = very severe).
	3. Overall Patient Symptom Score (erythema, thickness, burning, flaking, etc): 7-pt continuous scale (0 = none to 6 = severe)
	4. Success rates
	5. Participant satisfaction (cosmetic acceptability)
	6. Dermatology Quality of Life Index (DLQI) (0 to 30, where higher scores indicate poorer QoL)
	7. Recurrence rates
	  • loss of PASI 50 response achieved at wk 12
	  • PGA score at wk18 = score at wk 0

Notes	NeoStrata company, Inc. sponsored the trial. There was significant improvement in DLQI scores relative to baseline in both groups.

Alora-Palli 2010 *(Continued)*

Compliance: 96% of participants in both groups reported they applied the study medication twice daily on most days.

Recurrence rates (loss of PASI50 response): C: 7/9; T: 4/16

Recurrence rates (PGA): C: 14/20; T: 5/22

The trial author supplied unpublished data.

There was SD imputation (TSS).

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Unclear risk	The trial reported insufficient details.
Blinding (performance bias and detection bias) All outcomes	High risk	The study was single-blind (investigator).
Randomisation method reported	Low risk	A computer-generated list was used for randomisation.
Loss to follow up	Low risk	8.3%
Baseline assessments	Low risk	The trial reported demographic and clinical characteristics.
Baseline comparability demonstrated	Low risk	This was demonstrated.

Austad 1998

Methods	**DESIGN** Within-patient Participant delivery **ALLOCATION** Random Method of randomisation: not stated Concealment: unclear **BLINDING** Double-blind (participant/investigator) **WITHDRAWAL/DROPOUT** Described
Participants	N: 49 Treatment duration: 6 wks; FU: 10 wks LF: 3 (6.1%) BC: yes Age: 42.4 (13.9SD; range = 18 to 68) Gender (per cent men): 63% Severity: TSS (0 to 9) = 6.4 (0.5SD; range = 6.0 to 8.0)

Austad 1998 *(Continued)*

	Duration: 15.6 (12.3SD; range = 1 to 57) **INCLUSION CRITERIA** • Adults • Symmetrical plaque psoriasis • Total Severity Score ≥ 6/9 **EXCLUSION CRITERIA** • Widespread psoriasis • Hypercalcaemia • Liver or renal disease • Risk of pregnancy • Pregnancy • Relevant concomitant medication or conditions • Previous adverse response
Interventions	• Clobetasol propionate ointment 0.05% BD (2/52), followed by calcipotriol 50 mcg/g BD (4/52) (CP) • Calcipotriol 50 mcg/g BD (6/52) (C)
Outcomes	1. Overall severity score (0 to 9) 2. Investigator Global Assessment (6-pt: worsened to cleared) 3. Treatment preferences, investigator 4. Treatment preferences, patients 5. Compliance
Notes	Glaxo Wellcome Research and Development, Norway, sponsored the trial.

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Unclear risk	The trial reported insufficient details.
Blinding (performance bias and detection bias) All outcomes	Low risk	The trial was double-blind (participant/investigator).
Randomisation method reported	High risk	The trial did not report this.
Loss to follow up	Low risk	6.1%
Baseline assessments	Low risk	The trial did not report these.
Baseline comparability demonstrated	Low risk	-

Baiocchi 1997

Methods	**DESIGN** Within-patient Participant delivery

Baiocchi 1997 *(Continued)*

	ALLOCATION Random Method of randomisation: block randomisation (4 participants) Concealment: unclear **BLINDING** Open **WITHDRAWAL/DROPOUT** Described
Participants	N: 132 Treatment duration: 8 wks; FU: 8 wks LF: 2 (1.5%) BC: yes Age: 46.8 (15.2SD; range = 18 to 89) Gender (per cent men): 67.4% Severity: PASI = 4.4 (2.1SD) **INCLUSION CRITERIA** • Adult • Symmetrical mild-to-moderate chronic plaque psoriasis **EXCLUSION CRITERIA** • Recent topical or systemic antipsoriatic therapy • Rapidly worsening psoriasis • Concurrent vitamin D • Renal or hepatic disease • Pregnancy • Lactation
Interventions	• Calcipotriol ointment 50 mcg/g OD (C1) • Calcipotriol ointment 50 mcg/g BD (C2)
Outcomes	1. PASI 2. Severity: erythema, scaling, induration (0 to 4 each) 3. Global improvement score (7-pt: 0% to 90 - 100%) 4. Cosmetic acceptability
Notes	The trial did not report on sponsorship. All participants had a bath with salicylic acid 3 to 4 days before starting study treatments.

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Unclear risk	The trial reported insufficient details.
Blinding (performance bias and detection bias) All outcomes	High risk	The trial was open.

Baiocchi 1997 *(Continued)*

Randomisation method reported	Low risk	Block randomisation was used.
Loss to follow up	Low risk	1.5%
Baseline assessments	Low risk	These were reported.
Baseline comparability demonstrated	Low risk	-

Barker 1999 (H)

Methods	**DESIGN** Within-patient Participant delivery Method of randomisation: unclear Concealment: unclear **BLINDING** Double-blind (participant/assessor) **WITHDRAWAL/DROPOUT** Described
Participants	N: 30 Treatment duration: 8 wks; FU: 8 wks LF: 4 (13.3%) BC: demographics similar; clinical characteristics not reported Age: 47.2 (14.5SD, N = 144) (range = 20 to 75) Gender (per cent men): 59.7% (86/144) Severity: not reported **INCLUSION CRITERIA** • Chronic plaque psoriasis • Stable bilateral lesions affecting < 20% total body surface area • Adult (aged 18 to 85) **EXCLUSION CRITERIA** • Pregnancy • Concomitant disease • Known hypersensitivity to vitamin D derivatives • Systemic treatments within previous 1 mth • Systemic retinoids within previous 2 mths • Plaques < 10 cm^2 or > 150 cm^2
Interventions	Dose-ranging study including placebo; calcipotriol 50 mcg/g; maxacalcitol 6, 12.5, 25, and 50 mcg/g OD. Contrast included the following: • maxacalcitol 25 mcg/g OD

Barker 1999 (H) *(Continued)*

- Calcipotriol 50 mcg/g OD

Outcomes	1. Psoriasis Severity Index (PSI): sum scores for erythema, induration, and scaling (0 to 24) 2. IAGI (6-pt: worse to cleared) 3. PAGI (6-pt: worse to cleared) 4. Investigator side preference 5. Patient side preference
Notes	Non-target plaques received emollient or coal tar throughout. Chugai Pharma Europe sponsored the trial.

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Unclear risk	The trial reported insufficient details.
Blinding (performance bias and detection bias) All outcomes	Low risk	The trial was double-blind (participant/assessor).
Randomisation method reported	Unclear risk	The trial did not report this.
Loss to follow up	Low risk	13.3%
Baseline assessments	Low risk	These were partially reported (demographics only).
Baseline comparability demonstrated	Unclear risk	This was partially demonstrated.

Barker 1999 (P)

Methods	**DESIGN** Between-patient Participant delivery **ALLOCATION** Random Method of randomisation: unclear Concealment: unclear **BLINDING** Double-blind (unclear) **WITHDRAWAL/DROPOUT** Described
Participants	N: 60 Treatment duration: 8 wks; FU: 8 wks LF: 6 (10.0%) BC: demographics similar; clinical characteristics not reported Age: 47.2 (14.5SD, N = 144) (range = 20 to 75) Gender (per cent men): 59.7% (86/144)

Barker 1999 (P) *(Continued)*

	Severity: not reported **INCLUSION CRITERIA** • Chronic plaque psoriasis • Stable bilateral lesions affecting < 20% total body surface area • Adult (aged 18 to 85) **EXCLUSION CRITERIA** • Pregnancy • Concomitant disease • Known hypersensitivity to vitamin D derivatives • Systemic treatments within previous 1 mth • Systemic retinoids within previous 2 mths • Plaques < 10 cm^2 or > 150 cm^2
Interventions	Dose-ranging study including placebo; calcipotriol 50 mcg/g; maxacalcitol ointment 6, 12.5, 25, and 50 mcg/g OD. Contrast included the following: • Calcipotriol ointment 50 mcg/g OD (C) • Placebo ointment (vehicle) (P)
Outcomes	1. Psoriasis Severity Index (PSI): sum scores for erythema, induration and scaling (0 to 24) 2. IAGI (6-pt: worse to cleared) 3. PAGI (6-pt: worse to cleared) 4. Investigator side preference 5. Patient side preference
Notes	Non-target plaques received emollient or coal tar throughout the study. Chugai Pharma Europe sponsored the trial.

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Unclear risk	The trial reported insufficient details.
Blinding (performance bias and detection bias) All outcomes	Low risk	The trial was double-blind (participant/assessor).
Randomisation method reported	Unclear risk	The trial did not report this.
Loss to follow up	Low risk	10.0%
Baseline assessments	Low risk	These were partially reported (demographics only).
Baseline comparability demonstrated	Unclear risk	These were partially done.

Barrett 2005

Methods	**DESIGN** Between-patient Participant delivery **ALLOCATION** Random Method of randomisation: not stated Concealment: unclear **BLINDING** Open **WITHDRAWAL/DROPOUT** Not described
Participants	N: 420 Treatment duration: 8 wks; FU: 8 wks LF: unclear BC: not reported Age: not reported Gender (per cent men): not reported Severity: not reported **INCLUSION CRITERIA** • People with mild plaque psoriasis **EXCLUSION CRITERIA** • Not reported
Interventions	• Calcipotriol scalp 50 mcg/g solution BD, plus non-medicated shampoo twice/wk (Johnson's baby shampoo®) (CP) • Calcipotriol scalp 50 mcg/g solution BD, plus tar shampoo (Polytar liquid ®) twice/wk (CT) At visit 1, all participants were treated with calcipotriol scalp solution twice daily. Participants were randomly assigned to treatment with either twice-weekly Polytar® liquid or a non-medicated shampoo twice weekly.
Outcomes	1. Investigator assessment of global improvement (6-pt: worse to cleared) 2. Total Sign Score (scale: 0 to 12)
Notes	Leo Pharmaceuticals sponsored the trial. The sponsor supplied unpublished outcomes data.

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Unclear risk	The trial did not report this.
Blinding (performance bias and detection bias) All outcomes	High risk	The trial was open (impossible to blind participants when tar-based products are used).

Barrett 2005 *(Continued)*

Randomisation method reported	Unclear risk	The trial did not report this.
Loss to follow up	Unclear risk	The trial did not report this.
Baseline assessments	Unclear risk	The trial did not report these.
Baseline comparability demonstrated	Unclear risk	The trial did not report this.

Bernhard 1991 (1)

Methods	**DESIGN** Within-patient Delivery unclear **ALLOCATION** Random Method of randomisation: not reported Concealment: unclear **BLINDING** Double-blind (participant/investigator) **WITHDRAWAL/DROPOUT** Described
Participants	N: 100 Treatment duration: 2 wks; FU: 2 wks LF: 4 (4%) BC: yes Age: 49 (range = 20 to 77) Gender (per cent men): 61.5% Severity: at least 2 signs or symptoms ≥ 2 on a 4-pt scale Duration (yrs): 18.2 (range = 1 to 53) **INCLUSION CRITERIA** • Bilateral, comparable psoriasis of at least moderate severity • Adult • At least 2 signs or symptoms ≥ 2 on a 4-pt scale **EXCLUSION CRITERIA** • Not reported
Interventions	• Halobetasol 0.05% ointment BD (H) • Placebo (Vehicle) (P)
Outcomes	1. Signs: erythema, plaque elevation, scaling, overall lesion severity 2. Patient Global Assessment (5-pt: poor to excellent) 3. Skin atrophy
Notes	Westwood-Squibb Pharmaceuticals (BMS) sponsored the trial with an educational grant.

Bernhard 1991 (1) *(Continued)*

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Unclear risk	The trial reported insufficient details.
Blinding (performance bias and detection bias) All outcomes	Unclear risk	The trial was double-blind (participant/investigator).
Randomisation method reported	Unclear risk	The trial did not report this.
Loss to follow up	Low risk	4.0%
Baseline assessments	Low risk	These were reported.
Baseline comparability demonstrated	Low risk	-

Bernhard 1991(2)

Methods	**DESIGN** Between-patient Delivery unclear **ALLOCATION** Random Method of randomisation: not reported Concealment: unclear **BLINDING** Double-blind (participant/investigator) **WITHDRAWAL/DROPOUT** Described
Participants	N: 72 Treatment duration: 2 wks; FU: 2 wks LF: 0 (0%) BC: yes (demographics); clinical comparability unclear Age: 53 (range = 23 to 86) Gender (per cent men): 52.8% Severity: signs > = 4 on a 7-pt scale; BSA = 1% to 20% Duration: 22.7 (range = 1 to 62) **INCLUSION CRITERIA** • Plaque psoriasis of at least moderate severity • Adult • Signs ≥ 4 on a 7-pt scale • BSA 1% to 20%

Bernhard 1991(2) *(Continued)*

	EXCLUSION CRITERIA • Not reported
Interventions	• Halobetasol 0.05% ointment, BD (H) • Placebo (Vehicle) (P)
Outcomes	1. Signs: erythema, induration, scaling 2. Investigator Global Assessment (5-pt: worse to clear)
Notes	Westwood-Squibb Pharmaceuticals (BMS) sponsored the trial with an educational grant.

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Unclear risk	The trial reported insufficient details.
Blinding (performance bias and detection bias) All outcomes	Low risk	The trial was double-blind (participant/investigator).
Randomisation method reported	Unclear risk	The trial did not report this.
Loss to follow up	Low risk	0.0%
Baseline assessments	Low risk	These were reported.
Baseline comparability demonstrated	Unclear risk	This was partially demonstrated.

Bernstein 2006

Methods	**DESIGN** Between-patient Participant delivery **ALLOCATION** Random Method of randomisation: not stated Concealment: unclear **BLINDING** Double-blind (participant/investigator) **WITHDRAWAL/DROPOUT** Described
Participants	N: 200 Treatment duration: 12 wks; FU: 12 wks LF: 29 (14.5%) BC: yes Age: 48.3 (13.9SD) Gender (per cent men): 46.5%

Bernstein 2006 *(Continued)*

	Severity: PASI (0 to 12) = 6.89 (2.8SD); QLI (0 to 120) = 58.74 (31.5SD) **INCLUSION CRITERIA** • People aged 18 to 80 with mild to moderate plaque psoriasis (BSA < 15%) • Good general health **EXCLUSION CRITERIA** • Painful/inflamed lesions • Intertriginous psoriasis • Hypertrophic lesions • Severe psoriasis • Use of topical antipsoriatics within previous 2 wks • Use of systematic antipsoriatics within previous 4 wks • Concurrent use of steroids, immunosuppressants, COX2s • Pregnancy or risk thereof • Lactation
Interventions	• *Mahonia aquifolium* (Reliéva™) in Novasome cream® BD (MA) • Placebo (vehicle) BD (P)
Outcomes	1. PASI, assessed by physician on a 4 x 4 cm section of skin "typical of the patient's psoriasis involvement" (E+I+S) x per cent involvement (0 to 12) 2. QLI (Quality of Life Index) assessed by participant. 12 questions each scored 0 (not at all) to 10 (very much). Maximum score = 120 (equating to very poor quality of life) 3. Also covers adverse events.
Notes	Apollo Pharmaceuticals sponsored the trial. 'PASI' is similar to TSS (range = 0 to 12) as it examines small BSA. However, the PASI score was also adjusted by area.

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Unclear risk	The trial reported insufficient details.
Blinding (performance bias and detection bias) All outcomes	Low risk	The trial was double-blind (participant/investigator).
Randomisation method reported	Unclear risk	The trial did not report this.
Loss to follow up	Low risk	14.5%
Baseline assessments	Low risk	The trial reported this.
Baseline comparability demonstrated	Low risk	-

Berth Jones 1992b

Methods	**DESIGN** Between-patient Participant delivery **ALLOCATION** Random Method of randomisation: balanced blocks of 4 using computer-generated random numbers Concealment: unclear **BLINDING** Open **WITHDRAWAL/DROPOUT** Described
Participants	N: 478 Treatment duration: 8 wks; FU: 8 wks LF: for PASI: 56 (11.7%); for Response: 20 (4.2%) BC: yes Age: 44 (range = 18 to 85) Gender (per cent men): 55% Severity: PASI = 9.3 Duration (yrs): 18 (12SD) **INCLUSION CRITERIA** • Outpatients • Adults • Chronic stable plaque psoriasis **EXCLUSION CRITERIA** • Previous non-response to study medications • Recent systemic treatment • Hypercalcaemia • Abnormal renal/hepatic function • Calcium or vitamin D intake • Relevant concomitant medication • Pregnancy • Risk of pregnancy
Interventions	• Calcipotriol ointment 50 mcg/g BD (C) • Dithranol cream (dose titration 0.1% to 2%) OD (D)
Outcomes	1. PASI 2. Investigator Global Assessment (5-pt: worse to cleared) 3. Patient Global Assessment (5-pt: worse to cleared) 4. Cosmetic acceptability 5. Compliance
Notes	Leo Pharmaceutical Products, Denmark, sponsored the trial.
Risk of bias	

Berth Jones 1992b *(Continued)*

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Unclear risk	The trial reported insufficient details.
Blinding (performance bias and detection bias) All outcomes	High risk	The trial was open.
Randomisation method reported	Low risk	A computer-generated block list was used for randomisation.
Loss to follow up	Low risk	11.7%
Baseline assessments	Low risk	These were reported.
Baseline comparability demonstrated	Low risk	-

Beutner 2006

Methods	**DESIGN** Within-patient Participant delivery **ALLOCATION** Random Method of randomisation: not stated Concealment: unclear **BLINDING** Double-blind (participant/investigator) **WITHDRAWAL/DROPOUT** Described
Participants	N: 27 Treatment duration: 4 wks; FU: 4 wks LF: 2 (7.4%) BC: yes Age: 51.6 (12.8SD); range = 21 to 75 Gender (per cent men): 67% Ethnicity (% white): 85% Severity: overall target severity score (0 to 4) = 2.67 (0.58SD) **INCLUSION CRITERIA** • People aged > = 18 with moderate to severe plaque psoriasis (overall plaque severity score (0 to 8) > = 5) • 2 bilateral plaques of equivalent size (5 cm^2 to 10 cm^2) **EXCLUSION CRITERIA** • Use of topical antipsoriatic therapy or UV exposure within previous 4 wks • Pregnancy or risk thereof

Beutner 2006 *(Continued)*

Interventions	• Clobetasol propionate 0.05% spray BD (CP) • Placebo (vehicle) spray BD (P)
Outcomes	1. Overall target plaque severity score using a collapsed 9-pt scale: none (0 to 1), mild (2 to 3), moderate (4 to 5), severe (6 to 7), and very severe (8) 2. Signs: scaling, erythema, and plaque elevation (each scored 0 to 8) 3. Adverse events (burning, stinging, pruritus, telangiectasias, skin atrophy)
Notes	Galderma Laboratories, L.P. sponsored the study. There was SD imputation (TSS).

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Unclear risk	The trial reported insufficient details.
Blinding (performance bias and detection bias) All outcomes	Low risk	The trial was double-blind (participant/investigator).
Randomisation method reported	Unclear risk	The trial did not report this.
Loss to follow up	Low risk	7.4%
Baseline assessments	Low risk	These were reported.
Baseline comparability demonstrated	Low risk	-

Bourke 1993b

Methods	**DESIGN** Within-patient Participant delivery **ALLOCATION** Random Method of randomisation: participants were randomised into groups A and B, then randomised to left/right application with sealed envelopes Concealment: unclear **BLINDING** Single-blind (investigator) **WITHDRAWAL/DROPOUT** Described
Participants	N: 19 (evaluable) Treatment duration: 8 wks; FU: 8 wks LF: NR BC: yes (clinical only) Age: not reported

Bourke 1993b *(Continued)*

	Gender (per cent men): not reported Severity: TSS = 7.9 **INCLUSION CRITERIA** • Adult • Symmetrical chronic plaque psoriasis • Outpatients **EXCLUSION CRITERIA** • UV or systemic antipsoriatic therapy
Interventions	• Calcipotriol BD (C) • Calcipotriol BD plus polythene film at night (O)
Outcomes	1. Signs: erythema, induration, scale 2. Total Sign Score (0 to 12)
Notes	Participants were randomised into groups A (calcipotriol BD) and B (occlusion ON), then each participant was randomised to left/right application: group A (occlusion ON/no occlusion); group B (calcipotriol BD or placebo BD). The study reported findings for group A. The trial did not report sponsorship.

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Unclear risk	The trial reported insufficient details.
Blinding (performance bias and detection bias) All outcomes	Low risk	The trial was single-blind (investigator).
Randomisation method reported	Low risk	Envelopes were used.
Loss to follow up	Unclear risk	The trial did not report this.
Baseline assessments	Low risk	These were partially done.
Baseline comparability demonstrated	Unclear risk	This was partially demonstrated.

Bourke 1997

Methods	**DESIGN** Between-patient Participant delivery **ALLOCATION** Random Method of randomisation: not reported Concealment: unclear **BLINDING** Double-blind (participant/assessor)

Bourke 1997 *(Continued)*

	WITHDRAWAL/DROPOUT Described
Participants	N: 24 Treatment duration: 8 wks LF: 4 (16.7%) BC: yes (clinical only reported) Age: not reported Gender (per cent men): 41.7% Severity: PASI mean = 14.0 **INCLUSION CRITERIA** • Adults • Symmetrical chronic moderate chronic plaque psoriasis **EXCLUSION CRITERIA** • Pregnancy • Lactation • Drugs affecting systemic calcium homeostasis • Recent systemic antipsoriatic or UVB therapy
Interventions	• Calcitriol 3 mcg/g BD (CL) • Calcipotriol 50 mcg/g BD (C)
Outcomes	1. PASI
Notes	Solvay-Duphar Ltd sponsored the trial.

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Unclear risk	The trial reported insufficient details.
Blinding (performance bias and detection bias) All outcomes	Low risk	The trial was double-blind (participant/assessor).
Randomisation method reported	Unclear risk	The trial did not report this.
Loss to follow up	Low risk	16.7%
Baseline assessments	Low risk	These were partially done.
Baseline comparability demonstrated	Unclear risk	This was partially demonstrated.

Brown 2005

Methods	**DESIGN** Between-patient Participant delivery **ALLOCATION** Random Method of randomisation: not stated Concealment: unclear **BLINDING** Double-blind (participant/investigator) **WITHDRAWAL/DROPOUT** Described
Participants	N: 30 Treatment duration: 12 wks; FU: 12 wks LF: 6 (20%) BC: unclear Age: 55 (12.6SD); range = 20 to 75 Gender (per cent men): 50% Ethnicity (% white): 46.7% Severity: TSS (0 to 16) mean = 6.97 **INCLUSION CRITERIA** • People with mild stable plaque psoriasis • BSA affected < 15% • General good health **EXCLUSION CRITERIA** • Pregnancy or risk thereof • Lactation • Phototherapy, topical therapy, or systemic therapy within previous 4 wks • Cancer • History of drug or alcohol abuse • Concomitant antipsoriatic therapy
Interventions	• Kukui nut oil TD (K) • Placebo (mineral oil, vehicle) TD (P)
Outcomes	1. Investigator assessment of PASI (scale unclear (0 to 64.8)) and Global Severity Score (5-pt: 0 = none to 4 = very severe) 2. Subject assessment of Global Severity Score (5-pt: 0 = none to 4 = very severe) 3. Total Severity Score (0 to 16; thickness + scaliness + erythema + itch) 4. Compliance also assessed (bottles weighed)
Notes	Hawaii Community Foundation sponsored the study. The trial author supplied unpublished data. There was SD imputation (TSS).
Risk of bias	

Brown 2005 *(Continued)*

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Unclear risk	The trial reported insufficient details.
Blinding (performance bias and detection bias) All outcomes	Low risk	The trial was double-blind (participant/investigator).
Randomisation method reported	Unclear risk	The trial did not report this.
Loss to follow up	Unclear risk	20%
Baseline assessments	Unclear risk	The trial did not report these.
Baseline comparability demonstrated	Unclear risk	The trial did not report this.

Bruce 1994

Methods	**DESIGN** Between-patient Participant delivery **ALLOCATION** Random Method of randomisation: not reported Concealment: unclear **BLINDING** Double-blind (participant/investigator) **WITHDRAWAL/DROPOUT** Described
Participants	N: 114 Treatment duration: 6 wks; FU: 6 wks LF: 15 (13.2%) BC: yes Age: 44.1 (14.6SD; range = 20 to 77) Gender (per cent men): 60.2% Severity: mean duration of current episode (days) = 142 (range = 0 to 601) Overall severity score (mean): 4.5 **INCLUSION CRITERIA** • Stable plaque psoriasis • Adults • At least mild overall severity • At least moderately severe plaque elevation **EXCLUSION CRITERIA**

Bruce 1994 *(Continued)*

	• Pregnancy • Lactation • Inadequate contraception • Sensitivity to test medications • Recent topical, UV, or systemic treatment • Recent involvement in other trials • Planned sun exposure
Interventions	• Calcipotriol ointment 0.005% BD (C) • Fluocinonide ointment 0.05% BD (F)
Outcomes	1. Sign: scaling, erythema, plaque elevation 2. Overall severity (Total Sign Score and per cent involvement) 3. Investigator Global Assessment
Notes	Westwood Squibb Pharmaceuticals Inc. sponsored the trial. There was SD imputation (TSS).

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Unclear risk	The trial reported insufficient details.
Blinding (performance bias and detection bias) All outcomes	Low risk	The trial was double-blind (participant/investigator).
Randomisation method reported	Unclear risk	The trial did not report this.
Loss to follow up	Low risk	13.2%
Baseline assessments	Low risk	-
Baseline comparability demonstrated	Low risk	-

Buckley 1978

Methods	**DESIGN** Within-patient Participant delivery **ALLOCATION** Random Method of randomisation: not reported Concealment: unclear **BLINDING** Double-blind (participant/investigator) **WITHDRAWAL/DROPOUT** Described
Participants	N: 10

Buckley 1978 *(Continued)*

	Treatment duration: 3 wks; FU: 3 wks LF: 2 (20%) BC: not reported Age: 21.4 (range = 9 to 41) Gender (per cent men): 50% Severity: not reported **INCLUSION CRITERIA** • Active chronic psoriasis • Lesions approximately symmetrically distributed **EXCLUSION CRITERIA** • Not reported
Interventions	• Dead Sea salts emollient lotion 30% (frequency of application not reported) (D) • Base emollient lotion (placebo) (P)
Outcomes	1. Jacoby assessment score (0 to 7 score transformed to per cent clinical improvement) 2. Photographic evaluation 3. Overall patient assessment (relative efficacy, speed of response, irritation, staining, ease of application)
Notes	The trial did not report sponsorship.

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Unclear risk	The trial reported insufficient details.
Blinding (performance bias and detection bias) All outcomes	Low risk	The trial was double-blind (participant/investigator).
Randomisation method reported	Unclear risk	The trial did not report this.
Loss to follow up	Low risk	20.0%
Baseline assessments	Low risk	These were partially done.
Baseline comparability demonstrated	Unclear risk	The trial did not report this.

Buckley 2008

Methods	**DESIGN** Between-patient Participant delivery **ALLOCATION**

Buckley 2008 *(Continued)*

	Random Method of randomisation: not stated Concealment: unclear **BLINDING** Double-blind (participant/investigator) **WITHDRAWAL/DROPOUT** Described
Participants	N: 218 Treatment duration: 8 wks; FU: 10 wks LF: 5 (2.3%) BC: yes Age: 48.4 (15.48SD) Gender (per cent men): 45.0% Ethnicity: 97.7% Severity: TSS (0 to 12) = 6.80 (1.58SD) Duration (yrs): 14.6 (13.87SD); range = 0 to 65 Extent of scalp psoriasis: 3.39 (1.36SD) **INCLUSION CRITERIA** • People aged > = 18 with scalp psoriasis affecting > = 10% scalp • Amenable to topical treatment with < = 100 g medication/wk • TSS (0 to 12) > = 4 • Each individual sign score (0 to 4) > = 1 • IGA at least mild (> = 3) **EXCLUSION CRITERIA** • Erythrodermic psoriasis • Pustular psoriasis • Systemic or PUVA therapy within previous 4 wks • UVB or grenz ray therapy on scalp, or topical scalp therapy within previous 2 wks • Severe renal impairment or severe hepatic disorders
Interventions	• Combined gel: calcipotriol 50 mcg/g + betamethasone dipropionate 0.5 mg/g OD (C-B) • Betamethasone dipropionate 0.5 mg/g gel OD (B) Participants achieving absence of disease (IGA = 5) at weeks 2 to 5 could withdraw from the study.
Outcomes	1. Signs: redness, thickness, scaliness (each sign scored on 5 pt scale 0 to 4) 2. Total Sign Score (TSS; 13-pt: 0 = none to 12 = very severe symptoms) 3. Investigator's Global Assessment (IGA): 0 = absence of disease to 5 = very severe disease. 4. Controlled disease: IGA < = 1 5. Investigator assessment of extent of scalp psoriasis: 0% to 100% (score of 3 corresponds to 30% to 49% involvement) 6. Patient's assessment of global improvement (PAGI): 7-pt scale: 0 = worse to 6 = cleared. Reported as dichotomised treatment success: PAGI > = 4 7. Treatment duration 8. Compliance (medication usage)

Buckley 2008 *(Continued)*

Notes	Leo Pharma A/S, Ballerup, Denmark, sponsored the study. Treatment duration (wks): C-B: 6.1 (2.4 SD), N = 108; B: 6.8 (2.2 SD), N = 110 Compliance (missed < = 20% applications): C-B: 93/108; B: 103/110 The sponsor supplied unpublished data.,

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Unclear risk	The trial reported insufficient details.
Blinding (performance bias and detection bias) All outcomes	Unclear risk	The trial was double-blind (participant/investigator).
Randomisation method reported	Unclear risk	The trial did not report this.
Loss to follow up	Low risk	2.3%
Baseline assessments	Low risk	These were reported.
Baseline comparability demonstrated	Low risk	-

Camarasa 2003

Methods	**DESIGN** Between-patient Participant delivery **ALLOCATION** Random Method of randomisation: not reported Conducted in 20 centres; stratification not reported Concealment: unclear **BLINDING** Double-blind (participant/investigator) **WITHDRAWAL/DROPOUT** Described
Participants	N: 258 Treatment duration: 6 wks; FU: 14 wks LF: 15 (5.8%) BC: yes Age: 43.5 (14.3SD: range = 15 to 83) Gender (per cent men): 64.3% Severity: per cent BSA = 25.5 (22.9SD: range = 1 to 95); PASI = 15.4 (10.6SD) Duration of psoriasis (mths) mean: 199.2 (157.5SD: range = 1 to 745)

Camarasa 2003 *(Continued)*

	INCLUSION CRITERIA • Adults • Moderate to severe chronic plaque psoriasis (≥ 2 on global severity score) **EXCLUSION CRITERIA** • Systemic or intralesional therapy or photo(chemo)therapy in previous 2 mths • Medications or conditions that might interfere with the assessment of study drugs Concomitant bacterial, fungal, or viral skin conditions • Clinically relevant abnormalities in laboratory parameters (calcium homeostasis and renal function) • Pregnancy or lactation • Absence of adequate contraception, where appropriate
Interventions	• Calcitriol 3 mcg/g ointment BD (C) • Betamethasone dipropionate 0.05% ointment BD (B)
Outcomes	1. IAGI (6-pt: worsening to clearance) 2. PASI 3. Overall global severity of lesions (5-pt: 0 = none to 4 = very severe) 4. Relapse rate 5. Proportion remaining in remission (non-randomised subgroup analysis)
Notes	There was a 1-wk run-in period without treatment, except tar shampoo and emollients. Follow up was for responders only (defined as achieving clearance or considerable improvement). The scalp was excluded. Galderma Laboratories sponsored the trial. There was SD imputation (TSS).

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Unclear risk	The trial reported insufficient details.
Blinding (performance bias and detection bias) All outcomes	Low risk	The trial was double-blind (participant/investigator).
Randomisation method reported	Unclear risk	The trial did not report this.
Loss to follow up	Low risk	5.8%
Baseline assessments	Low risk	-
Baseline comparability demonstrated	Low risk	-

Cheesbrough 1992

Methods	**DESIGN** Between-patient Participant delivery **ALLOCATION**

Cheesbrough 1992 *(Continued)*

	Random Method of randomisation: not reported Concealment: unclear **BLINDING** Double-blind (participant/investigator) **WITHDRAWAL/DROPOUT** Described
Participants	N: 24 Treatment duration: 12 wks; FU: 12 wks LF: 5 (20.8 %) BC: yes Age (mean): 47 Gender (per cent men): 54.2% Severity: PASI mean = 26 **INCLUSION CRITERIA** • Chronic stable plaque psoriasis **EXCLUSION CRITERIA** • Not reported
Interventions	• Dead sea salts emollient lotion 30% (frequency of application not reported) (D) • Base emollient lotion (placebo) (P)
Outcomes	1. PASI 2. Erythema, scaling, thickening, pruritus 3. Adverse events
Notes	Finders Dead Sea Salt Co and Dead Sea Salt works supplied the study treatments.

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Unclear risk	The trial reported insufficient details.
Blinding (performance bias and detection bias) All outcomes	Low risk	The trial was double-blind (participant/investigator).
Randomisation method reported	Unclear risk	The trial did not report this.
Loss to follow up	Unclear risk	20.8%
Baseline assessments	Low risk	These were reported.
Baseline comparability demonstrated	Low risk	-

Christensen 1999

Methods	**DESIGN** Between-patient Participant delivery **ALLOCATION** Random Method of randomisation: not reported Concealment: unclear **BLINDING** Single-blind at inclusion only (investigator) **WITHDRAWAL/DROPOUT** Described
Participants	N: 171 Treatment duration: 8 wks; FU: 16 wks (N = 95) LF: 5 (2.9%) BC: yes Age: 47.4 (range = 17 to 88) Gender (per cent men): 62.6% Severity: mean TSS (0 to 9) = 6.24; mean duration of psoriasis = 18.5 (range = 1 to 58) **INCLUSION CRITERIA** • Outpatients with mild to severe chronic stable chronic plaque psoriasis, not more than 10% BSA, Total Severity Score (0 to 9) ≥ 4, involving all 3 signs (erythema, scaling, infiltration) **EXCLUSION CRITERIA** • Systemic treatment within previous 4 wks • Topical treatment within previous 2 wks; receipt of oral retinoids within previous 2 mths
Interventions	• Short-contact dithranol (30 min) 1% to 3%, OD (D) • Calcipotriol 50 mcg/g BD (C)
Outcomes	1. Total Severity Score (0 to 9) 2. Pruritus (0 to 3) 3. Investigator's Global Assessment (7-pt: worse to completely clear) 4. Patient's Global Assessment (6-pt: worse to completely clear) 5. Adverse events
Notes	The study did not report sponsorship. The study also included 16-week follow-up data for consenting participants who achieved at least 50% improvement from baseline (Investigator scale). There was SD imputation (TSS).

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Unclear risk	The trial reported insufficient details.

Christensen 1999 *(Continued)*

Blinding (performance bias and detection bias) All outcomes	Low risk	The trial was single-blind (investigator).
Randomisation method reported	Unclear risk	The trial did not report this.
Loss to follow up	Low risk	2.9%
Baseline assessments	Low risk	-
Baseline comparability demonstrated	Low risk	-

Cook-Bolden 2010

Methods	**DESIGN** Between-patient Participant delivery **ALLOCATION** Random Method of randomisation: unclear Concealment: unclear **BLINDING** Double-blind (participant/investigator) **WITHDRAWAL/DROPOUT** Described
Participants	N: 81 Treatment duration: 4 wks; FU: 4 wks LF: 3 (4%) BC: yes Age: 43.7 (14.69SD) Ethnicity (% white): 78% Gender (per cent men): 39.5% Duration (yrs): 11.1 (10.5SD) Severity: GSS = 3 (moderate) (67.9%); GSS = 4 (severe) (32.1%) **INCLUSION CRITERIA** • People aged 18 or over with moderate to severe plaque psoriasis of the scalp (GSS = 3 or GSS = 4) **EXCLUSION CRITERIA** • Use of chemical hair process, steroid medication, ultraviolet B (UVB) treatment, or both; calcipotriene; other vitamin D analogues; anthralin/tar; all other anti-psoriasis medications (previous 2 wks) • Use of PUVA or other non-biological systemic treatments (previous 4 wks) • Use of biological therapies (previous 12 wks) • Pregnancy or risk thereof • Lactation
Interventions	• Clobetasol propionate spray 0.05% BD (CP) • Placebo (vehicle) spray BD (P) Max usage/wk: 50 g

Cook-Bolden 2010 *(Continued)*

	Participants achieving GSS = 0 at 2 wks completed ("withdrew" from) the study.
Outcomes	1. Global Severity Score (GSS) (6-pt: 0 = none to 5 = very severe), dichotomised as success (clear/almost clear) and failure 2. Scalp psoriasis sign scores: erythema, scaling, elevation (0 to 4, where 0 = none) 3. Pruritus (4-pt: 0 = no itching to 3 = intense itching that disrupts sleep) 4. Atrophy (0 to 3, where 0 = none) 5. Telangiectasias (0 to 3, where 0 = none) 6. Stinging/burning (0 to 3, where 0 = none) 7. Patient satisfaction with applicator 8. Scalpdex, a scalp dermatitis-specific quality of life instrument; 23 questions, each scored 0 (never) to 100 (all the time) 9. Compliance: yes if participant achieved 80% to 120% of expected applications
Notes	Galderma Laboratories, LP, sponsored the trial. Galderma supplied safety data for this study.

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Unclear risk	The trial reported insufficient details.
Blinding (performance bias and detection bias) All outcomes	Low risk	The trial was double-blind (participant/investigator).
Randomisation method reported	Unclear risk	The trial did not report this.
Loss to follow up	Low risk	4%
Baseline assessments	Low risk	These were made.
Baseline comparability demonstrated	Low risk	The trial demonstrated demographic and clinical comparability.

Crosti 1997

Methods	**DESIGN** Between-patient Participant delivery **ALLOCATION** Random Method of randomisation: not reported Concealment: unclear **BLINDING** Unclear **WITHDRAWAL/DROPOUT** Described
Participants	N: 160 Treatment duration: 6 wks; FU: 10 wks

Crosti 1997 *(Continued)*

	LF: 8 (5%) BC: yes Age: 49.9 (14.2SD) Gender (per cent men): 68.1% Severity: mean PASI = 7.6 **INCLUSION CRITERIA** • Mild stable chronic plaque psoriasis • Adult **EXCLUSION CRITERIA** • Recent topical or systemic treatments • Pregnancy • Lactation • Concomitant vitamin D or systemic steroids • Hepatic or renal failure
Interventions	• Calcipotriol ointment 50 mcg/g BD (C) • Betamethasone dipropionate + salicylic acid BD (B)
Outcomes	1. PASI 2. Investigator Global Assessment 3. Patient Global Assessment of acceptability of treatment (5-pt: nil to excellent)
Notes	The trial did not report sponsorship. There was SD imputation (PASI).

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Unclear risk	The trial reported insufficient details.
Blinding (performance bias and detection bias) All outcomes	Unclear risk	The trial did not report this.
Randomisation method reported	Unclear risk	The trial did not report this.
Loss to follow up	Low risk	5.0%
Baseline assessments	Low risk	-
Baseline comparability demonstrated	Low risk	-

Cunliffe 1992

Methods	**DESIGN**

Cunliffe 1992 *(Continued)*

	Between-patient Delivery unclear **ALLOCATION** Random Method of randomisation: balanced blocks of 10 according to a computer-generated random numbers table Concealment: unclear **BLINDING** Double-blind (participant/investigator) **WITHDRAWAL/DROPOUT** Described
Participants	N: 409 Treatment duration: 6 wks; FU: 6 wks LF: 8 (2.0%) BC: yes Age: 44.9 (range = 17 to 83) Gender (per cent men): 55.7% Severity: mean PASI = 9.0 (range = 0.6 to 41.2); mean duration psoriasis = 16.2 (range = 0.2 to 57) **INCLUSION CRITERIA** • Stable plaque psoriasis • Adults • Outpatients **EXCLUSION CRITERIA** • Risk of pregnancy • Pregnancy • Lactation • Recent systemic antipsoriatic treatment
Interventions	• Calcipotriol ointment 50 mcg/g BD (C) • Betamethasone 17-valerate 1 mg/g BD (B)
Outcomes	1. PASI 2. Patient overall assessment (5 pt: worse to clear)
Notes	Leo Pharmaceuticals sponsored the trial.

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Unclear risk	The trial reported insufficient details.
Blinding (performance bias and detection bias) All outcomes	Low risk	The trial was double-blind (participant/investigator).
Randomisation method reported	Low risk	A computer-generated block list was used for randomisation.

Cunliffe 1992 *(Continued)*

Loss to follow up	Low risk	2.0%
Baseline assessments	Low risk	-
Baseline comparability demonstrated	Low risk	-

De Simone 1993

Methods	**DESIGN** Between-patient Participant delivery **ALLOCATION** Random Method of randomisation: not stated Concealment: unclear **BLINDING** Blinding unclear **WITHDRAWAL/DROPOUT** Not described
Participants	N: 30 Treatment duration: 6 wks; FU: 10 wks LF: 0 (0%) BC: not reported Age: range = 18 to 84 Gender (per cent men): 70.0% Severity: PASI range = 2.7 to 24.3 **INCLUSION CRITERIA** • Chronic plaque psoriasis **EXCLUSION CRITERIA** • Pregnancy • Lactation • Hepatic or renal disease • Recent systemic or topical therapy • High intake of vitamin D or calcium
Interventions	• Calcipotriol ointment 50 mcg/g BD (C) • Coal tar 5% in Lassar's paste (T)
Outcomes	1. Investigator Global Assessment (estimated from PASI score)
Notes	The trial did not report sponsorship.

Risk of bias

Bias	Authors' judgement	Support for judgement

De Simone 1993 *(Continued)*

Allocation concealment (selection bias)	Unclear risk	The trial reported insufficient details.
Blinding (performance bias and detection bias) All outcomes	Unclear risk	The trial did not report this.
Randomisation method reported	Unclear risk	The trial did not report this.
Loss to follow up	Low risk	0.0%
Baseline assessments	Low risk	These were partially done.
Baseline comparability demonstrated	Unclear risk	The trial did not report this.

Decroix 2004

Methods	**DESIGN** Between-patient Participant delivery **ALLOCATION** Random Method of randomisation: not stated Concealment: unclear **BLINDING** Single-blind (investigator); as cream and lotion were compared, not possible to blind participants **WITHDRAWAL/DROPOUT** Described
Participants	N: 222 Treatment duration: 4 wks; FU: 4 wks LF: 0 (0%) BC: yes Age: 48.4 (15.0SD) Gender (per cent men): 55.9% Ethnicity (% white): 100% Severity: DSS (0 to 12) = 8.44 (1.45SD); atrophy (0 to 3) = 1.01; telangiectasia (0 to 3) = 0.01 **INCLUSION CRITERIA** • People aged > = 18 with stable moderate to severe plaque psoriasis • Target lesion diameter > 3 cm • Lesion not localised to scalp, face, hands, or feet • BSA > = 10%; • (Women participants only) negative pregnancy test **EXCLUSION CRITERIA** • Use of topical treatments and phototherapy within previous 2 wks

Decroix 2004 *(Continued)*

	• Use of systemic therapies within previous 2 to 16 wks • Regular sun exposure within previous 2 wks
Interventions	• Clobetasol propionate lotion/cream BD (CP) • Placebo (vehicle lotion) BD (P) Participants were randomised to clobetasol propionate cream or lotion; results were aggregated for review purposes.
Outcomes	1. Erythema, plaque elevation, scaling pruritus: each scored on 5-pt scale (0 to 4) 2. Dermatological Sum Score (DSS: erythema, elevation, scaling): 0 to 12 3. Global severity (GSS): 0 (none) to 4 (severe) 4. Dichotomised as success (GSS = 0, 0.5, or 1) or failure (GSS = 2 to 4) 5. Investigator's Assessment of Global Improvement (IAGI): -1 (worse) to 5 (clear) 6. Per cent BSA involvement: rule of nines 7. Safety: telangiectasia (0 to 3), atrophy (0 to 3); adverse events 8. Compliance (assessment method not reported) 9. Cosmetic acceptability (questionnaire survey)
Notes	Galderma R&D, Sophia Antipolis, France, sponsored the trial. There was SD imputation (TSS).

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Unclear risk	The trial reported insufficient details.
Blinding (performance bias and detection bias) All outcomes	Unclear risk	The study was single-blind (investigator); as the cream and lotion were compared, it was not possible to blind participants.
Randomisation method reported	Unclear risk	The trial did not report this.
Loss to follow up	Low risk	0%
Baseline assessments	Low risk	These were reported.
Baseline comparability demonstrated	Low risk	This was demonstrated.

Douglas 2002

Methods	**DESIGN** Between-patient Participant delivery **ALLOCATION** Random Method of randomisation: computer-generated randomisation schedule Concealment: unclear **BLINDING** Double-blind (participant/investigator)

Douglas 2002 *(Continued)*

	WITHDRAWAL/DROPOUT Described
Participants	N: 1106 Treatment duration: 4 wks; FU: 4 wks LF: 86 (7.8%) BC: yes Age: mean = 47.1 (range = 18 to 89) Gender (per cent men): 59.8% Severity: PASI = 10.7 (range = 2.1 to 39.6) Duration: mean = 18.4 (range = 0 to 65) **INCLUSION CRITERIA** • Chronic plaque psoriasis • Aged at least 18 years • Use of systemic antipsoriatic treatment/phototherapy in previous 6 weeks • Treatment of lesions contraindicated for topical corticosteroid therapy **EXCLUSION CRITERIA** • Pregnancy • Lactation • Current participation in other trial • Abnormality of calcium metabolism • Hypercalcaemia
Interventions	• Calcipotriol (50 mcg/g)/betamethasone (0.5 mg/g) combination ointment (Daviobet®) BD (D) • Calcipotriol ointment (Daivonex®) 50 mcg/g BD (C) • Betamethasone dipropionate ointment (Diprosone®) 0.5 mg/g BD (B) All groups then received 4 weeks of maintenance therapy with calcipotriol BD.
Outcomes	1. PASI (modified) (0 to 64.8) 2. Redness, thickness, scaling (0 to 8 each) 3. Investigator Global Assessment (6-pt: worse to cleared) 4. Patient's assessment of treatment response (6-pt: worse to cleared) 5. Adverse events
Notes	Leo Pharmaceuticals sponsored the trial. 4-week follow-up study also reported (open design: all participants received calcipotriol).

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Unclear risk	The trial reported insufficient details.
Blinding (performance bias and detection bias) All outcomes	Low risk	The trial was double-blind (participant/investigator).

Douglas 2002 *(Continued)*

Randomisation method reported	Low risk	Randomisation was computer-generated.
Loss to follow up	Low risk	7.8%
Baseline assessments	Low risk	-
Baseline comparability demonstrated	Low risk	-

Dubertret 1992

Methods	**DESIGN** Within-patient Participant delivery **ALLOCATION** Random Method of randomisation: unclear Concealment: unclear **BLINDING** Double-blind (participant/investigator) **WITHDRAWAL/DROPOUT** Described
Participants	N: 66 Treatment duration: 4 wks; FU: 8 wks LF: 6 (9.1%) BC: yes Age: 43 (range = 21 to 84) Gender (per cent men): 69.7% Severity: PASI mean = 14.15 Duration: 13.3 (range = 0.3 to 40.0) **INCLUSION CRITERIA** • Bilateral stable symmetric chronic plaque psoriasis of the arms, limbs, or trunk • Adult **EXCLUSION CRITERIA** • Guttate or pustular psoriasis • Psoriasis restricted to the scalp, face, elbows, or knees • Recent systemic or UV therapy in the previous 10 weeks • Calcium, vitamin D daily or other medications • Hepatic or renal impairment • Pplanned exposure to sun
Interventions	• Calcipotriol ointment 50 mcg/gm BD (C) • Placebo (vehicle) (P)
Outcomes	1. Severity [erythema, infiltration, desquamation]

Dubertret 1992 *(Continued)*

2. Modified PASI
3. Preferred treatment
4. Investigator Global Assessment (5-pt: cleared to worse)
5. Patient Global Assessment (5-pt: cleared to worse)

Notes	Leo Pharmaceuticals sponsored the trial. We contacted Leo for patient outcome data. There was the SD imputation (TSS).

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Unclear risk	The trial reported insufficient details.
Blinding (performance bias and detection bias) All outcomes	Low risk	The trial was double-blind (participant/investigator).
Randomisation method reported	Unclear risk	The trial did not report this.
Loss to follow up	Low risk	9.1%
Baseline assessments	Low risk	-
Baseline comparability demonstrated	Low risk	-

Durakovic 2001

Methods	**DESIGN** Within-patient Participant delivery **ALLOCATION** Random Method of randomisation: not stated Concealment: unclear **BLINDING** Double-blind (participant/investigator) **WITHDRAWAL/DROPOUT** Described
Participants	N: 15 Treatment duration: 12 wks; FU: 20 wks LF: 0 (0%) BC: yes Age: 49 (range = 27 to 76) Gender (per cent men): 80% Severity: TSS (0 to 24) = 13.7 (14.7SD)

Durakovic 2001 *(Continued)*

	INCLUSION CRITERIA • Chronic plaque psoriasis involving at least 5% BSA • Bilateral lesions of approximately 25 cm^2 **EXCLUSION CRITERIA** • Systemic treatment within previous 30 days • Topical treatment within previous 1 day • History of hepatic or renal failure • Nephrolithiasis; hypercalcaemia • Hypercalciuria • Pregnancy • Lactation • Unwillingness in women to use effective contraception
Interventions	• Hexafluoro-1,25-dihydroxyvitamin D_3 5 mcg/g in 0.1g of ointment BD (F6) • Placebo ointment BD (P)
Outcomes	1. Total Severity Score (0 to 24) 2. PASI (0 to 72) 3. Investigator's assessment of global improvement (5-pt: worsening to excellent improvement)
Notes	National Institutes of Health and by Penederm Inc. sponsored the trial. 8-week follow up (open design: all participants received study drug) study also reported.

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Unclear risk	The trial reported insufficient details.
Blinding (performance bias and detection bias) All outcomes	Low risk	The trial was double-blind (participant/investigator).
Randomisation method reported	Unclear risk	The trial did not report this.
Loss to follow up	Low risk	0.0%
Baseline assessments	Low risk	-
Baseline comparability demonstrated	Low risk	-

Durakovic 2004

Methods	**DESIGN** Within-patient Participant delivery **ALLOCATION** Random Method of randomisation: not reported

Durakovic 2004 *(Continued)*

	Concealment: unclear **BLINDING** Double-blind (participant/investigator) **WITHDRAWAL/DROPOUT** Described
Participants	N: 11 Treatment duration: 12 wks; FU: 12 wks LF: 0 (0%) BC: yes Age: 46 (range = 29 to 65) Gender (per cent men): 72.7% Severity: TSS (0 to 12) = 9.30 **INCLUSION CRITERIA** • Moderate plaque psoriasis • BSA ≥ 5%; 2 target lesions with diameter ≥ 5cm • Severity score (0 to 4) ≥ 2 for each of plaque elevation, scaling, and erythema **EXCLUSION CRITERIA** • Previous topical therapy within previous 2 wks • Systemic therapy within previous 4 wks • Pregnancy or risk thereof • Lactation • Hepatic failure • Renal failure • Hypercalcaemia • Hypercalciuria • Hyperphosphataemia • Concurrent calcium supplements or drugs influencing calcium metabolism
Interventions	• Paricalcitol (19-nor-1 alpha,25-dihydroxyvitamin D_2) ointment 15 mcg/g OD (PC) • Placebo ointment OD (P)
Outcomes	1. Global severity score (0 to 12) (erythema, plaque elevation, scaling) 2. Global treatment success rates (IAGI) (4-pt: excellent, moderate, mild, or no improvement)
Notes	The trial was sponsored in part by grant from the National Institutes for Health. US Abbott Laboratories supplied the study drug.

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Unclear risk	The trial reported insufficient details.
Blinding (performance bias and detection bias) All outcomes	Low risk	The trial was double-blind (participant/investigator).
Randomisation method reported	Unclear risk	The trial did not report this.
Loss to follow up	Low risk	0.0%

Durakovic 2004 *(Continued)*

Baseline assessments	Low risk	-
Baseline comparability demonstrated	Low risk	-

Duweb 2000

Methods	**DESIGN** Between-patient Participant delivery **ALLOCATION** Random Method of randomisation: not reported Concealment: unclear **BLINDING** Unclear **WITHDRAWAL/DROPOUT** Described
Participants	N: 42 Treatment duration: 6 wks; FU: unclear LF: 0 (0%) BC: clinical only Age: 33.5 (range = 6 to 61) Gender (per cent men): 69% Severity: TSS (0 to 12) = 5.2 **INCLUSION CRITERIA** • Psoriasis of the scalp **EXCLUSION CRITERIA** • Not reported
Interventions	• Calcipotriol 50 mcg/g/ml solution BD (C) • Betamethasone valerate 1% lotion BD (B)
Outcomes	1. Redness, thickness, scaliness (0 to 4) 2. Total Severity Score (0 to 12) 3. Adverse events
Notes	Leo Pharmaceuticals sponsored the trial. There was SD imputation (TSS).

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Unclear risk	The trial reported insufficient details.

Duweb 2000 *(Continued)*

Blinding (performance bias and detection bias) All outcomes	Unclear risk	The trial did not report this.
Randomisation method reported	Unclear risk	The trial did not report this.
Loss to follow up	Low risk	0.0%
Baseline assessments	Low risk	-
Baseline comparability demonstrated	Low risk	This was partially demonstrated.

Elie 1983

Methods	**DESIGN** Between-patient Participant delivery **ALLOCATION** Random Method of randomisation: unclear Concealment: unclear **BLINDING** Double-blind (participant/investigator) **WITHDRAWAL/DROPOUT** Described
Participants	N: 40 (55% psoriasis) Treatment duration: 3 wks; FU: 3 wks LF: not reported BC: yes Age: 36.5 (range = 20 to 63) Gender (per cent men): 40% Severity: not reported **INCLUSION CRITERIA** • Moderate to severe psoriasis, seborrhoeic dermatitis, or neurodermatitis of the scalp • Adult **EXCLUSION CRITERIA** • None reported
Interventions	• Betamethasone-17,21-dipropionate, 0.05% BD (B) • Salicylic acid 2% BD (S) • Betamethasone-17,21-dipropionate, 0.05% + Salicylic acid 2% BD (BS) • Placebo (vehicle) (P)
Outcomes	1. Investigator Global Assessment (5-pt: very severe to clear) 2. Severity (redness; scaling; pruritis)

Elie 1983 *(Continued)*

	3. Area of lesion (cm^2)
Notes	Schering Canada Inc. sponsored the trial. This was a scalp trial. There was SD imputation (TSS/IAGI).

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Unclear risk	The trial reported insufficient details.
Blinding (performance bias and detection bias) All outcomes	Low risk	The trial was double-blind (participant/investigator).
Randomisation method reported	Unclear risk	The trial did not report this.
Loss to follow up	Unclear risk	The trial did not report this.
Baseline assessments	Low risk	These were partially done.
Baseline comparability demonstrated	Low risk	-

Ellis 1988

Methods	**DESIGN** Between-patient Participant delivery **ALLOCATION** Random Method of randomisation: computer-generated randomisation list (1:1) Concealment: unclear **BLINDING** Double-blind (participant/investigator) **WITHDRAWAL/DROPOUT** Described
Participants	N: 165 Treatment duration: 3 wks; FU: 3 wks LF: 33 (20%) BC: yes Age: 49.1 (range = 19 to 82) Gender (per cent men): 51.6% Severity: not reported **INCLUSION CRITERIA** • Psoriasis of the scalp

Ellis 1988 *(Continued)*

- Adult
- TSS (0 to 12) ≥ 6
- Particpants required to have psoriatic lesions elsewhere

EXCLUSION CRITERIA

- Acute systemic illness
- Active skin infection
- Concomitant antihistamine, topical, or systemic corticosteroid, antimetabolites, PUVA, or other dermatological treatment
- Recalcitrant psoriasis
- Intolerance or hypersensitivity to topical corticosteroids
- Pregnant or lactating

Interventions	• Amcinonide lotion 0.1% OD (A) • Placebo (vehicle) (P)
Outcomes	1. Severity (erythema; excoriation; scaling; induration, pruritis) 2. Total Sign Score (erythema; scaling; induration, pruritis) 3. Investigator's Overall Evaluation (7-pt: cleared to exacerbation) 4. Patient's Overall Evaluation (4-pt: poor to excellent) 5. Patient Acceptability Evaluation
Notes	The trial did not report sponsorship. Compliance was checked by counting returned bottles. This was a scalp trial. There was SD imputation (TSS).

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Unclear risk	The trial reported insufficient details.
Blinding (performance bias and detection bias) All outcomes	Low risk	The trial was double-blind (participant/investigator).
Randomisation method reported	Low risk	Randomisation was computer-generated.
Loss to follow up	Low risk	20.0%
Baseline assessments	Low risk	-
Baseline comparability demonstrated	Low risk	-

Escobar 1992

Methods	**DESIGN** Within-patient Participant delivery **ALLOCATION**

Escobar 1992 *(Continued)*

	Random Method of randomisation: 'randomised code' Concealment: unclear **BLINDING** Single-blind (investigator) **WITHDRAWAL/DROPOUT** Described
Participants	N: 25 Treatment duration: 4 wks; FU: 8 wks LF: 0 (0%) BC: yes Age: 40.3 (14.1SD); range = 18 to 66 Gender (per cent men): 56.0% Severity: mean TSS (0 to 12) = 7.83 **INCLUSION CRITERIA** • Clinical and histopathological diagnosis of psoriasis **EXCLUSION CRITERIA** • Systemic cytostatic/corticosteroid therapy within previous year • Renal, hepatic, haematological disease • NSAIDs, beta adrenergic receptor blockers, antimalarial drugs
Interventions	• Fish oil plus 6-hour occlusion OD (FO) • Liquid paraffin plus 6-hour occlusion OD (LP)
Outcomes	1. Erythema, scaling, thickening (0 to 4) 2. Pruritis (VAS) 3. Patient acceptability
Notes	The trial did not report sponsorship. There was SD imputation (TSS).

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Unclear risk	The trial reported insufficient details.
Blinding (performance bias and detection bias) All outcomes	Low risk	The trial was single-blind (investigator).
Randomisation method reported	Unclear risk	The trial did not report this.
Loss to follow up	Low risk	0.0%
Baseline assessments	Low risk	-

Escobar 1992 *(Continued)*

Baseline comparability demonstrated	Low risk	-

Farkas 1999

Methods	**DESIGN** Between-patient Delivery unclear **ALLOCATION** Random Method of randomisation: computer programme randomised participants in blocks of 10 Concealment: unclear **BLINDING** Open **WITHDRAWAL/DROPOUT** Described
Participants	N: 84 Treatment duration: 8 wks; FU: 12 wks LF: 0 (0%) BC: yes Age: 45.1 (range = 18 to 69) Gender (per cent men): 60.7% Severity: mean PASI = 13.2%; BSA (mean) = 16.5% **INCLUSION CRITERIA** • Chronic stable plaque psoriasis • Adults • White participants = 30% BSA • mPASI > 10 • In- and outpatients **EXCLUSION CRITERIA** • Recent topical, systemic, or UV therapies • Sensitivity to study medications • Concurrent medication • Abnormal hepatic or renal function • Risk of pregnancy • Pregnancy • Lactation Serious co-morbidity
Interventions	• Tacalcitol ointment 4 mcg/g OD (T) • Dithranol stick 1.5% or 3% OD (D)
Outcomes	1. PASI (modified to exclude head) 2. Total Sign Score (erythema, infiltration, and desquamation) 3. Investigator Global Assessment

Farkas 1999 *(Continued)*

	4. Patients evaluation of benefit (10-pt) 5. Investigator evaluation of efficacy and tolerability (1 = very good to 4 = very bad) 6. Patient evaluation of efficacy and tolerability (1 = very good to 4 = very bad)
Notes	Hermal sponsored the trial.

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Unclear risk	The trial reported insufficient details.
Blinding (performance bias and detection bias) All outcomes	High risk	The trial was open.
Randomisation method reported	Low risk	A computer-generated block list was used for randomisation.
Loss to follow up	Low risk	0.0%
Baseline assessments	Low risk	-
Baseline comparability demonstrated	Low risk	-

Feldman 2010 (1)

Methods	**DESIGN** Between-patient Participant delivery **ALLOCATION** Random Method of randomisation: not stated Concealment: unclear **BLINDING** Double-blind (participant/investigator) **WITHDRAWAL/DROPOUT** Described
Participants	N: 323 Treatment duration: 8 wks; FU: 8 wks LF: 7 (2.2%) BC: yes Age: 47.8 (15.2SD) Gender (per cent men): 48.3% Per cent white: 90.7% Severity: ISGA = mild disease: 26.9%; ISGA = moderate disease: 73.1%; SGA = 3.69 (0.89SD); % BSA = 6.4% (4.9SD) **INCLUSION CRITERIA** • People aged ≥12 with mild to moderate plaque psoriasis • BSA: 2% to 20% • ISGA: 2 to 3

Feldman 2010 (1) *(Continued)*

	EXCLUSION CRITERIA • Known allergy to any component of formulation • Hypercalcaemia or history thereof • Pregnancy or risk thereof • Topical or systemic therapy within previous 4 wks • Previous participation in trial of study medication
Interventions	• Calcipotriol foam 0.005% BD (C) • Placebo foam BD (P)
Outcomes	1. Investigator Static Global Assessment (IGSA): scale unclear 2. Treatment success: ISGA < = 1 (clear/almost clear) and minimum improvement from baseline of 2 points. 3. Subject Global Assessment (SGA) (6-pt: 0 = clear to 5 = severe) 4. Signs: erythema, scaling, thickness (0 to 4)
Notes	STUDY 1: nCT00689481 Stiefel Laboratories, a GSK Company, sponsored the trial. Atrophy was not reported. We sought data, but they were not received. No usable effectiveness data were reported or available from sponsor.

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Unclear risk	The trial reported insufficient details.
Blinding (performance bias and detection bias) All outcomes	Low risk	The trial was double-blind (participant/investigator).
Randomisation method reported	Unclear risk	The trial did not report this.
Loss to follow up	Low risk	2.2%
Baseline assessments	Low risk	These were reported.
Baseline comparability demonstrated	Low risk	This was demonstrated.

Feldman 2010 (2)

Methods	**DESIGN** Between-patient Participant delivery **ALLOCATION** Random Method of randomisation: not stated Concealment: unclear

Feldman 2010 (2) *(Continued)*

	BLINDING Double-blind (participant/investigator) **WITHDRAWAL/DROPOUT** Described
Participants	N: 336 Treatment duration: 8 wks; FU: 8 wks LF: 6 (1.8%) BC: yes Age: 48.7 (14.4SD) Gender (per cent men): 60.4% % white: 86.0% Severity: ISGA = mild disease: 31.8%; ISGA = moderate disease: 68.2%; SGA = 3.69 (0.83SD); % BSA = 6.2% (4.8SD) **INCLUSION CRITERIA** • People aged ≥12 with mild to moderate plaque psoriasis • BSA: 2% to 20% • ISGA: 2 to 3 **EXCLUSION CRITERIA** • Known allergy to any component of formulation • Hypercalcaemia or history thereof • Pregnancy or risk thereof • Topical or systemic therapy within previous 4 wks • Previous participation in trial of study medication
Interventions	• Calcipotriol foam 0.005% BD (C) • Placebo foam BD (P)
Outcomes	1. Investigator Static Global Assessment (IGSA): scale unclear 2. Treatment success: ISGA < = 1 (clear/almost clear) and minimum improvement from baseline of 2 points 3. Subject Global Assessment (SGA) (6-pt: 0 = clear to 5 = severe) 4. Signs: erythema, scaling, thickness (0 to 4)
Notes	STUDY 2: nCT00688519 Stiefel Laboratories, a GSK Company, sponsored the trial. Atrophy was not reported. We sought data, but they were not received. No usable effectiveness data were reported or available from sponsor.

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Unclear risk	The trial reported insufficient details.
Blinding (performance bias and detection bias) All outcomes	Low risk	The trial was double-blind (participant/investigator).

Feldman 2010 (2) *(Continued)*

Randomisation method reported	Unclear risk	The trial did not report this.
Loss to follow up	Low risk	1.8%
Baseline assessments	Low risk	These were reported.
Baseline comparability demonstrated	Low risk	This was demonstrated.

Fleming 2010 (H)

Methods	**DESIGN** Between-patient Participant delivery **ALLOCATION** Random Method of randomisation: computer-generated schedule Concealment: unclear **BLINDING** Double-blind (participant/investigator) **WITHDRAWAL/DROPOUT** Described
Participants	N: 364 Treatment duration: 8 wks; FU: 10 wks LF: 2 (0.5%) BC: yes Age: 51.1 (14.7SD) Gender (per cent men): 58.8% Per cent white: 98.1% Severity: PASI (0 to 64.8) = 7.8 (4.4SD), range = 1 to 25; IGA = 2.97 (0.66SD), range = mild (2) to very severe (5) Duration (yrs): 18.9 (13.8SD) **INCLUSION CRITERIA** • People aged > = 18 with psoriasis vulgaris affecting the trunk and or limbs, amenable to treatment with < = 100 g topical medication/w • IGA at least mild **EXCLUSION CRITERIA** • Guttate, erythrodermic, exfoliative or pustular psoriasis • Use of biological therapy within previous 6 mths • Use of systemic antipsoriatic therapy, PUVA, or grenz ray therapy with previous 4 wks • Topical or UVB therapy within previous 2 wks • Concomitant use of emollients during study
Interventions	• Calcipotriol gel 50 mcg/g plus betamethasone dipropionate gel 0.5 mg/g OD (C-B)

Fleming 2010 (H) *(Continued)*

- Calcipotriol gel 50 mcg/g OD (C)
- Betamethasone dipropionate gel 0.5 mg/g OD (B)

Concomitant use of corticosteroids (WHO group I or II), dithranol, tar, and retinoids on face, scalp, and flexures was permitted.

Outcomes	1. Investigator's Global Assessment (IGA) of disease severity; 6-pt (clear, minimal disease, mild, moderate, severe, very severe); rescaled as clear (0) to very severe (5) 2. Responder (IGA): If IGA moderate at wk 0: clear/minimal at wk 4 or 8. If IGA mild at wk 0: clear at wk 4 or 8 3. PASI (modified) (0 to 64.8): change from baseline 4. Treatment success: PASI75 5. Adverse events 6. Compliance
Notes	Leo Pharma, Ballerup, Denmark, sponsored the trial. Compliance: mean weekly us =: C-B: 22.7 g; C: 22.4g; B: 25.9 g Most participants (73.5% to 80%) were fully compliant and those non-compliant missed < 10% applications. Safety data were available for 362/364 participants. Leo Pharmaceuticals supplied unpublished data.

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Unclear risk	The trial reported insufficient details.
Blinding (performance bias and detection bias) All outcomes	Low risk	The trial was double-blind (participant/investigator).
Randomisation method reported	Low risk	A computer-generated randomisation schedule was used.
Loss to follow up	Low risk	0.5%
Baseline assessments	Low risk	These were reported.
Baseline comparability demonstrated	Low risk	This was demonstrated.

Fleming 2010 (P)

Methods	**DESIGN** Between-patient Participant delivery **ALLOCATION** Random Method of randomisation: computer-generated schedule Concealment: unclear **BLINDING** Double-blind (participant/investigator)

Fleming 2010 (P) *(Continued)*

WITHDRAWAL/DROPOUT
Described

Participants	N: 364 Treatment duration: 8 wks; FU: 10 wks LF: 2 (0.5%) BC: yes Age: 51.1 (14.7SD) Gender (per cent men): 58.8% Per cent white: 98.1% Severity: PASI (0 to 64.8) = 7.8 (4.4SD), range = 1 to 25; IGA = 2.97 (0.66SD), range = mild (2) to very severe (5) Duration (yrs): 18.9 (13.8SD) **INCLUSION CRITERIA** • People aged > = 18 with psoriasis vulgaris affecting the trunk and or limbs, amenable to treatment with < = 100 g topical medication/w • IGA at least mild **EXCLUSION CRITERIA** • Guttate, erythrodermic, exfoliative or pustular psoriasis • Use of biological therapy within previous 6 mths • Use of systemic antipsoriatic therapy, PUVA, or grenz ray therapy with previous 4 wks • Topical or UVB therapy within previous 2 wks • Concomitant use of emollients during study
Interventions	• Calcipotriol gel 50 mcg/g plus betamethasone dipropionate gel 0.5 mg/g OD (C-B) • Calcipotriol gel 50 mcg/g OD (C) • Betamethasone dipropionate gel 0.5 mg/g OD (B) • Placebo gel OD (P) Concomitant use of corticosteroids (WHO group I or II), dithranol, tar, and retinoids on face, scalp, and flexures were permitted.
Outcomes	1. Investigator's Global Assessment (IGA) of disease severity; 6-pt (clear, minimal disease, mild, moderate, severe, very severe); rescaled as clear (0) to very severe (5) 2. Responder (IGA): If IGA moderate at wk 0: clear/minimal at wk 4 or 8. If IGA mild at wk 0: clear at wk 4 or 8 3. PASI (modified) (0 to 64.8): change from baseline 4. Treatment success: PASI75 5. Adverse events 6. Compliance
Notes	Leo Pharma, Ballerup, Denmark, sponsored the trial. Compliance: mean weekly us =: C-B: 22.7 g; C: 22.4g; B: 25.9 g; P: 26.1 g Most participants (73.5% to 80%) were fully compliant and those non-compliant missed < 10% applications. Safety data were available for 362/364 participants. Leo Pharmaceuticals supplied unpublished data.

Risk of bias

Bias	Authors' judgement	Support for judgement

Fleming 2010 (P) *(Continued)*

Allocation concealment (selection bias)	Unclear risk	The trial reported insufficient details.
Blinding (performance bias and detection bias) All outcomes	Low risk	The trial was double-blind (participant/investigator).
Randomisation method reported	Low risk	A computer-generated randomisation schedule was used.
Loss to follow up	Low risk	0.5%
Baseline assessments	Low risk	These were reported.
Baseline comparability demonstrated	Low risk	This was demonstrated.

Franz 1999

Methods	**DESIGN** Between-patient Participant delivery **ALLOCATION** Random Method of randomisation: unclear Concealment: unclear **BLINDING** Double-blind (participant/investigator) **WITHDRAWAL/DROPOUT** Described
Participants	N: 190 Treatment duration: 2 wks; FU: 4 wks LF: 18 (9.5%) BC: yes Age: 49.6 Gender (per cent men): 49.3% Severity: mean TSS (0 to 12) = 7.92 **INCLUSION CRITERIA** • Moderate to severe scalp psoriasis (each of 3 primary signs ≥ 2) • Scalp involvement ≥10% • Adults **EXCLUSION CRITERIA** • Systemic psoriatic therapy within previous 4 wks • Topical scalp preparations within previous 2 wks
Interventions	• Betamethasone valerate foam 0.1% BD • Placebo foam BD

Franz 1999 *(Continued)*

- Betamethasone valerate lotion 0.1% BD
- Placebo lotion BD

Findings reported for foam and lotion combined:

- Betamethasone (B)
- Placebo (P)

Outcomes	1. Erythema, scaling, thickness, pruritis 2. IAGI (7-pt: worse to completely clear) 3. PAGI (7-pt: worse to completely clear)
Notes	Connectics Corporation sponsored by the trial. This was a scalp trial. There was SD imputation (TSS).

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Unclear risk	The trial reported insufficient details.
Blinding (performance bias and detection bias) All outcomes	Low risk	The trial was double-blind (participant/investigator).
Randomisation method reported	Unclear risk	The trial did not report this.
Loss to follow up	Low risk	9.5%
Baseline assessments	Low risk	-
Baseline comparability demonstrated	Low risk	-

Franz 2000

Methods	**DESIGN** Between-patient Participant delivery **ALLOCATION** Random Method of randomisation: not reported Concealment: unclear **BLINDING** Double-blind (participant/investigator) **WITHDRAWAL/DROPOUT** Described
Participants	N: 188 Treatment duration: 2 wks; FU: 4 wks LF: 0 (0%)

Franz 2000 *(Continued)*

	BC: unclear Age: not reported Gender (per cent men): 49.5% Severity: mean TSS (0 to 12) = 7.25 **INCLUSION CRITERIA** • Moderate to severe scalp psoriasis (each of 3 primary signs ≥ 2) • Scalp involvement ≥10% • Adults **EXCLUSION CRITERIA** • Not reported
Interventions	• Clobetasol propionate foam 0.05% BD • Placebo foam BD • Clobetasol propionate lotion 0.05% BD • Placebo lotion BD *Findings reported for foam and lotion combined:* • Clobetasol (C) • Placebo (P)
Outcomes	1. Signs: erythema, scaling, thickness, pruritis 2. TSS (0 to 12) 3. IAGI (7-pt: worse to completely clear) 4. PAGI (7-pt: worse to completely clear)
Notes	Connectics Corporation sponsored by the trial. This was a scalp trial. There was SD imputation (TSS).

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Unclear risk	The trial reported insufficient details.
Blinding (performance bias and detection bias) All outcomes	Low risk	The trial was double-blind (participant/investigator).
Randomisation method reported	Unclear risk	The trial did not report this.
Loss to follow up	Low risk	0.0%
Baseline assessments	Low risk	These were partially done.
Baseline comparability demonstrated	Unclear risk	The trial did not report this.

Geilen 2000

Methods	**DESIGN** Within-patient Nurse delivery **ALLOCATION** Random Method of randomisation: not reported Concealment: unclear **BLINDING** Double-blind (participant/investigator) **WITHDRAWAL/DROPOUT** Described
Participants	N: 7 Treatment duration: 3 wks; FU: 3 wks LF: 0 (0%) BC: yes Age: 36 to 67 Gender (per cent men): 100% Severity: TSS (0 to 8) = 6.72 (0.76SD) **INCLUSION CRITERIA** • Chronic plaque psoriasis **EXCLUSION CRITERIA** • Not reported
Interventions	• Mycophenolic acid ointment 1% plus occlusion OD (M) • Placebo ointment plus occlusion OD (P)
Outcomes	1. TSS (erythema induration) (0 to 8)
Notes	The trial did not report sponsorship.

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Unclear risk	The trial reported insufficient details.
Blinding (performance bias and detection bias) All outcomes	Low risk	The trial was double-blind (participant/investigator).
Randomisation method reported	Unclear risk	The trial did not report this.
Loss to follow up	Low risk	0.0%
Baseline assessments	Low risk	These were partially done.

Geilen 2000 *(Continued)*

Baseline comparability demonstrated	Low risk	-

Gottlieb 2003

Methods	**DESIGN** Between-patient Participant delivery **ALLOCATION** Random Method of randomisation: not reported Conducted in 17 centres; stratification not reported Concealment: unclear **BLINDING** Double-blind (participant/investigator) **WITHDRAWAL/DROPOUT** Described
Participants	N: 279 Treatment duration: 2 wks; FU: 4 wks LF: 8 (2.9%) BC: yes (clinical only) Age: 47 (range = 19 to 82) Gender (per cent men): 57% Severity: BSA = 6.7% **INCLUSION CRITERIA** • Aged 18 to over • Mild to moderate chronic plaque psoriasis of non-scalp regions • 2 > PSGA > 3; BSA < = 20% • Target lesion > 2 cm^2 on trunk or extremities with PGSA between 2 and 3 for each of erythema, scaling, and plaque thickness **EXCLUSION CRITERIA** • Known allergy to study medications or other topical corticosteroids • Systemic therapy within previous 8 wks • Topical corticosteroid therapy or retinoids within previous 4 wks • Other topical therapy within previous 2 wks • Expected exposure to strong sunlight/UVB therapy during study period • Pregnancy or risk thereof • Lactation
Interventions	• Clobetasol foam (OLUX®) 0.05% BD (C) • Placebo foam BD (P) Limit of 50 g of medication/wk to non-scalp sites only
Outcomes	1. Signs and symptoms of psoriasis (6-pt scale for each: induration, erythema, scaling, pruritis) 2. Physician's Static Global Assessment (PGSA) (6-pt: 0 = clear to 5 = majority of lesions have individual scores that average 5 on a 6-pt scale)

Gottlieb 2003 *(Continued)*

3. Proportion of patients with PSGA score < = 1 at 2 wks
4. Mean change in Total Sign Scores (0 to 15)
5. Patient Global Assessment (PGA) (6-pt: 0 = no psoriasis; 5 = worst during current exacerbation)
6. Patient assessment of likely compliance
7. Patient assessment of cosmetic acceptability

Notes	Connetics Corporation sponsored the trial. There was SD imputation (TSS).

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Unclear risk	The trial reported insufficient details.
Blinding (performance bias and detection bias) All outcomes	Low risk	The trial was double-blind (participant/investigator).
Randomisation method reported	Unclear risk	The trial did not report this.
Loss to follow up	Low risk	-
Baseline assessments	Low risk	-
Baseline comparability demonstrated	Low risk	This was partially demonstrated.

Grattan 1997 (H)

Methods	**DESIGN** Within-patient Delivery unclear **ALLOCATION** Random Method of randomisation: pre-determined randomisation schedule Concealment: unclear **BLINDING** Open **WITHDRAWAL/DROPOUT** Described
Participants	N: 25 Treatment duration: 4 wks; FU: 16 weeks LF: not reported BC: yes Age: 44.0 (range = 20 to 72) Gender (per cent men): 52.0%) Severity: BSA = 16.1% (range = 4.1% to 47.8%); TSS (target sites) = 6.3 (range = NR)

Grattan 1997 (H) *(Continued)*

	INCLUSION CRITERIA • Bilateral stable chronic plaque psoriasis • Adult • Hospitalised for routine dithranol treatment **EXCLUSION CRITERIA** • Intolerance of dithranol • Unstable or pustular psoriasis • Calcium metabolism disorders • Systemic psoriasis treatment • Recent UVB or PUVA therapy • Pregnancy or lactation
Interventions	• Calcipotriol ointment 0.005% BD (C) • Dithranol in aqueous gel (dose titration 0.1% to 2.0%) BD (D)
Outcomes	1. Severity (erythema; scaling; palpability) 2. Total Severity Score 3. Patient assessment of irritation (VAS) 4. Investigator assessment of skin staining (none, mild, moderate, or severe)
Notes	There was inpatient treatment to ensure high level of compliance. Dermal Laboratories sponsored the trial.

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Unclear risk	The trial reported insufficient details.
Blinding (performance bias and detection bias) All outcomes	High risk	The trial was open.
Randomisation method reported	Unclear risk	The trial did not report this.
Loss to follow up	Unclear risk	The trial did not report this.
Baseline assessments	Low risk	These were reported.
Baseline comparability demonstrated	Low risk	This was demonstrated.

Grattan 1997 (P)

Methods	**DESIGN** Within-patient Delivery unclear **ALLOCATION** Random Method of randomisation: pre-determined randomisation schedule

Grattan 1997 (P) *(Continued)*

	Concealment: unclear **BLINDING** Open **WITHDRAWAL/DROPOUT** Described
Participants	N: 12 Treatment duration: 4 wks: FU: 16 wks LF: 0 (0%) BC: yes Age: 50.3 (range = 33 to 75) Gender (per cent men): 33% (4/12) Severity: BSA 17.1% (range = 4.7% to 45.7%); TSS = 6.3 (range = 5 to 7) **INCLUSION CRITERIA** • Bilateral stable chronic plaque psoriasis • Adult • Hospitalised for routine dithranol treatment **EXCLUSION CRITERIA** • Intolerance of dithranol • Unstable or pustular psoriasis • Calcium metabolism disorders • Systemic psoriasis treatment • Recent UVB or PUVA therapy • Pregnancy or lactation
Interventions	• Dithranol in aqueous gel (dose titration 0.1 to 2.0%) BD (D) • Placebo (vehicle) (P)
Outcomes	1. Severity (erythema; scaling; palpability) 2. Total Severity Score, patient assessment of irritation (VAS) 3. Investigator assessment of skin staining (none, mild, moderate, or severe)
Notes	There was inpatient treatment to ensure high level of compliance. Dermal Laboratories sponsored the trial.

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Unclear risk	The trial reported insufficient details.
Blinding (performance bias and detection bias) All outcomes	High risk	The trial was open.
Randomisation method reported	Unclear risk	The trial did not report this.

Grattan 1997 (P) *(Continued)*

Loss to follow up	Low risk	0.0%
Baseline assessments	Low risk	-
Baseline comparability demonstrated	Low risk	-

Green 1994

Methods	**DESIGN** Between-patient Participant delivery **ALLOCATION** Random Method of randomisation: not reported Concealment: unclear **BLINDING** Double-blind (participant/investigator) **WITHDRAWAL/DROPOUT** Described
Participants	N: 49 Treatment duration: 4 wks; FU: 4 wks LF: 3 (6.1%) BC: unclear Age: not reported Gender (per cent men): not reported Severity: mean TSS (0 to 12) = 6.7 **INCLUSION CRITERIA** • Mild to moderate scalp psoriasis and a history of psoriasis elsewhere on the body • Adult **EXCLUSION CRITERIA** • Excessively thick scalp psoriasis • Other scalp disease • Marked deterioration of scalp psoriasis at entry • Recent systemic or UV therapy • Concurrent topical corticosteroid use • Vitamin D or calcium supplement • Medications that could affect the course of the disease • Hypercalcaemia • Hepatic or renal disease • At risk of pregnancy
Interventions	• Calcipotriol solution 50 mcg/ml BD (C) • Placebo (vehicle) (P)
Outcomes	1. Signs (erythema; thickness; scaliness; flaking; itching)

Green 1994 *(Continued)*

	2. Total Sign Score (redness, thickness, scaliness) 3. Investigator Global Assessment 4. Patient Global Assessment
Notes	Leo Pharmaceutical Products sponsored the trial. Compliance was assessed by unused medication returned at each visit. The compliance rate for participants in each group was > 90%. This was a scalp trial.

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Unclear risk	The trial reported insufficient details.
Blinding (performance bias and detection bias) All outcomes	Low risk	The trial was double-blind (participant/investigator).
Randomisation method reported	Unclear risk	The trial did not report this.
Loss to follow up	Low risk	6.1%
Baseline assessments	Low risk	These were partially done.
Baseline comparability demonstrated	Unclear risk	The trial did not report this.

Greenspan 1993

Methods	**DESIGN** Between-patient Participant delivery **ALLOCATION** Random Method of randomisation: not reported Concealment: unclear **BLINDING** Double-blind (participant/investigator) **WITHDRAWAL/DROPOUT** Described
Participants	N: 80 Treatment duration: 3 wks; FU: 3 wks LF: 9 (11.3%) BC: unclear Age: 51.5 (range = 20 to 77) Gender (per cent men): 43.8% Severity: not reported

Greenspan 1993 *(Continued)*

	INCLUSION CRITERIA • Mild to moderate psoriasis **EXCLUSION CRITERIA** • Recent systemic or topical treatment for psoriasis • Contraindication to low-potency corticosteroids • Pregnant, nursing, or planning pregnancy
Interventions	• Desonide lotion 0.05% TDS (DL) • Desonide cream 0.05% TDS (DC) • Placebo (vehicle lotion) (P)
Outcomes	1. Severity (erythema; scaling; induration; pruritis) 2. Investigator Global Assessment
Notes	The trial did not report sponsorship, but 3 of the authors were employed by Owen/Galderma laboratories. There was SD imputation (IAGI).

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Unclear risk	The trial reported insufficient details.
Blinding (performance bias and detection bias) All outcomes	Low risk	The trial was double-blind (participant/investigator).
Randomisation method reported	Unclear risk	The trial did not report this.
Loss to follow up	Low risk	11.3%
Baseline assessments	Low risk	These were partially done.
Baseline comparability demonstrated	Unclear risk	The trial did not report this.

Gribetz 2004

Methods	**DESIGN** Between-patient Participant delivery **ALLOCATION** Random Method of randomisation: 'validated system that automates the random assignment of treatment codes' Concealment: adequate **BLINDING** Double-blind (participant/investigator) **WITHDRAWAL/DROPOUT** Described

Gribetz 2004 *(Continued)*

Participants	N: 57 Treatment duration: 8 wks; FU: 8 wks LF: 6 (10.5%) BC: yes Age: 47.8 (range = 21 to 88) Gender (per cent men): 50.9% Severity: PGA, per cent moderate = 72%; PGA, per cent severe = 29.8%; TSS = 5.34 (range = 3.0 to 9.0) **INCLUSION CRITERIA** • Stable chronic plaque psoriasis • Moderate to severe inverse psoriasis affecting axillae, inguinal, inframammary, or gluteal cleft regions (duration ≥ 6 mths) • PGA ≥ 3 • Erythema ≥ 2 • Aged ≥ 18 **EXCLUSION CRITERIA** • Clinically significant laboratory abnormalities • Hypersensitivity to study drug or vehicle • Systemic, phototherapy, or immuno-modifying agents within previous 30 dys • Topical therapies within previous 14 dys • Unstable plaque psoriasis, pustular, drug associated or erythrodermic psoriasis
Interventions	• Pimecrolimus cream (Elidel®) 1% BD (PM) • Placebo cream BD (P)
Outcomes	1. Investigator's Global Assessment of overall severity (PGA) (5-pt: clear to severe disease) 2. Target Area Score (TSS) (erythema, induration, scaling) (0 to 9) 3. Patient Self-Assessment (control of psoriasis over previous 1 wk) (4-pt: 0 = complete control; 3 = uncontrolled)
Notes	Novartis Pharmaceuticals Group sponsored the trial. No instances of skin atrophy were reported. This was an inverse psoriasis trial.

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Low risk	Novartis supplied identical tubes identified only by randomisation number (participants and investigators blinded to tube contents).
Blinding (performance bias and detection bias) All outcomes	Low risk	The trial was double-blind (participant/investigator).
Randomisation method reported	Low risk	Randomisation was by a validated system that automated the random assignment of treatment codes.
Loss to follow up	Low risk	10.5%

Gribetz 2004 *(Continued)*

Baseline assessments	Low risk	These were reported.
Baseline comparability demonstrated	Low risk	-

Guenther 2000

Methods	**DESIGN** Between-patient Participant delivery **ALLOCATION** Random Method of randomisation: not reported Concealment: unclear **BLINDING** Single-blind (investigator) **WITHDRAWAL/DROPOUT** Described
Participants	N: 120 Treatment duration: 8 wks; FU: 20 wks LF: 14 (11.7%) BC: yes Age: 48.5 Gender (per cent men): 60.8% Severity: not reported **INCLUSION CRITERIA** • Stable chronic plaque psoriasis • BSA involvement between 5% and 20% • Adult **EXCLUSION CRITERIA** • Pregnancy • Lactation • Unreliable contraception • Unstable plaque psoriasis • Other types of psoriasis or other concomitant dermatological disorder • Hypercalaemia • Uncontrolled systemic disease • Likelihood of prolonged UV exposure • Concomitant systemic or topical therapies that might affect psoriasis • Adherence to washout requirements
Interventions	• Tazarotene gel, 0.1% ON, plus mometasone furoate cream 0.1% OM (TM) • Calcipotriol ointment 0.005% BD (C) 12 weeks' maintenance for both groups with emollient only.

Guenther 2000 *(Continued)*

Outcomes	1. IAGI (0 to 6; exacerbation to complete clearance) 2. Erythema, scaling, thickness (0 to 4 for each) 3. BSA involvement 4. Patient assessments (efficacy, comfort of skin; outlook for long-term control; overall impression of treatment) 5. Adverse events
Notes	Allergan Inc. sponsored the trial.

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Unclear risk	The trial reported insufficient details.
Blinding (performance bias and detection bias) All outcomes	Unclear risk	The trial was single-blind (investigator).
Randomisation method reported	Unclear risk	The trial did not report this.
Loss to follow up	Low risk	11.7%
Baseline assessments	Low risk	-
Baseline comparability demonstrated	Low risk	-

Guenther 2002 (H)

Methods	**DESIGN** Between-patient Participant delivery **ALLOCATION** Random Method of randomisation: computer-generated random numbers table Concealment: adequate **BLINDING** Double-blind (participant/investigator) **WITHDRAWAL/DROPOUT** Described
Participants	N: 828 Treatment duration: 4 wks; FU: 4 wks LF: 10 (1.2%) BC: yes Age: 48.5 (14.3SD) Gender (per cent men): 64.0% Severity: mean PASI = 10.5; mean duration psoriasis = 18.3 yrs

Guenther 2002 (H) *(Continued)*

	INCLUSION CRITERIA • Aged 18 to 86 • Chronic plaque psoriasis • BSA involvement ≥ 10% **EXCLUSION CRITERIA** • Systemic therapy within previous 6 wks • Topical antipsoriatic therapy within previous 2 wks • Concurrent use of type III/IV topical corticosteroids • Recent UV exposure • Pregnancy • Lactation • Concurrent use of other medicines that could affect course of psoriasis
Interventions	• Calcipotriol (50 mcg/g) and betamethasone dipropionate (0.5 mg/g) ointment ON, plus placebo OM (D1) • Calcipotriol (50 mcg/g) and betamethasone dipropionate (0.5 mg/g) ointment BD (D2) • Calcipotriol BD (C) • Placebo BD (P)
Outcomes	1. PASI (head excluded) 2. IAGI (6-pt: worse to clearance) 3. PAGI (6-pt: worse to clearance) 4. Percentage change in thickness score 5. Speed of response (PASI) at 1 week 6. Adverse events 7. Quality of life: Psoriasis Disability Index; EQ-5D and EQ-VAS (reported in van de Kerkhof 2004)
Notes	Leo Pharmaceuticals sponsored the trial. The trial was conducted across 57 centres in 8 countries.

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Low risk	All study personnel and participants were blinded to treatment assignment for the duration of the study.
Blinding (performance bias and detection bias) All outcomes	Low risk	The trial was double-blind (participant/investigator).
Randomisation method reported	Low risk	Randomisation was computer-generated.
Loss to follow up	Low risk	1.2%
Baseline assessments	Low risk	-
Baseline comparability demonstrated	Low risk	-

Guenther 2002 (P)

Methods	**DESIGN** Between-patient Participant delivery **ALLOCATION** Random Method of randomisation: computer-generated random numbers table Concealment: adequate **BLINDING** Double-blind (participant/investigator) **WITHDRAWAL/DROPOUT** Described
Participants	N: 828 Treatment duration: 4 wks; FU: 4 wks LF: 10 (1.2%) BC: yes Age: 48.5 (14.3SD) Gender (per cent men): 64.0% Severity: mean PASI = 10.5; mean duration psoriasis = 18.3 yrs **INCLUSION CRITERIA** • Aged 18 to 86 • Chronic plaque psoriasis • BSA involvement ≥ 10% **EXCLUSION CRITERIA** • Systemic therapy within previous 6 wks • Topical antipsoriatic therapy within previous 2 wks • Concurrent use of type III/IV topical corticosteroids • Recent UV exposure • Pregnancy • Lactation • Concurrent use of other medicines that could affect course of psoriasis
Interventions	• Calcipotriol (50 mcg/g) and betamethasone diproprionate (0.5 mg/g) ointment ON, plus placebo, OM (D1) • Calcipotriol (50 mcg/g) and betamethasone diproprionate (0.5 mg/g) ointment BD (D2) • Calcipotriol BD (C) • Placebo BD (P)
Outcomes	1. PASI (head excluded) 2. IAGI (6-pt: worse to clearance) 3. PAGI (6-pt: worse to clearance) 4. Percentage change in thickness score 5. Speed of response (PASI) at 1 week 6. Adverse events 7. Quality of life: Psoriasis Disability Index; EQ-5D and EQ-VAS (reported in van de Kerkhof 2004)
Notes	Leo Pharmaceuticals sponsored the trial. The trial was conducted across 57 centres in 8 countries.

Risk of bias

Bias	Authors' judgement	Support for judgement

Guenther 2002 (P) *(Continued)*

Allocation concealment (selection bias)	Low risk	All study personnel and participants were blinded to treatment assignment for the duration of the study.
Blinding (performance bias and detection bias) All outcomes	Low risk	The trial was double-blind (participant/investigator).
Randomisation method reported	Low risk	Randomisation was computer-generated.
Loss to follow up	Low risk	1.2%
Baseline assessments	Low risk	These were reported.
Baseline comparability demonstrated	Low risk	-

Han 2001

Methods	**DESIGN** Between-patient Participant delivery **ALLOCATION** Random Method of randomisation: not reported Concealment: unclear **BLINDING** Open **WITHDRAWAL/DROPOUT** Described
Participants	N: 208 Treatment duration: 12 wks; FU: 12 wks LF: 9 (4.3%) BC: yes Age: 40.4 (8.9SD) Gender (per cent men): 59.8% Severity: TSS (0 to 20) = 16.1 (11.0SD) Duration (yrs): 9.4 (8.9SD) **INCLUSION CRITERIA** • People with chronic plaque psoriasis • Aged between 18 and 65 • BSA between 2% and 30% **EXCLUSION CRITERIA** • Known allergy to study drug constituents • History of other skin diseases • Pustular or erythrodermic psoriasis

Han 2001 *(Continued)*

	• Topical treatments within previous 2 wks • PUVA within previous 4 wks • UVB within previous 2 wks • Alcohol or drug abuse • Renal, hepatic, or immunity disorder • Pregnancy or risk thereof • Lactation • Participation in another clinical trial within previous 4 wks • Other morbidity likely to affect outcome or raise safety issues
Interventions	• Tazarotene gel 0.05% OD (T) • Calcipotriol ointment 5 mcg/g BD (C)
Outcomes	1. TSS (0 to 20) 2. Proportion of patients achieving effective response 3. Curative rate
Notes	The trial did not report sponsorship. Translation support was received for data extraction.

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Unclear risk	The trial reported insufficient details.
Blinding (performance bias and detection bias) All outcomes	High risk	The trial was open.
Randomisation method reported	Unclear risk	The trial did not report this.
Loss to follow up	Low risk	4.3%
Baseline assessments	Low risk	These were reported.
Baseline comparability demonstrated	Low risk	-

Harrington 1996a

Methods	**DESIGN** Between-patient Participant delivery **ALLOCATION** Random Method of randomisation: not reported Concealment: unclear **BLINDING** Double-blind (participant/investigator) **WITHDRAWAL/DROPOUT**

Harrington 1996a *(Continued)*

	Described
Participants	N: 413 Treatment duration: 8 wks; FU: 8 wks LF: 47 (11.4%) BC: yes, except average age in placebo group higher than for A and B (P = 0.02) Age: 44.6 Gender (per cent men): 52.8% Severity: PASI (modified) = 8.3 (range = 0.6 to 59.4) Duration (yrs): 17.7 (range = 0.04 to 70) **INCLUSION CRITERIA** • Stable chronic plaque psoriasis on trunk or limbs • Adult **EXCLUSION CRITERIA** • Recent systemic medication or phototherapy for psoriasis • Hepatic or renal disease • Raised serum calcium • Calcium supplements or vitamin D

Interventions	• Calcipotriol cream 50 mcg/g BD as follows:
	  • Cream A (dissolved) (CA)
	  • Cream B (suspended) (CB)
	• Placebo (vehicle of A) (P)

Outcomes	1. PASI (modified to exclude head) 2. Investigator Global Assessment 3. Patient Global Assessment
Notes	Leo Pharmaceuticals sponsored the trial.

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Unclear risk	The trial reported insufficient details.
Blinding (performance bias and detection bias) All outcomes	Low risk	The trial was double-blind (participant/investigator).
Randomisation method reported	Unclear risk	The trial did not report this.
Loss to follow up	Low risk	11.4%
Baseline assessments	Low risk	-

Harrington 1996a *(Continued)*

Baseline comparability demonstrated	Unclear risk	This was partially demonstrated.

Helfrich 2007

Methods	**DESIGN** Between-patient Participant delivery **ALLOCATION** Random Method of randomisation: unclear (method inadequately described) Concealment: unclear (inadequately described) **BLINDING** Double-blind (participant/investigator/assessor) **WITHDRAWAL/DROPOUT** Described
Participants	N: 185 Treatment duration: 8 wks; FU: 8 wks LF: 3 (1.6%) BC: yes Age: 49.0 (range = 19 to 83) Gender (per cent men): 56.8% Severity: PGA = 3.2 (range = 3 to 4); PSS = 8.1 (range = 4.7 to 12) Ethnicity (per cent white): NR Duration: 17.3 (range = 0.5 to 65) **INCLUSION CRITERIA** • People aged 18 and over with chronic plaque psoriasis affecting 2% to 10% BSA with severity "appropriate" for topical therapy • PGA score: > = 3 **EXCLUSION CRITERIA** • Topical therapies within previous 2 wks • Systemic/UV therapy within previous 4 wks • Biological within previous 6 mths • Oral vitamin D (> 400 IU/day), oral calcium (> 1200 mg/day) within previous 30 days • Pregnancy or risk thereof • Lactation • Significant medial comorbidity • Sensitivity to study drug • Concomitant antipsoriatics therapy, immunosuppressive drugs, lithium, hydoxycholoroquine, or biologicals • Non-compliance with dosing of study medication
Interventions	• Becocalcidiol ointment 75 mcg/g BD (B2) • Becocalcidiol ointment 75 mcg/g ON and placebo OM (B1) • Placebo ointment BD (P)

Helfrich 2007 *(Continued)*

	Max: 8 g ointment/day Participants were permitted concurrent oral vitamin D (= < 400 IU/day), oral calcium (< = 1200 mg/day), or both; or tar shampoo for scalp psoriasis.
Outcomes	1. Physician's Static Global Assessment of Overall Lesion Severity (PGA) (6-point scale: clear to very severe) 2. Psoriasis Symptom Severity (PSS) score (0 to 12): sum of scores for erythema, scaling, induration (each scored 0 to 4) 3. Adverse events 4. Laboratory evaluations 5. Compliance (participants who missed > 6 consecutive doses discontinued the study)
Notes	QuatRx Pharmaceuticals (product now owned by Deltanoid Pharmaceuticals) sponsored the trial. The sponsor supplied unpublished data.

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Unclear risk	The trial reported insufficient details.
Blinding (performance bias and detection bias) All outcomes	Low risk	The trial was double-blind (participant and investigator/assessor).
Randomisation method reported	Unclear risk	The trial did not report this.
Loss to follow up	Low risk	1.6%
Baseline assessments	Low risk	These were reported.
Baseline comparability demonstrated	Low risk	This was demonstrated (clinical and demographic).

Henneicke-v. Z. 1993

Methods	**DESIGN** Within-patient (placebo) Between-patient (active) Participant delivery **ALLOCATION** Random Method of randomisation: not reported Concealment: unclear **BLINDING** Double-blind (participant/investigator) **WITHDRAWAL/DROPOUT** Described
Participants	N: 73 Treatment duration: 8 wks; FU: 8 wks

Henneicke-v. Z. 1993 *(Continued)*

	LF: 21 (28.8%) BC: yes Age: 40.5 (median); range = 18 to 71 (N = 52) Gender (per cent men): 65.8% (N = 73) Severity: TSS (0 to 12) = 7.4 **INCLUSION CRITERIA** • Aged 18 to 71 • Moderate plaque psoriasis • 9 >TSS ≥ 4 **EXCLUSION CRITERIA** • Systemic antipsoriatic drugs within previous 4 wks • UV therapy within previous wk • Drug-induced psoriasis • Cancer • Pregnancy • Lactation • Severe organ dysfunction • Metabolic disorders • Abuse of drugs or alcohol
Interventions	• Omega-3-polyunsaturated fatty acids ointment 1% BD (O3(1)) • Placebo (vehicle) 1% BD • Omega-3-polyunsaturated fatty acids ointment 10% BD (O3(10)) • Placebo (vehicle) 10% BD (P)
Outcomes	1. Local psoriasis severity index (TSS equivalent): erythema, induration, desquamation 2. Area of indicator lesion 3. Pruritis 4. Investigator's subjective intra-individual comparison (left side better than right side) 5. Patient's subjective intra-individual comparison (left side better than right side) 6. Compliance: tube weight compared with expected use
Notes	The trial did not report sponsorship.

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Unclear risk	The trial reported insufficient details.
Blinding (performance bias and detection bias) All outcomes	Low risk	The trial was double-blind (participant/investigator).
Randomisation method reported	Unclear risk	The trial did not report this.
Loss to follow up	High risk	28.8%

Henneicke-v. Z. 1993 *(Continued)*

Baseline assessments	Low risk	These were reported.
Baseline comparability demonstrated	Low risk	-

Highton 1995

Methods	**DESIGN** Between-patient Participant delivery **ALLOCATION** Random Method of randomisation: not reported Concealment: unclear **BLINDING** Double-blind (participant/investigator) **WITHDRAWAL/DROPOUT** Described
Participants	N: 277 Treatment duration: 8 wks LF: 30 (10.8%) BC: clinical severity comparable, demographics unclear Age: not reported Gender (per cent men): not reported Severity: TSS (0 to 8) = 3.90; BSA = 9.1% **INCLUSION CRITERIA** • Moderately severe stable plaque psoriasis • Plaque elevation score greater than or equal to 4 (0 to 8) • Not pregnant or nursing during the duration of the study **EXCLUSION CRITERIA** • Recent topical or systemic psoriasis treatment, prolonged exposure to sunlight, phototherapy • Photochemotherapy • Hypercalcemia • Erythrodermic or pustular psoriasis • Calcium, vitamin A or D supplements
Interventions	• Calcipotriene ointment 0.005% BD (C) • Placebo (vehicle) (P)
Outcomes	1. Severity (erythema; plaque elevation; scaling; overall disease severity) 2. 75% improvement scores 3. Investigator Global Assessment (7-pt: worse to completely clear)
Notes	Bristol Myers Squibb sponsored the trial. There was SD imputation (TSS).

Highton 1995 *(Continued)*

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Unclear risk	The trial reported insufficient details.
Blinding (performance bias and detection bias) All outcomes	Low risk	The trial was double-blind (participant/investigator).
Randomisation method reported	Unclear risk	The trial did not report this.
Loss to follow up	Low risk	10.8%
Baseline assessments	Low risk	These were partially done.
Baseline comparability demonstrated	Unclear risk	This was partially demonstrated.

Hindsén 2006 (H)

Methods	**DESIGN** Between-patient Participant delivery **ALLOCATION** Random Method of randomisation: not stated Concealment: unclear **BLINDING** Double-blind (participant/investigator) **WITHDRAWAL/DROPOUT** Not described
Participants	N: 360 Treatment duration: 2 or 6 wks; FU: 6 or 10 wks LF: NR BC: not demonstrated Age: NR Gender (per cent men): NR Severity: NR **INCLUSION CRITERIA** • People with moderately severe plaque psoriasis on elbows, knees, or both **EXCLUSION CRITERIA** • Not stated
Interventions	• Calcipotriol ointment 50 mcg/g BD (no occlusion) for 6 wks (C)

Hindsén 2006 (H) *(Continued)*

	• Calcipotriol ointment 50 mcg/g plus occlusion, once/week for 2 wks (CO) [Placebo ointment plus occlusion, once/week for 2 wks (P)]
Outcomes	1. Total Sign Score (redness, thickness, scaliness) (TSS): 0 to 24
Notes	Leo Pharma, Ballerup, sponsored the trial. It was unclear how participants were blinded to treatment options where 2/3 involved occlusion. The sponsor supplied unpublished data.

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Unclear risk	The trial reported insufficient details.
Blinding (performance bias and detection bias) All outcomes	Unclear risk	The trial was reported to be double-blind (participant/investigator), but it was unclear how they blinded participants to treatment options where 2/3 involved occlusion.
Randomisation method reported	Unclear risk	The trial did not report this.
Loss to follow up	Unclear risk	The trial did not report this.
Baseline assessments	Unclear risk	The trial did not report these.
Baseline comparability demonstrated	Unclear risk	This was not demonstrated.

Hindsén 2006 (P)

Methods	**DESIGN** Between-patient Participant delivery **ALLOCATION** Random Method of randomisation: not stated Concealment: unclear **BLINDING** Double-blind (participant/investigator) **WITHDRAWAL/DROPOUT** Not described
Participants	N: 360 Treatment duration: 2 or 6 wks; FU: 6 or 10 wks LF: NR BC: not demonstrated Age: NR Gender (per cent men): NR Severity: NR **INCLUSION CRITERIA** • People with moderately severe plaque psoriasis on elbows, knees, or both

Hindsén 2006 (P) *(Continued)*

	EXCLUSION CRITERIA • Not stated
Interventions	• Calcipotriol ointment 50 mcg/g, BD (no occlusion) for 6 wks (C) • Calcipotriol ointment 50 mcg/g plus occlusion, once/week for 2 wks (CO) • Placebo ointment plus occlusion, once/week for 2 wks (P)
Outcomes	1. Total Sign Score (redness, thickness, scaliness) (TSS): 0 to 24
Notes	Leo Pharma, Ballerup, sponsored the trial. It was unclear how participants were blinded to treatment options where 2/3 involved occlusion. The sponsor supplied unpublished data.

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Unclear risk	The trial reported insufficient details.
Blinding (performance bias and detection bias) All outcomes	Unclear risk	The trial was reported to be double-blind (participant/investigator), but it was unclear how they blinded participants to treatment options where 2/3 involved occlusion.
Randomisation method reported	Unclear risk	The trial did not report this.
Loss to follow up	Unclear risk	The trial did not report this.
Baseline assessments	Unclear risk	The trial did not report these.
Baseline comparability demonstrated	Unclear risk	This was not demonstrated.

Holick 2003

Methods	**DESIGN** Within-patient Participant delivery **ALLOCATION** Random Method of randomisation: not reported Concealment: unclear **BLINDING** Double-blind (participant/investigator) **WITHDRAWAL/DROPOUT** Described
Participants	N: 15 Treatment duration: 8 wks; FU: 8 wks LF: 0 (0%) BC: not reported

Holick 2003 *(Continued)*

	Age: 56 (range = 25 to 74) Gender (per cent men): 67 % Severity: not reported **INCLUSION CRITERIA** • Chronic plaque psoriasis • 2 symmetrically comparable plaques • Failure to respond to at least 1 standard treatment **EXCLUSION CRITERIA** • Kidney disease, hypercalcaemia, hypercalciuria • Systemic therapy within previous 30 days • Topical therapy within previous 14 days • Concomitant medications that interfere with calcium metabolism
Interventions	• Parathyroid hormone (PTH) (1 to 34) 20 mcg/g in Novasome A® liposomal cream BD (PTH) • Novasome A® liposomal cream BD (P)
Outcomes	1. Global severity score (0 to 24) 2. PASI (for open trial phase only)
Notes	The National Institutes for Health (Department of Health and Human Services) and the Department of Defense Small Business Innovation Research (SBIR) Program sponsored the trial through grants. The trial also reported a uncontrolled open, large area, study for N = 10 (PTH applied OD for up to 11 months).

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Unclear risk	The trial reported insufficient details.
Blinding (performance bias and detection bias) All outcomes	Low risk	The trial was double-blind (participant/investigator).
Randomisation method reported	Unclear risk	The trial did not report this.
Loss to follow up	Low risk	0.0%
Baseline assessments	Low risk	These were partially done.
Baseline comparability demonstrated	Unclear risk	The trial did not report this.

Huang 2009

Methods	**DESIGN** Between-patient Participant delivery **ALLOCATION**

Huang 2009 *(Continued)*

	Random Method of randomisation: unclear Concealment: unclear **BLINDING** Double-blind (participant/investigator) **WITHDRAWAL/DROPOUT** Described
Participants	N: 320 Treatment duration: 4 wks; FU: 4 wks LF: 0 (0%) BC: stated no significant difference in clinical or demographic characteristics (data not shown) Age: NR Gender (per cent men): NR Severity: NR **INCLUSION CRITERIA** • Chinese people aged 18 to 65 with stable plaque psoriasis • At least 1 area (or arm, leg, body) with mPASI score > = 2 (i.e. % BSA > = 10% of affected area) **EXCLUSION CRITERIA** • Psoriasis of the face • Severe disease requiring steroids or other systemic medication • % BSA > = 30% • Use of systemics during previous 4 weeks, topicals during previous 2 weeks • Participation in another trial during previous 3 months • Iodine deficiency, hypercalcaemia, Cushing's Syndrome, diabetes, or other metabolic disease • Heart disease, kidney disease, liver disease • Immunesuppression • Cancer • Mental disorder • Failure to consent • Pregnancy or risk thereof • Lactation • Investigator opinion of unsuitability
Interventions	• Calcipotriol ointment BD (C) • Calcipotriol betamethasone ointment ON, placebo OM (C-B) Participant gave written consent to use < = 100 g/wk.
Outcomes	1. mPASI (0 to 64.8) 2. Treatment success: PASI75 3. TSS (redness, thickness, scaliness) (0 to 12) 4. DLQI 5. Adverse events 6. Laboratory tests: urine, blood, biochemistry, liver function, electrolytes, serum calcium 7. Atrophy, telangiectasias
Notes	The trial did not report sponsorship.

Huang 2009 *(Continued)*

We received translation support from native speaker.

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Unclear risk	The trial reported insufficient details.
Blinding (performance bias and detection bias) All outcomes	Low risk	The trial was double-blind (participant/investigator).
Randomisation method reported	Unclear risk	The trial did not report this.
Loss to follow up	Low risk	0%
Baseline assessments	Unclear risk	The trial authors state these were undertaken.
Baseline comparability demonstrated	Unclear risk	The trial authors state that groups were comparable at baseline (not demonstrated).

Hutchinson 2000

Methods	**DESIGN** Between-patient Participant delivery **ALLOCATION** Random Method of randomisation: not reported Concealment: unclear **BLINDING** Open **WITHDRAWAL/DROPOUT** Described
Participants	N: 114 Treatment duration: 8 wks; FU: 8 wks LF: 28 (24.6%) BC: yes Age: 42.3 Gender (per cent men): 74.4% Severity: PASI (mean) = 11.8 Duration of psoriasis (mths) (mean): 185.1 (range = 1 to 85) **INCLUSION CRITERIA** • Chronic plaque psoriasis of at least moderate severity • Aged over 18 • White or Asian origin

Hutchinson 2000 *(Continued)*

	EXCLUSION CRITERIA • Systemic or intralesional therapy or photo-chemotherapy within previous 2 mths • Topical antipsoriatics within previous wk or concomitant • Other medications that could affect psoriasis • Pregnancy • Inadequate contraception
Interventions	• Calcitriol ointment 3 mcg/g BD (C) • Short contact dithranol 0.25 to 2% OD (D)
Outcomes	1. PASI 2. IAGI (6-pt: worse to clearing) 3. Overall global severity (5-pt: none to very severe) 4. Psoriasis Disability Index (quality of life) (scale NR) 5. Cosmetic acceptability (1 = good/none to 3 = not acceptable): staining, irritation 6. Adverse events
Notes	The trial did not report sponsorship.

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Unclear risk	The trial reported insufficient details.
Blinding (performance bias and detection bias) All outcomes	High risk	The trial was open.
Randomisation method reported	Unclear risk	The trial did not report this.
Loss to follow up	Unclear risk	24.6%
Baseline assessments	Low risk	These were reported.
Baseline comparability demonstrated	Low risk	This was demonstrated.

Jarratt 2004

Methods	**DESIGN** Between-patient Participant delivery **ALLOCATION** Random Method of randomisation: computer-generated list Concealment: unclear **BLINDING** Double-blind (participant/investigator) **WITHDRAWAL/DROPOUT** Unclear

Jarratt 2004 *(Continued)*

Participants	N: 142 Treatment duration: 4 wks; FU: 6 wks LF: 1 (0.7%) BC: yes Age: 45.1 (15.37SD) Gender (per cent men): 42.3% Severity: TSS (0 to 9) = 6.6; GSS (6-pt (rescaled: 0 = very severe to 5 = clear) = 1.65 (0.61SD), N = 142 **INCLUSION CRITERIA** • Aged 12 or over • Moderate to severe scalp psoriasis (global severity score ≥ 3) • Compliance with wash-out periods for systemic therapies (details not reported) **EXCLUSION CRITERIA** • Pregnancy or risk thereof • Known allergy to test products • Need for systemic therapy or other concomitant antipsoriatics • Excessive UV exposure
Interventions	• Clobetasol propionate shampoo 0.05% OLUX® OD (C) • Placebo shampoo OD (P) • Treatments applied OD, left to dry for 15 minutes, then washed out • Placebo represented by vehicle for clobetasol propionate
Outcomes	1. Global severity score (GSS) (6-pt: 0 = clear to 5 = very severe) 2. Total Severity Score (erythema, thickening, scaling) (TSS) (0 to 9) 3. Individual sign scores for erythema, thickening, scaling pruritis, per cent scalp involvement (4-pt: 0 = none to 3 = severe) 4. IAGI (5-pt: worse to clear) 5. PAGI (5-pt: worse to clear)
Notes	Galderma R&D Inc sponsored the trial. Missing data imputed using last observation carried forward. No cases of skin atrophy, teleangiectasia, or acne were reported. This was a scalp trial. There was SD imputation (TSS).

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Unclear risk	The trial reported insufficient details.
Blinding (performance bias and detection bias) All outcomes	Low risk	The trial was double-blind (participant/investigator).
Randomisation method reported	Low risk	-

Jarratt 2004 *(Continued)*

Loss to follow up	Low risk	0.7%
Baseline assessments	Low risk	-
Baseline comparability demonstrated	Low risk	-

Jarratt 2006

Methods	**DESIGN** Between-patient Participant delivery **ALLOCATION** Random Method of randomisation: not stated Concealment: unclear **BLINDING** Double-blind (participant/investigator) **WITHDRAWAL/DROPOUT** Described
Participants	N: 120 Treatment duration: 4 wks; FU: 8 wks LF: 0 (0%) BC: yes Age: 48.0 (12.9SD) Gender (per cent men): 60.0% Severity: % BSA = 7.69% (6.17%SD); ODS (moderate) = 90.8%; ODS (severe/very severe) = 9.2% Ethnicity (per cent white): 94.2% Duration: NR **INCLUSION CRITERIA** • People aged 18 and over with moderate to severe chronic plaque psoriasis • BSA > = 2% (excluding face, scalp, groin, axillae, and other intertriginous areas) • Overall disease severity score (0 to 4) > = 3 **EXCLUSION CRITERIA** • Non-compliance with treatment specific wash-out periods on topical and systemic treatments or phototherapy or natural UV light (periods NS) • Pregnancy or risk thereof
Interventions	• Clobetasol propionate 0.05% spray BD (CP) • Placebo spray BD (P) Then 4-week treatment-free follow-up period. There was 8 hrs between applications, and the treated area was unwashed for 4 hours after application.

Jarratt 2006 *(Continued)*

Outcomes	1. Scaling, erythema, plaque elevation, pruritus, overall disease severity (ODS) each scored on 5-pt scale (0 = clear to 4 = severe/very severe) 2. Success rate: ODS < = 2 at wk 2 and ODS < = 1 at wk 4 3. ODS at wk 1 and wk 8 4. Signs at wk 1 and wk 8 5. ODS < = 1 at wk 8 6. Adverse events (atrophy, telangiectasia, burning/stinging, folliculitis); HPA axis suppression
Notes	Galderma Pharmaceuticals sponsored the trial. The trial also reported CIC data on a safety RCT (2 or 4 wks with clobetasol propionate 0.05% spray, < = 50 g/wk): 8/36 had HPA suppression; all returned to normal within 2 wks of end of treatment (EOT). The trialist supplied unpublished data.

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Unclear risk	The trial reported insufficient details.
Blinding (performance bias and detection bias) All outcomes	Low risk	The trial was double-blind (participant/investigator).
Randomisation method reported	Unclear risk	The trial did not report this.
Loss to follow up	Low risk	0%
Baseline assessments	Low risk	The trial reported these.
Baseline comparability demonstrated	Low risk	This was demonstrated.

Jekler 1992

Methods	**DESIGN** Within-patient Participant delivery **ALLOCATION** Random Method of randomisation: not reported Concealment: unclear **BLINDING** Double-blind (participant/investigator) **WITHDRAWAL/DROPOUT** Described
Participants	N: 30 Treatment duration: 8 wks LF: 3 (10%) BC: not reported

Jekler 1992 *(Continued)*

	Age: 45.2 (14.0SD; N = 27) Gender (per cent men): 77.8%; N = 27 Severity: severity (mean score, 0 to 3) = 1.9; N = 27 Duration disease (years): 20.5 (14.8SD; N = 27) Duration exacerbation (mths): 5.1 (6.4SD; N = 27) **INCLUSION CRITERIA** • Chronic plaque-type psoriasis with bilateral lesions of equal clinical severity • Adult. **EXCLUSION CRITERIA** • Topical or systemic corticosteroids • Recent phototherapy
Interventions	• Dithranol 2% ointment 1 minute therapy OD (D) • Placebo (vehicle) (P)
Outcomes	1. Severity (pruritis; erythema; scaling; infiltration; overall result) 2. Investigator's assessment of degree of clearing 3. Patient's assessment of degree of clearing
Notes	E Merck AB sponsored the trial.

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Unclear risk	The trial reported insufficient details.
Blinding (performance bias and detection bias) All outcomes	Low risk	The trial was double-blind (participant/investigator).
Randomisation method reported	Unclear risk	The trial did not report this.
Loss to follow up	Low risk	10.0%
Baseline assessments	Low risk	-
Baseline comparability demonstrated	Unclear risk	The trial did not report this.

Jemec 2008 (H)

Methods	**DESIGN** Between-patient Participant delivery **ALLOCATION** Random Method of randomisation: pre-planned computer-generated randomisation code list (2:4:4:1)

Jemec 2008 (H) *(Continued)*

	Concealment: unclear **BLINDING** Double-blind (participant/investigator) **WITHDRAWAL/DROPOUT** Described
Participants	N: 1505 Treatment duration: 8 wks; FU: 8 wks LF: 32 (2.1%) BC: yes Age: 49.0 (15.8SD); range = 17 to 97 Gender (per cent men): 44.8% Ethnicity (per cent white): 96.3% Severity: IGA mild disease = 6.5%; IGA moderate disease = 56.2%; IGA severe disease = 31.6%; IGA very severe disease = 5.7%; TSS (0 to 12) = 6.82 (1.85SD) Duration (yrs): 16.5 (13.6SD) **INCLUSION CRITERIA** • People aged > = 18 with scalp plaque psoriasis involving > = 10% scalp • Amenable to topical treatment with < = 100 g medication/wk • Diagnosis of psoriasis vulgaris on trunk/limbs • Score at least moderate in 1 sign (erythema, thickness, scaliness) and at least slight for other signs • IGA mild to very severe **EXCLUSION CRITERIA** • PUVA or grenz ray or relevant systemic therapy within previous 4 wks • UVB or topical scalp antipsoriatic therapy or topical very potent (WHO group IV) corticosteroid on face/body within previous 2 wks • Biological therapy within previous 6 mths • Planned initiation of/changes to concomitant medication that could affect scalp psoriasis • Planned exposure to sun • Erythrodermic, exfoliative, or postural psoriasis • Viral lesions • Skin infections • Parasitic infections • Atrophic skin on scalp • Known/suspected abnormality of calcium homeostasis • Severe renal insufficiency • Severe hepatic disorder
Interventions	• Calcipotriol 50 mcg/g gel OD (C) • Betamethasone dipropionate 0.5 mg/g gel OD (B) • Combined gel: calcipotriol 50 mcg/g + betamethasone dipropionate 0.5 mg/g OD (C-B) • Placebo gel OD (P)
Outcomes	1. Total Sign Score (0 to 12) 2. Investigator's Global Assessment of Disease Severity of the scalp (IGA): 6-pt: absence of disease to very severe disease 3. Treatment success: IGA absence of disease or very mild disease

Jemec 2008 (H) *(Continued)*

4. Patient overall assessment of treatment response on a 7-pt scale (worse, unchanged, slight improvement, moderate improvement, marked improvement, almost clear, cleared)
5. Compliance (self-report)
6. Adverse events
7. Laboratory tests (serum calcium, serum albumin)

Notes	Leo Pharma A/S, Ballerup, Denmark, sponsored the trial. The sponsor supplied unpublished data.

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Unclear risk	The trial reported insufficient details.
Blinding (performance bias and detection bias) All outcomes	Low risk	The trial was double-blind (participant/investigator).
Randomisation method reported	Low risk	A preplanned computer-generated randomisation code list was used.
Loss to follow up	Low risk	2.1%
Baseline assessments	Low risk	These were reported.
Baseline comparability demonstrated	Low risk	This was demonstrated.

Jemec 2008 (P)

Methods	**DESIGN** Between-patient Participant delivery **ALLOCATION** Random Method of randomisation: pre-planned computer-generated randomisation code list (2:4:4:1) Concealment: unclear **BLINDING** Double-blind (participant/investigator) **WITHDRAWAL/DROPOUT** Described
Participants	N: 1505 Treatment duration: 8 wks; FU: 8 wks LF: 32 (2.1%) BC: yes Age: 49.0 (15.8SD); range = 17 to 97 Gender (per cent men): 44.8% Ethnicity (% white): 96.3% Severity: IGA mild disease = 6.5%; IGA moderate disease = 56.2%; IGA severe disease = 31.6%; IGA very severe disease = 5.7%; TSS (0 to 12) = 6.82 (1.85SD) Duration (yrs): 16.5 (13.6SD)

Jemec 2008 (P) *(Continued)*

INCLUSION CRITERIA

- People aged > = 18 with scalp plaque psoriasis involving > = 10% scalp
- Amenable to topical treatment with < = 100 g medication/wk
- Diagnosis of psoriasis vulgaris on trunk/limbs
- Score at least moderate in 1 sign (erythema, thickness, scaliness) and at least slight for other signs
- IGA mild to very severe

EXCLUSION CRITERIA

- PUVA or grenz ray or relevant systemic therapy within previous 4 wks
- UVB or topical scalp antipsoriatic therapy or topical very potent (WHO group IV) corticosteroid on face/body within previous 2 wks
- Biological therapy within previous 6 mths
- Planned initiation of/changes to concomitant medication that could affect scalp psoriasis
- Planned exposure to sun
- Erythrodermic, exfoliative, or postural psoriasis
- Viral lesions
- Skin infections
- Parasitic infections
- Atrophic skin on scalp
- Known/suspected abnormality of calcium homeostasis
- Severe renal insufficiency
- Severe hepatic disorder

Interventions	• Calcipotriol 50 mcg/g gel OD (C) • Betamethasone dipropionate 0.5 mg/g gel OD (B) • Combined gel: calcipotriol 50 mcg/g + betamethasone dipropionate 0.5 mg/g OD (C-B) • Placebo gel OD (P)
Outcomes	1. Total Sign Score (0 to 12) 2. Investigator's Global Assessment of Disease Severity of the scalp (IGA): 6-pt: absence of disease to very severe disease 3. Treatment success: IGA absence of disease or very mild disease 4. Patient overall assessment of treatment response on a 7-pt scale (worse, unchanged, slight improvement, moderate improvement, marked improvement, almost clear, cleared) 5. Compliance (self-report) 6. Adverse events 7. Laboratory tests (serum calcium, serum albumin)
Notes	Leo Pharma A/S, Ballerup, Denmark, sponsored the trial. The sponsor supplied unpublished data.

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Unclear risk	The trial reported insufficient details.
Blinding (performance bias and detection bias) All outcomes	Low risk	The trial was double-blind (participant/investigator).

Jemec 2008 (P) *(Continued)*

Randomisation method reported	Low risk	A preplanned computer-generated randomisation code list was used.
Loss to follow up	Low risk	2.1%
Baseline assessments	Low risk	These were reported.
Baseline comparability demonstrated	Low risk	This was demonstrated.

Ji 2008

Methods	**DESIGN** Between-patient Participant delivery **ALLOCATION** Random Method of randomisation: not stated Concealment: unclear **BLINDING** Single-blind (investigator) **WITHDRAWAL/DROPOUT** Described
Participants	N: 250 Treatment duration: 12 wks; FU: 12 wks LF: 7 (2.8%) BC: yes Age: 41.7 (12.2SD) Gender (per cent men): 65.6% Ethnicity (per cent Asian): 100% Severity: per cent BSA = 18%, range = 1% to 35%; DSS (0 to 12) = 8.12 (1.97SD), range = 3 to 12 **INCLUSION CRITERIA** • People aged 18 to 65 with stable mild to moderate plaque psoriasis • BSA < = 35% • Diameter of target lesions > = 3 cm **EXCLUSION CRITERIA** • Pregnancy or risk thereof • Acute guttate psoriasis • Erythrodermic, pustular, arthropathic psoriasis • Hypercalcaemia • Renal dysfunction • Calcium nephrolithiasis • Use of topical antipsoriatic therapy within previous 2 wks • Use of systemic antipsoriatic therapy within previous 8 wks
Interventions	• Calcipotriol 50 mcg/g ointment BD (C1) • Calcitriol 3 mcg/g BD (C2) Usage restrictions: • < = 210 g/wk calcitriol

Ji 2008 *(Continued)*

- < = 100 g/wk calcipotriol

Outcomes	1. Investigator's Assessment of Global Improvement (IAGI; 4-pt: 0 = worse/no change to 3 = clear/almost clear) 2. Subject's Assessment of Global Improvement (PAGI) (4-pt: 0 = worse/no change to 3 = clear/almost clear) 3. Dermatological Sum Score (DSS): erythema, plaque elevation, scaling: 0 to 12 4. Local: cutaneous safety (investigator): 5-pt: 0 (none) to 4 (very severe); cutaneous discomfort (subject): 5-pt: 0 (none) to 4 (very severe) 5. Adverse events 6. Systemic: routine blood and urine safety parameters, albumin-adjusted serum total calcium 7. Compliance (medication usage)
Notes	Galderma Laboratories LP sponsored the trial. The trial was set in China. We received translation support for data extraction.

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Unclear risk	The trial reported insufficient details.
Blinding (performance bias and detection bias) All outcomes	High risk	The study was single-blind (investigator).
Randomisation method reported	Unclear risk	The trial did not report this.
Loss to follow up	Low risk	2.8%
Baseline assessments	Low risk	These were reported.
Baseline comparability demonstrated	Low risk	This was demonstrated.

Jin 2001

Methods	**DESIGN** Between-patient Participant delivery **ALLOCATION** Random Method of randomisation: Not stated Concealment: unclear **BLINDING** Double-blind (participant/investigator) **WITHDRAWAL/DROPOUT** Described
Participants	N: 96

Jin 2001 *(Continued)*

	Treatment duration: 6 wks; FU: 6 wks LF: 7 (7.3%) BC: yes Age: 35.8 (range = 18 to 65) Gender (per cent men): 57.3% Severity: TSS (0 to 20) = 9.4 **INCLUSION CRITERIA** • Chronic plaque psoriasis • Aged over 18? (cannot translate) **EXCLUSION CRITERIA** • (cannot translate)
Interventions	• Anti-IL-8 monoclonal antibody cream (M) • Placebo (P)
Outcomes	1. Efficacy rate 2. Cure rate 3. Erythema, infiltration, scaling, pruritis 4. TSS (skin damage, erythema, infiltration, thickness, scaling) 5. IAGI (4-pt: failure to cure)
Notes	Biological Technical Medical Trade Limited sponsored the trial. We received translation support for data extraction.

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Unclear risk	The trial reported insufficient details.
Blinding (performance bias and detection bias) All outcomes	Low risk	The trial was double-blind (participant/investigator).
Randomisation method reported	Unclear risk	The trial did not report this.
Loss to follow up	Low risk	7.3%
Baseline assessments	Low risk	These were reported.
Baseline comparability demonstrated	Low risk	-

Jorizzo 1997

Methods	**DESIGN**

Jorizzo 1997 *(Continued)*

	Between-patient Participant delivery **ALLOCATION** Random Method of randomisation: not reported Concealment: unclear **BLINDING** Double-blind (participant/investigator) **WITHDRAWAL/DROPOUT** Described
Participants	N: 89 Treatment duration: 4 wks; FU: 6 wks LF: Unclear BC: yes Age: 49.7 (range = 21 to 84) Gender (per cent men): 65% Severity: per cent BSA affected = 8.1% Duration of psoriasis (range, years): 1 to 57 Duration of exacerbation (range, wks): 3 to 2080 **INCLUSION CRITERIA** • Moderate to severe plaque type psoriasis • Non-hospitalised men or non-pregnant; non-lactating women ≥ 12 yrs • Baseline morning serum cortisol concentration of 5 to 18 mcg/100 mL **EXCLUSION CRITERIA** • Recent topical antipsoriatic medication or other drug that could alter psoriatic status
Interventions	• Clobetasol propionate emollient 0.05% BD (C) • Placebo (vehicle) (P)
Outcomes	1. Severity (erythema; skin thickening; scaling; pruritis) 2. Total Severity Score (0 to 12) 3. Investigator Global Assessment of improvement (6-pt: worse to cleared) 4. Patient Global Assessment of improvement (5-pt: worse to excellent)
Notes	Glaxo Wellcome Inc. sponsored the trial. There was SD imputation (TSS).

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Unclear risk	The trial reported insufficient details.
Blinding (performance bias and detection bias) All outcomes	Low risk	The trial was double-blind (participant/investigator).

Jorizzo 1997 *(Continued)*

Randomisation method reported	Unclear risk	The trial did not report this.
Loss to follow up	Unclear risk	The trial did not report this.
Baseline assessments	Low risk	These were reported.
Baseline comparability demonstrated	Low risk	-

Jorizzo 2007

Methods	**DESIGN** Between-patient Participant delivery **ALLOCATION** Random Method of randomisation: not stated Concealment: unclear **BLINDING** Double-blind (participant/investigator) **WITHDRAWAL/DROPOUT** Not described
Participants	N: 379 Treatment duration: 6 wks; FU: 6 wks LF: NR BC: yes (only clinical comparability demonstrated) Age: NR Gender (per cent men): NR Severity: PASI = 7.9 (5.3SD); IGA moderate = 76.2%; IGA severe = 22.2% **INCLUSION CRITERIA** • People with moderate to severe plaque psoriasis **EXCLUSION CRITERIA** • Not stated
Interventions	• Calcipotriene 0.005% ointment (C) • Calcipotriene 0.005% plus betamethasone dipropionate 0.064% ointment (C-B) < = 100 g/wk - the daily dose was not specified.
Outcomes	1. PASI 2. Investigator Global Assessment (IGA) 3. Controlled disease (IGA: absence. very mild disease) 4. Patient Global Assessment of Improvement (PAGI) 5. Treatment success (PAGI marked improvement/cleared)
Notes	Warner-Chilcott sponsored the trial.

Jorizzo 2007 *(Continued)*

This was a conference abstract only.

We sought data but received no response.

There was SD imputation (PASI).

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Unclear risk	The trial reported insufficient details.
Blinding (performance bias and detection bias) All outcomes	Low risk	The trial was double-blind (participant/investigator).
Randomisation method reported	Unclear risk	The trial did not report this.
Loss to follow up	Unclear risk	The trial did not report this.
Baseline assessments	Unclear risk	The trial only reported clinical assessments (demographic characteristics not reported).
Baseline comparability demonstrated	Unclear risk	This was partially demonstrated (demographic characteristics not assessed).

Kang 1998

Methods	**DESIGN** Between-patient Participant delivery **ALLOCATION** Random Method of randomisation: identical tubes with computer-generated codes Concealment: adequate **BLINDING** Double-blind (participant/investigator) **WITHDRAWAL/DROPOUT** Described
Participants	N: 30 Treatment duration: 6 wks LF: 0 (0%) BC: psoriasis comparable, demographics unclear Age: 41 (range = 18 to 66) Gender (per cent men): 66.7% Severity: TSS (0 to 24) = 12.27 **INCLUSION CRITERIA** • Mild to moderate stable plaque-type psoriasis

Kang 1998 *(Continued)*

	• Adult **EXCLUSION CRITERIA** • Recent systemic therapy, UV, or topical therapy for psoriasis (excluding emollient) • Pregnant or breast-feeding women
Interventions	• Calcipotriene ointment 0.005% BD (C) • Placebo (vehicle) (P)
Outcomes	1. Signs (erythema; thickness; scaling) 2. TSS (0 to 24) 3. Investigator Global Assessment (7-pt: worse to clear)
Notes	Bristol-Myers Squibb Corporation and from Babcock Dermatologic Endowment (University of Michigan) sponsored the trial through grants.

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Low risk	Participants were assigned by computer-generated code.
Blinding (performance bias and detection bias) All outcomes	Low risk	The trial was double-blind (participant/investigator).
Randomisation method reported	Low risk	Randomisation was computer-generated.
Loss to follow up	Low risk	0.0%
Baseline assessments	Low risk	-
Baseline comparability demonstrated	Unclear risk	This was partially demonstrated.

Kanzler 1993

Methods	**DESIGN** Within-patient Participant delivery **ALLOCATION** Random Method of randomisation: identical containers labelled right and left; labelling method not reported Concealment: unclear **BLINDING** Double-blind (participant/investigator) **WITHDRAWAL/DROPOUT** Not described
Participants	N: 18 Treatment duration: 4 wks; FU: 4 wks LF: 0 (0%)

Kanzler 1993 *(Continued)*

	BC: not reported Age: 45.4 (range = 21 to 66) Gender (per cent men): 55.6% Severity: not reported **INCLUSION CRITERIA** • Bilaterally similar chronic stable plaque psoriasis **EXCLUSION CRITERIA** • Recent topical or systemic therapy
Interventions	• Tar (liquor carbonis detergens) 5% BD (T) • Placebo (vehicle) (P)
Outcomes	1. Severity (erythema; induration; scaling; pruritis) 2. Total Severity Score (0 to 12) 3. Investigator Global Assessment: per cent improvement from baseline, based on TSS
Notes	The trial did not report sponsorship. Compliance was assessed by unused medication returned at each visit. The compliance rate for participants in each group was > 90%. This was a scalp trial.

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Unclear risk	The trial reported insufficient details.
Blinding (performance bias and detection bias) All outcomes	Low risk	The trial was double-blind (participant/investigator).
Randomisation method reported	Unclear risk	The trial did not report this.
Loss to follow up	Low risk	0.0%
Baseline assessments	Low risk	These were partially done.
Baseline comparability demonstrated	Unclear risk	The trial did not report this.

Katz 1987a

Methods	**DESIGN** Between-patient Participant delivery **ALLOCATION** Random Method of randomisation: not reported

Katz 1987a *(Continued)*

	Concealment: unclear **BLINDING** Double-blind (participant/investigator) **WITHDRAWAL/DROPOUT** Described
Participants	N: 40 Treatment duration: 12 wks; FU: 12 wks LF: 2 (5%) BC: yes Age: 46.7 Gender (per cent men): 60% Severity: per cent participants with BSA affected < 10% = 68% Duration (years): 20.8 **INCLUSION CRITERIA** • Plaques psoriasis in remission (> 85% resolution) after 2 to 3 weeks treatment with Betamethasone dipropionate Note: 38/59 (64%) achieved remission during the acute phase **EXCLUSION CRITERIA** • Not achieving remission during acute phase treatment
Interventions	• Betamethasone dipropionate, intermittent maintenance (3 doses at 12-hour intervals each weekend) (B) • Placebo (vehicle) (P)
Outcomes	1. Signs (erythema; induration; scaling) 2. Area adjusted clinical score 3. Relapse (adjusted clinical score > 35% of baseline score)
Notes	The trial was supported in part by a grant from Schering Plough Corporation. There was SD imputation (TSS).

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Unclear risk	The trial reported insufficient details.
Blinding (performance bias and detection bias) All outcomes	Low risk	The trial was double-blind (participant/investigator).
Randomisation method reported	Unclear risk	The trial did not report this.
Loss to follow up	Low risk	5.0%
Baseline assessments	Low risk	-

Katz 1987a *(Continued)*

Baseline comparability demonstrated	Low risk	-

Katz 1991a

Methods	**DESIGN** Between-patient Participant delivery **ALLOCATION** Random Method of randomisation: computer-generated code Concealment unclear **BLINDING** Double-blind (participant/investigator) **WITHDRAWAL/DROPOUT** Described
Participants	N: 94 Treatment duration: 24 wks; FU: 24 wks LF: 4 (4.3%) BC: yes Age: 46.0 (range = 21 to 86) Gender (per cent men): 67.8% Severity: overall score not reported **INCLUSION CRITERIA** • Plaques psoriasis in remission after 3 to 4 weeks treatment with Betamethasone dipropionate (erythema score = 1; induration = 0.5; scaling = 0) Note: 94/123 (76%) achieved remission during acute phase **EXCLUSION CRITERIA** • Recent topical or systemic treatment • Pregnant • Nursing • Intent to conceive • Not achieving remission during acute phase treatment
Interventions	• Betamethasone dipropionate, intermittent maintenance (3 doses at 12-hour intervals once a week) (B) • Placebo (vehicle) (P)
Outcomes	1. Signs (erythema; induration; scaling) 2. TSS (0 to 9) 3. Area adjusted clinical score 4. Treatment failure (adjusted clinical score ≥ 2.5, or overall disease status moderate or severe) 5. Overall disease status 6. Patient evaluation of effectiveness. 7. Time to relapse

Katz 1991a *(Continued)*

Notes	The trial did not report sponsorship, but the Schering Corporation employed the corresponding author.

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Unclear risk	The trial reported insufficient details.
Blinding (performance bias and detection bias) All outcomes	Low risk	The trial was double-blind (participant/investigator).
Randomisation method reported	Low risk	Randomisation was computer-generated.
Loss to follow up	Low risk	4.3%
Baseline assessments	Low risk	These were reported.
Baseline comparability demonstrated	Low risk	-

Katz 1991b

Methods	**DESIGN** Within-patient Participant delivery **ALLOCATION** Random Method of randomisation: identical tubes labelled by computer-generated code Concealment: unclear **BLINDING** Double-blind (participant/investigator) **WITHDRAWAL/DROPOUT** Described
Participants	N: 110 Treatment duration: 2 wks LF: 2 (1.8%) BC: inadequately reported Age: 51.7 (range = 19 to 84) Gender (per cent men): 80.6% Severity: Total Severity Score (0 to 12) (median) = 8 Duration of disease (years): 21 (range 1 to 57) Duration of exacerbation (years): 15.4 (range < 1 to 57) **INCLUSION CRITERIA** • Comparable bilateral lesions of moderate or greater severity of plaque psoriasis

Katz 1991b *(Continued)*

	• Adult • At least 2 signs or symptoms of at least moderate severity • Lesions ≥10 cm^2 **EXCLUSION CRITERIA** • Pustular or erythodermic psoriasis • Recent topical or systemic medication • Women at risk of pregnancy
Interventions	• Halobetasol propionate cream 0.05% BD (H) • Placebo (vehicle) (P)
Outcomes	1. Severity (0 to 3) (erythema; plaque elevation; scaling pruritis) 2. Total Severity Score (0 to 12) 3. Patient Global Assessments of effectiveness and overall rating (5-pt: poor to excellent)
Notes	The trial was supported by an educational grant from Westwood-Squibb Pharmaceuticals, a Bristol-Myers Squibb company.

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Unclear risk	The trial reported insufficient details.
Blinding (performance bias and detection bias) All outcomes	Low risk	The trial was double-blind (participant/investigator).
Randomisation method reported	Low risk	Randomisation was computer-generated.
Loss to follow up	Low risk	1.8%
Baseline assessments	Low risk	-
Baseline comparability demonstrated	Unclear risk	The trial did not report this.

Kaufmann 2002 (H)

Methods	**DESIGN** Between-patient Participant delivery **ALLOCATION** Random Method of randomisation: computer-generated randomisation schedule Concealment: unclear **BLINDING** Double-blind (participant/assessor) **WITHDRAWAL/DROPOUT** Described
Participants	N: 1603

Kaufmann 2002 (H) *(Continued)*

Treatment duration: 4 wks; FU: 4 wks

LF: 0 (0%)

BC: yes

Age: 48.4 (range = 17 to 90)

Gender (per cent men): 60.5%

Severity: PASI mean = 10.0 (range = 1.2 to 49.5)

Duration: 19.2 (range = 0 to 75)

INCLUSION CRITERIA

- People aged 18 and over with chronic plaque psoriasis
- BSA at least 10%

EXCLUSION CRITERIA

- Unstable psoriasis in treatment areas
- Other skin diseases that could confound treatment assessments
- Concomitant antipsoriatic therapy
- Hypercalcaemia
- Application of study corticosteroid to untargeted lesion
- Pregnancy
- Lactation

Interventions	• Calcipotriol 50 mcg/g + betamethasone dipropionate 0.5 mg/g combination ointment OD (D) • Calcipotriol 50 mcg/g, in combination vehicle ointment OD (C) • Betamethasone dipropionate 0.5 mg/g, in combination vehicle ointment OD (B) • Placebo (combination vehicle) ointment OD (P)
Outcomes	1. PASI, modified (change score) 2. Investigator's Global Assessment of Disease Severity (6-pt: disease absent to very severe) 3. Patient's global assessment of disease severity (6-pt: worse to cleared)
Notes	Leo Pharmaceuticals sponsored the trial. Compliance rates were reported for each regimen.

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Unclear risk	The trial reported insufficient details.
Blinding (performance bias and detection bias) All outcomes	Low risk	The trial was double-blind (participant/assessor).
Randomisation method reported	Low risk	Randomisation was computer-generated.
Loss to follow up	Low risk	0.0%
Baseline assessments	Low risk	These were reported.

Kaufmann 2002 (H) *(Continued)*

Baseline comparability demonstrated	Low risk	-

Kaufmann 2002 (P)

Methods	**DESIGN** Between-patient Participant delivery **ALLOCATION** Random Method of randomisation: computer-generated randomisation schedule Concealment: unclear **BLINDING** Double-blind (participant/assessor) **WITHDRAWAL/DROPOUT** Described
Participants	N: 1603 Treatment duration: 4 wks; FU: 4 wks LF: 0 (0%) BC: yes Age: 48.4 (range = 17 to 90) Gender (per cent men): 60.5% Severity: PASI mean = 10.0 (range = 1.2 to 49.5) Duration: 19.2 (range = 0 to 75) **INCLUSION CRITERIA** • People aged 18 and over with chronic plaque psoriasis • BSA at least 10% **EXCLUSION CRITERIA** • Unstable psoriasis in treatment areas • Other skin diseases that could confound treatment assessments • Concomitant antipsoriatic therapy • Hypercalcaemia • Application of study corticosteroid to untargeted lesion • Pregnancy • Lactation
Interventions	• Calcipotriol 50 mcg/g + betamethasone dipropionate 0.5 mg/g combination ointment, OD (D) • Calcipotriol 50 mcg/g, in combination vehicle ointment OD (C) • Betamethasone dipropionate 0.5 mg/g, in combination vehicle ointment OD (B) • Placebo (combination vehicle) ointment OD (P)
Outcomes	1. PASI, modified (change score) 2. Investigator's Global Assessment of Disease Severity (6-pt: disease absent to very severe) 3. Patient's global assessment of disease severity (6-pt: worse to cleared)
Notes	Leo Pharmaceuticals sponsored the trial. Compliance were rates reported for each regimen.
Risk of bias	

Kaufmann 2002 (P) *(Continued)*

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Unclear risk	The trial reported insufficient details.
Blinding (performance bias and detection bias) All outcomes	Low risk	The trial was double-blind (participant/assessor).
Randomisation method reported	Low risk	Randomisation was computer-generated.
Loss to follow up	Low risk	0.0%
Baseline assessments	Low risk	These were reported.
Baseline comparability demonstrated	Low risk	-

Kim 1994

Methods	**DESIGN** Within-patient Participant delivery **ALLOCATION** Random Method of randomisation: unclear Concealment: unclear **BLINDING** Double-blind (unclear who was blinded) **WITHDRAWAL/DROPOUT** Not described
Participants	N: 10 Treatment duration: 8 wks; FU: 8 wks LF: 0 (0%) BC: yes Age: 32.1 (range 20 to 52) Gender (per cent men): 60% Severity: PASI = 10.49 (1.60SD) Duration: 6.7 years (range 0.2 to 15) **INCLUSION CRITERIA** • Psoriasis **EXCLUSION CRITERIA** • Not identifiable
Interventions	• Calcipotriol ointment 50 mcg/g BD (C)

Kim 1994 *(Continued)*

	• Desoxymethasone ointment 2.5 mg/g BD (D)
Outcomes	1. PASI 2. Erythema, infiltration, desquamation (0 to 9)
Notes	The trial did not report sponsorship.

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Unclear risk	The trial reported insufficient details.
Blinding (performance bias and detection bias) All outcomes	Low risk	The trial was double-blind (unclear who was blinded).
Randomisation method reported	Unclear risk	The trial did not report this.
Loss to follow up	Low risk	0.0%
Baseline assessments	Low risk	These were reported.
Baseline comparability demonstrated	Low risk	-

Kiss 1996

Methods	**DESIGN** Between-patient Participant delivery **ALLOCATION** Random Method of randomisation: not reported Concealment: unclear **BLINDING** Double-blind (participant/investigator) **WITHDRAWAL/DROPOUT** Described
Participants	N: 239 Treatment duration: 8 wks LF: 29 (12.1%) BC: not reported Age: not reported Gender (per cent men): not reported Severity: not reported **INCLUSION CRITERIA**

Kiss 1996 *(Continued)*

- Moderate scalp psoriasis
- Adult
- Overall disease severity ≥ 4

EXCLUSION CRITERIA

- None reported

Interventions	• Calcipotriene solution 0.0025% and 0.005% BD (C) • Placebo (vehicle) (P)
Outcomes	1. Severity (scaling; erythema; plaque elevation; pruritis) 2. Overall severity (9-pt: none to very severe) 3. Investigator Global Assessment (4-pt: worsened to cleared)
Notes	Bristol Myers Squibb Pharmaceuticals sponsored the trial. Carder 1996 reports finding for subgroup (N = 29). This was a scalp trial.

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Unclear risk	The trial reported insufficient details.
Blinding (performance bias and detection bias) All outcomes	Low risk	The trial was double-blind (participant/investigator).
Randomisation method reported	Unclear risk	The trial did not report this.
Loss to follow up	Low risk	12.1%
Baseline assessments	Unclear risk	The trial did not report these.
Baseline comparability demonstrated	Unclear risk	The trial did not report this.

Klaber 1994

Methods	**DESIGN** Between-patient Participant delivery **ALLOCATION** Random Method of randomisation: Concealment: unclear **BLINDING** Double-blind (participant/assessor) **WITHDRAWAL/DROPOUT** Described
Participants	N: 474

Klaber 1994 *(Continued)*

Treatment duration: 4 wks

LF: assessment = 6 (1.3%)

TSS: 29 (6.1%)

BC: yes

Age: 44.1 (range = 18 to 90)

Gender (per cent men): 51.5%

Severity: TSS (0 to 12) = 6.5 (range = 2 to 12)

Duration of scalp psoriasis (yrs): 13.1 (range = 0.1 to 67.0)

INCLUSION CRITERIA

- Adults
- Stable, mild-to-moderate scalp psoriasis
- History of psoriasis on body

EXCLUSION CRITERIA

- More extensive, severe, or infected psoriasis
- Recent systemic antipsoriatic treatment or UV
- Concurrent vitamin D, calcium, or other relevant medication
- Significant hepatic or renal disease
- Hypercalcaemia
- Risk of pregnancy
- Pregnancy
- Lactation

Interventions	• Calcipotriol solution 50 mcg/ml BD (C) • Betamethasone 17-valerate solution 1 mg/ml BD (B)
Outcomes	1. Investigator Global Assessment (5-pt: worse to cleared) 2. Patient Global Assessment (5-pt: worse to cleared) 3. Total Sign Score (erythema, thickness, scaliness) (0 to 12) 4. Assessment of extent of scalp psoriasis 5. Assessment of acceptability
Notes	Leo Pharmaceutical Products sponsored the trial. This was a scalp trial.

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Unclear risk	The trial reported insufficient details.
Blinding (performance bias and detection bias) All outcomes	Low risk	The trial was double-blind (participant/assessor).
Randomisation method reported	Unclear risk	The trial did not report this.

Klaber 1994 *(Continued)*

Loss to follow up	Low risk	1.3%
Baseline assessments	Low risk	reported
Baseline comparability demonstrated	Low risk	-

Klaber 2000b

Methods	**DESIGN** Between-patient Participant delivery **ALLOCATION** Random Method of randomisation: not reported Concealment: unclear **BLINDING** Open **WITHDRAWAL/DROPOUT** Described
Participants	N: 475 Treatment duration: 8 wks; FU: 24 wks (N = 166) LF: 52 (10.9%) BC: yes Age: 45.3 Gender (per cent men): 52.0% Severity: Total Severity Score (0 to 12) = 5.1 **INCLUSION CRITERIA** • Mild or moderate scalp psoriasis **EXCLUSION CRITERIA** • Other forms of psoriasis • Topical antipsoriatic treatment within previous 2 wks • Systemic antipsoriatic treatment or UV therapy within previous 4 wks • Concomitant vitamins, calcium, or other medications that could affect the course of psoriasis • Known hypersensitivity to study medications • Pregnancy • Inadequate contraception • Lactation • Hypercalaemia • Significant renal or hepatic disease
Interventions	• Calcipotriol solution 50 mcg/g (Dovonex®) BD (C) • Coal tar 1%, coconut oil 1%, salicylic acid 0.5%, shampoo (Capasal ®) OD (T)
Outcomes	1. IAGI (6-pt: worse to cleared) 2. TSS (0 to 12)

Klaber 2000b *(Continued)*

	3. Patients global assessment of disease severity (VAS)
Notes	Leo Pharmaceuticals sponsored the trial. All participants who achieved at least a slight improvement in scalp psoriasis then received 16 weeks of treatment with calcipotriol BD. This was a scalp trial.

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Unclear risk	The trial reported insufficient details.
Blinding (performance bias and detection bias) All outcomes	High risk	The trial was open.
Randomisation method reported	Unclear risk	The trial did not report this.
Loss to follow up	Low risk	10.9%
Baseline assessments	Low risk	These were reported.
Baseline comparability demonstrated	Low risk	-

Koo 2006

Methods	**DESIGN** Between-patient Participant delivery **ALLOCATION** Random Method of randomisation: not stated (1:1:2) Concealment: unclear **BLINDING** Double-blind (participant/investigator) **WITHDRAWAL/DROPOUT** Described
Participants	N: 86 Treatment duration: 2 wks; FU: 2 wks LF: 0 (0%) BC: not demonstrated Age: NR Gender (per cent men): NR Severity: NR **INCLUSION CRITERIA** • People aged > = 18 with plaque psoriasis

Koo 2006 *(Continued)*

	• Good general health • Target lesions on trunk and extremities with severity score > = 2 for each sign (erythema, induration, scaling; 0 to 4) **EXCLUSION CRITERIA** • Pregnancy or risk thereof • Lactation • Use of investigational drug within previous 30 dys • Systemic or phototherapy within previous 30 dys • Use of topical or intralesional therapies (other than emollients) within previous 2 wks • Guttate, erythrodermic, pustular psoriasis • BSA > 20% (excluding face/scalp) • Known hypersensitivity to study medications • Concomitant topical/systemic medication that might affect target lesions Concomitant phototherapy
Interventions	Part 1 • Calcipotriene 0.005% ointment BD (C) • Clobetasol propionate foam 0.05% BD (CP) • Calcipotriene 0.005% ointment plus clobetasol propionate foam 0.05% BD (CC) Part 2 • Follow-up maintenance study based on responders from combination group (CC)
Outcomes	1. Total Severity Score, based on Psoriasis Grading Scale (erythema, induration, scaling, each 0 to 4) (TSS; 0 to 12). Scores adjusted for baseline differences. TSS reported separately for trunk and extremity lesions 2. Remission: per cent reduction in TSS > = 50%, IGA reduction of 3 points, or PGA reduction of 3 points 3. Investigator Global Severity Assessment (IGA); 7-pt: 0 (clear) to 6 (severe) 4. Subject Global Severity Assessment (PGA); 7-pt: 0 (clear) to 6 (severe) 5. Adverse events 6. Skin atrophy 7. Safety
Notes	Connetics Corporation, Palo Alto, California, US, sponsored the trial. We sought data, but we received no response. There was SD imputation (IGA/PGA).

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Unclear risk	The trial reported insufficient details.
Blinding (performance bias and detection bias) All outcomes	Low risk	The trial was double-blind (participant/investigator).
Randomisation method reported	Unclear risk	The trial did not report this.
Loss to follow up	Low risk	0%

Koo 2006 *(Continued)*

Baseline assessments	Unclear risk	The trial did not report these.
Baseline comparability demonstrated	Unclear risk	This was not demonstrated.

Kragballe 1988b

Methods	**DESIGN** Within-patient Participant delivery **ALLOCATION** Random Method of randomisation: not reported Concealment: unclear **BLINDING** Double-blind (participant/investigator) **WITHDRAWAL/DROPOUT** Not described
Participants	N: 30 Treatment duration: 6 wks LF: 3 (10%) BC: yes Age: 39 (range = 18 to 65) Gender (per cent men): 30.0% Severity: TSS (0 to 9) = 6.9; per cent BSA = 18.7% (range = 12% to 50%) Duration (yrs): 15.3 (range = 1 to 35) **INCLUSION CRITERIA** • Stable symmetrically distributed moderate • Chronic plaque-type psoriasis • Outpatients • Adult • Women above child bearing age or using adequate contraception **EXCLUSION CRITERIA** • Recent topical, systemic, intralesional, or UV radiation therapy (excluding bland emollients) • Non-normal serum levels of calcium and creatinine • Taking calcium tablets
Interventions	• Calcipotriol cream 10 mcg/g, 33 mcg/g, or 100 mcg/g BD C (10); C (33); C (100) • Placebo (vehicle) (P)
Outcomes	1. Severity (erythema; thickness; scaling) 2. TSS (0 to 9) 3. Investigator Global Assessment (5-pt: worse to clear) 4. Patient Global Assessment (5-pt: worse to clear)

Kragballe 1988b *(Continued)*

Notes	The trial did not report sponsorship.

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Unclear risk	The trial reported insufficient details.
Blinding (performance bias and detection bias) All outcomes	Low risk	The trial was double-blind (participant/investigator).
Randomisation method reported	Unclear risk	The trial did not report this.
Loss to follow up	Low risk	10.0%
Baseline assessments	Low risk	-
Baseline comparability demonstrated	Low risk	-

Kragballe 1991a

Methods	**DESIGN** Within-patient Participant delivery **ALLOCATION** Random Method of randomisation: not stated Concealment: unclear **BLINDING** Double-blind (participant/assessor) **WITHDRAWAL/DROPOUT** Described
Participants	N: 345 Treatment duration: 6 wks LF: 3 (0.9%) BC: yes Age: 45.2 (range = 18 to 90) Gender (per cent men): 58.8% Severity: PASI = 8.35 (range = 0.60 to 48.5) Duration (yrs): 19.5 (range = 0.5 to 76) **INCLUSION CRITERIA** • Adult • Symmetrical chronic plaque psoriasis • Inpatients and outpatients

Kragballe 1991a *(Continued)*

	EXCLUSION CRITERIA • Unstable psoriasis • Recent systemic or UV therapy • Hypercalcaemia • Impaired renal/hepatic function • High dose calcium/Vitamin D intake • Unresponsive to corticosteroids • Concomitant medication
Interventions	• Calcipotriol ointment 50 mcg/g BD (C) • Betamethasone valerate ointment 0.1% BD (B)
Outcomes	1. PASI 2. Total Sign Score (erythema, thickness, scaliness) (0 to 12) 3. Patient assessment of response
Notes	Leo Pharmaceuticals sponsored the trial Trial participants were inpatients and outpatients. There was SD imputation (TSS).

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Unclear risk	The trial reported insufficient details.
Blinding (performance bias and detection bias) All outcomes	Low risk	The trial was double-blind (participant/assessor).
Randomisation method reported	Unclear risk	The trial did not report this.
Loss to follow up	Low risk	0.9%
Baseline assessments	Low risk	-
Baseline comparability demonstrated	Low risk	-

Kragballe 1998b

Methods	**DESIGN** Between-patient Participant delivery **ALLOCATION** Random Method of randomisation: not stated Concealment: not stated **BLINDING** Double-blind (participant/assessor) **WITHDRAWAL/DROPOUT** Described

Kragballe 1998b *(Continued)*

Participants	N: 699 Treatment duration: 8 wks; FU: 8 wks LF: 8 (1.1%) BC: psoriasis comparable, demographics unclear Age: not stated Gender (per cent men): not stated Severity: not stated **INCLUSION CRITERIA** • Adult • Stable chronic plaque psoriasis on trunk and limbs **EXCLUSION CRITERIA** • Pregnancy • Risk of pregnancy • Lactation • Recent systemic or UV therapy • Concomitant medication • Hypercalcaemia or renal disease • Planned exposure to sun
Interventions	• Calcipotriol cream 50 mcg/g BD (C2) • Calcipotriol cream 50 mcg/g OM, plus clobetasone17-butyrate cream,0.5 mg/g ON (CL) • Calcipotriol cream 50 mcg/g OM, plus betamethasone 17-valerate cream 1 mg/g ON (CB) • Calcipotriol cream 50 mcg/g OM, plus vehicle ON (C1)
Outcomes	1. PASI 2. Investigator overall assessment of response (6-pt: worse to clearance) 3. Patient overall assessment of response (6-pt: worse to clearance)
Notes	Leo Pharmaceuticals sponsored the trial

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Unclear risk	The trial reported insufficient details.
Blinding (performance bias and detection bias) All outcomes	Low risk	The study was double-blind (participant/assessor).
Randomisation method reported	Unclear risk	The trial did not report this.
Loss to follow up	Low risk	1.1%
Baseline assessments	Unclear risk	The trial did not report these.

Kragballe 1998b *(Continued)*

Baseline comparability demonstrated	Unclear risk	This was partially demonstrated.

Kragballe 2004

Methods	**DESIGN** Between-patient Participant delivery **ALLOCATION** Random Method of randomisation: computer-generated randomisation schedule, using centralised telephone voice response system Concealment: adequate **BLINDING** Double-blind (participant/investigator) (Groups A and B) Single-blind (investigator) (Group C) **WITHDRAWAL/DROPOUT** Described
Participants	N: 972 Treatment duration: 8 wk; FU: 12 wks LF: 99 (10.2%) BC: yes Age: 47.7 (range = 18 to 97) Gender (per cent men): 63.8% Severity: PASI = 10.5 (range = 2 to 49); per cent with moderate disease = 64.3% Duration (yrs): 18.5 (range = 0 to 70) **INCLUSION CRITERIA** • Aged 18 and over • Chronic plaque psoriasis amenable to topical treatment • BSA ≥ 10% of at least 1 body region (arms, trunk, legs) **EXCLUSION CRITERIA** • Pregnancy or risk thereof • Lactation • Unstable psoriasis or other inflammatory skin disease • Concurrent systemic or UV therapy • Concurrent topical therapy for trunk or limbs • Abnormal calcium homeostasis
Interventions	• TCP OD for 8 wks then calcipotriol ointment 50 mcg/g OD for 4 wks (A) • TCP OD for 4 wks then calcipotriol ointment 50 mcg/g OD (weekdays) and TCP OD (weekends) for 8 wks (B) • Calcipotriol ointment 50 mcg/g BD for 12 wks (C) • TCP: calcipotriol ointment 50 mcg/g, plus betamethasone dipropionate 0.5 mg/g ointment
Outcomes	1. PASI 2. Investigator's global assessment of severity (PGA) (6-pt: absence of disease to very severe disease)

Kragballe 2004 *(Continued)*

	3. Self-reported compliance with trial medication
Notes	Leo Pharmaceuticals sponsored the trial. Request data: none supplied Reversible skin atrophy: A: 1/322; B: 0/322; C: 0/327

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Low risk	A centralised telephone voice response system was used for the participant assignment, and this removed the opportunity for investigator bias during randomisation.
Blinding (performance bias and detection bias) All outcomes	Low risk	Groups A and B were double-blind (participant/investigator); group C was single-blind (investigator).
Randomisation method reported	Low risk	Randomisation was computer-generated.
Loss to follow up	Low risk	10.2%
Baseline assessments	Low risk	-
Baseline comparability demonstrated	Low risk	-

Kragballe 2006

Methods	**DESIGN** Between-patient Participant delivery **ALLOCATION** Random Method of randomisation: computer-generated randomisation schedule (1:1:1) Concealment: unclear **BLINDING** Double-blind (participant/investigator) **WITHDRAWAL/DROPOUT** Described
Participants	N: 634 Treatment duration: 52 wks; FU: 52 wks LF: 8 (1.3%) BC: yes Age: 48.7 (14.2SD) Gender (per cent men): 61.0% Ethnicity (per cent white): 97.3% Severity: per cent IGA moderate = 69.1%; per cent IGA severe = 27.9%; per cent IGA very severe = 3.0% Duration (yrs): mean = 19.7; median = 17.0; range = 1 to 65 Use of topical corticosteroids during last decade (mths): 33.8 **INCLUSION CRITERIA** • Outpatients aged > = 18 with plaque psoriasis of trunk and limbs • IGA at least moderate.

Kragballe 2006 *(Continued)*

	EXCLUSION CRITERIA • Erythrodermic, exfoliative, and pustular psoriasis • Skin infection, use of systemic or topical antipsoriatic therapy • Use of PUVA or UVB • BSA > = 30% (and requiring treatment) • Calcium metabolic disorder • Pregnancy • Lactation
Interventions	1. Calcipotriol ointment 50 mcg/g plus betamethasone dipropionate ointment 0.5 mg/g OD (C-B) 2. Alternating every 4 weeks: calcipotriol ointment 50 mcg/g plus betamethasone dipropionate ointment 0.5 mg/g OD (4 wks) then calcipotriol 50 mcg/g (4 wks) (A) 3. Calcipotriol ointment 50 mcg/g plus betamethasone dipropionate ointment 0.5 mg/g, OD (4 wks) then calcipotriol ointment 50 mcg/g (48 wks) (C) < = 100 g/wk
Outcomes	1. Investigator's Global Assessment (IGA): 6-pt (absent, very mild, mild, moderate, severe, very severe) 2. Treatment success: IGA absent, very mild, or mild 3. Independent assessment of adverse events by non-investigator clinicians: adjudicated corticosteroid reactions 4. Patient Global Assessment (PGA): 3-pt (satisfactory, not satisfactory, not applicable (not used)) 5. Compliance (medication usage) 6. HPA assessed in subgroup of 19 participants
Notes	Leo Pharma A/S sponsored the trial. The sponsor supplied unpublished data.

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Unclear risk	The trial reported insufficient details.
Blinding (performance bias and detection bias) All outcomes	Low risk	The trial was double-blind (participant/investigator).
Randomisation method reported	Low risk	A computer-generated randomisation schedule was used (1:1:1).
Loss to follow up	Low risk	1.3%
Baseline assessments	Low risk	These were reported.
Baseline comparability demonstrated	Unclear risk	The trial only reported mean values (no measure of spread). They described groups as "well balanced".

Kragballe 2009

Methods	**DESIGN** Between-patient

Kragballe 2009 *(Continued)*

	Participant delivery **ALLOCATION** Random Method of randomisation: computer-generated schedule (1:2) Concealment: unclear **BLINDING** Single-blind (investigator) **WITHDRAWAL/DROPOUT** Described
Participants	N: 312 Treatment duration: 8 wks; FU: 16 wks LF: 2 (0.6%) BC: yes Age: 51.0 (15.4SD); range = 18 to 91 Gender (per cent men): 43.0% Ethnicity (per cent white): 99.0% Severity: IGA moderate = 56.7%; IGA severe = 35.9%; IGA very severe = 7.4%; TSS (0 to 12) = 7.3 (1.7SD) Duration (yrs): 18.7 (14.6SD); range = 0 to 70 **INCLUSION CRITERIA** • People with moderately severe scalp psoriasis amenable to treatment with < = 100 g medication/wk (combined product) or 60 mL solution/wk (calcipotriol) • Psoriasis of trunk/limbs • Scalp involvement > = 10% • Clinical signs > = moderate for > = 1 sign and > = slight for remaining signs • IGA > = moderate **EXCLUSION CRITERIA** • PUVA or grenz ray therapy within previous 4 wks • Topical scalp treatments or UVB therapy or very potent (WHO group IV) corticosteroids on body within previous 2 wks • Biologicals within previous 6 mths • Systemic therapies within previous 4 wks • Current diagnosis of unstable forms of psoriasis or other skin diseases confounding psoriasis assessment • Skin infections • Atrophy of the scalp • Calcium homeostasis abnormality • Severe renal or hepatic disorder • Concomitant use of medications that could affect scalp psoriasis • Pregnancy • Lactation
Interventions	• Calcipotriol solution 50 mcg/g BD (C) • Calcipotriol gel 50 mcg/g plus betamethasone dipropionate "scalp formulation" (gel) 0.5 mg/g OD (C-B) There was no concomitant topical treatment, emollient, or medicated shampoo or conditioner.

Kragballe 2009 *(Continued)*

Outcomes	1. Investigator's Global Assessment (IGA): 6-pt (absent (0), very mild, mild, moderate, severe, very severe (5)) 2. Treatment success: IGA clear or minimal 3. Total Sign Score (TSS): 0 to 12 4. Patient Global Assessment of Disease Severity (PGA). 5-pt scale (clear, very mild, mild, moderate, severe) 5. Patient assessment of itching (4-pt: none, mild, moderate, severe) 6. Compliance: self-report; use of study medication
Notes	Leo Pharma A/S, Ballerup, Denmark, sponsored the trial. The sponsor supplied unpublished data.

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Unclear risk	The trial reported insufficient details.
Blinding (performance bias and detection bias) All outcomes	Low risk	The trial was double-blind (participant/investigator).
Randomisation method reported	Low risk	A computer-generated randomisation schedule was used (1:2).
Loss to follow up	Low risk	0.6%
Baseline assessments	Low risk	These were reported.
Baseline comparability demonstrated	Low risk	This was demonstrated.

Kreuter 2006 (H)

Methods	**DESIGN** Between-patient Participant delivery **ALLOCATION** Random Method of randomisation: computer-generated randomisation lists Concealment: unclear **BLINDING** Double-blind (participant/investigator) **WITHDRAWAL/DROPOUT** Described
Participants	N: 80 Treatment duration: 4 wks; FU: 10 wks LF: 2 (2.5%) BC: yes Age: 52.4 (14.3SD); range = 28 to 87

Kreuter 2006 (H) *(Continued)*

	Gender (per cent men): 61.3% Ethnicity: NR Severity: mPASI = 21.2 (13.4SD); range = 3 to 54; VAS (0 to 10) = 4.8 (2.7SD); range = 1 to 10 **INCLUSION CRITERIA** • People aged > = 18 with inverse psoriasis that had been present for at least 6 mths • Good general health **EXCLUSION CRITERIA** • Systemic or phototherapies within previous 4 wks • Topical therapies within previous 2 wks • Acute guttate or pustular psoriasis • Pregnancy • Lactation • Severe concurrent infectious diseases • Diseases associated with immunesuppression or malignancy • Drug dependency • Mental dysfunction or other factors limiting compliance
Interventions	• Calcipotriol 0.005% ointment OD (C) • Betamethasone valerate 0.1% OD (B) • Pimecrolimus 1% cream OD (PM) • Placebo (vehicle for pimecrolimus) OD (P) No concomitant therapies were permitted (including emollients).
Outcomes	1. mPASI (0 to 72): assessment confined to body area affected. Each sign scored 0 to 4 and then multiplied by area affects (0 (0%) to 6 (90% to 100%)) 2. VAS (itching): 0 = absence to 10 = maximum 3. Adverse events
Notes	Novartis Pharma GmbH sponsored the trial. Atrophy was not reported. We sought unpublished data, but it was reported to be unavailable. There was SD imputation (PASI).

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Unclear risk	The trial reported insufficient details.
Blinding (performance bias and detection bias) All outcomes	Low risk	The trial was double-blind (participant/investigator).
Randomisation method reported	Low risk	Computer-generated randomisation lists were used.
Loss to follow up	Low risk	2.5%

Kreuter 2006 (H) *(Continued)*

Baseline assessments	Low risk	These were reported.
Baseline comparability demonstrated	Low risk	This was demonstrated.

Kreuter 2006 (P)

Methods	**DESIGN** Between-patient Participant delivery **ALLOCATION** Random Method of randomisation: computer-generated randomisation lists Concealment: unclear **BLINDING** Double-blind (participant/investigator) **WITHDRAWAL/DROPOUT** Described
Participants	N: 80 Treatment duration: 4 wks; FU: 10 wks LF: 2 (2.5%) BC: yes Age: 52.4 (14.3SD); range = 28 to 87 Gender (per cent men): 61.3% Ethnicity: NR Severity: mPASI = 21.2 (13.4SD), range = 3 to 54; VAS (0 to 10) = 4.8 (2.7SD), range = 1 to 10 **INCLUSION CRITERIA** • People aged > = 18 with inverse psoriasis that had been present for at least 6 mths • Good general health **EXCLUSION CRITERIA** • Systemic or phototherapies within previous 4 wks • Topical therapies within previous 2 wks • Acute guttate or pustular psoriasis • Pregnancy • Lactation • Severe concurrent infectious diseases • Diseases associated with immunesuppression or malignancy • Drug dependency • Mental dysfunction or other factors limiting compliance
Interventions	• Calcipotriol 0.005% ointment OD (C) • Betamethasone valerate 0.1% OD (B) • Pimecrolimus 1% cream OD (PM) • Placebo (vehicle for pimecrolimus) OD (P) No concomitant therapies were permitted (including emollients).
Outcomes	1. mPASI (0 to 72): assessment confined to body area affected. Each sign scored 0 to 4 and then multiplied by area affects (0 (0%) to 6 (90% to 100%)) 2. VAS (itching): 0 = absence to 10 = maximum

Kreuter 2006 (P) *(Continued)*

	3. Adverse events
Notes	Novartis Pharma GmbH sponsored the trial. Atrophy was not reported. We sought unpublished data, but it was reported to be unavailable. There was SD imputation (PASI).

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Unclear risk	The trial reported insufficient details.
Blinding (performance bias and detection bias) All outcomes	Low risk	The trial was double-blind (participant/investigator).
Randomisation method reported	Low risk	Computer-generated randomisation lists were used.
Loss to follow up	Low risk	2.5%
Baseline assessments	Low risk	These were reported.
Baseline comparability demonstrated	Low risk	This was demonstrated.

Krueger 1998

Methods	**DESIGN** Within-patient Participant delivery **ALLOCATION** Random Method of randomisation: not reported Concealment: unclear **BLINDING** Double-blind (participant/investigator) **WITHDRAWAL/DROPOUT** Described
Participants	N: 45 Treatment duration: 6 wks LF: 0 (0%) BC: reported to be similar Age: 50 (range = 23 to 83) Gender (per cent men): 84% Severity: not reported

Krueger 1998 *(Continued)*

	INCLUSION CRITERIA • Mild to moderate bilateral psoriatic plaques • Adult • Total Severity Score less than or equal to 6. **EXCLUSION CRITERIA** • Pregnant • Nursing or of likely to conceive • Recent use of certain topical agents • Recent systemic retinoids, UV phototherapy, or systemic antipsoriasis drugs
Interventions	• Tazarotene gel 0.01% or 0.05% BD (T) • Placebo (vehicle) (P)
Outcomes	1. Severity (erythema; plaque elevation; scaling) 2. TSS (0 to 12) 3. Investigator Global Assessment (6-pt: no change/worse to completely clear)
Notes	Allergan, Inc, California, sponsored the trial.

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Unclear risk	The trial reported insufficient details.
Blinding (performance bias and detection bias) All outcomes	Low risk	The trial was double-blind (participant/investigator).
Randomisation method reported	Unclear risk	The trial did not report this.
Loss to follow up	Low risk	0.0%
Baseline assessments	Unclear risk	These were partially done.
Baseline comparability demonstrated	Unclear risk	These were stated to be similar; comparability was not demonstrated.

Köse 1997

Methods	**DESIGN** Between-patient Delivery unclear **ALLOCATION** Random Method of randomisation: not stated Concealment: unclear **BLINDING** Unclear **WITHDRAWAL/DROPOUT**

Köse 1997 *(Continued)*

	Described
Participants	N: 43 Treatment duration: 10 days FU: 20 days LF: 0 (0%) BC: yes Age: not stated Gender (per cent men): not stated Severity: not stated **INCLUSION CRITERIA** • Psoriasis of the scalp **EXCLUSION CRITERIA** • Not reported
Interventions	• Calcipotriol ointment 50 mcg/g occluded ON (CO) • Clobetasol 17-propionate solution BD (CP)
Outcomes	1. TSS (0 to 9)
Notes	The trial did not report sponsorship. This was a scalp trial.

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Unclear risk	The trial reported insufficient details.
Blinding (performance bias and detection bias) All outcomes	Unclear risk	The trial did not report this.
Randomisation method reported	Unclear risk	The trial did not report this.
Loss to follow up	Low risk	0.0%
Baseline assessments	Unclear risk	The trial did not report these.
Baseline comparability demonstrated	Unclear risk	The trial reported baseline comparability (demographic/clinical), but it was not demonstrated.

Lahfa 2003

Methods	**DESIGN** Between-patient Participant delivery

Lahfa 2003 *(Continued)*

	ALLOCATION Random Method of randomisation: not stated Concealment: unclear **BLINDING** Single-blind (investigator) **WITHDRAWAL/DROPOUT** Described
Participants	N: 125 Treatment duration: 12 wks; FU: 12 wks LF: 5 (4.0%) BC: yes Age: 49.5 (15.1SD) Gender (per cent men): 55.2% Ethnicity (per cent white/Caucasoid): 97.6% Severity: PASI = 6.8; per cent BSA = 13.2 (7.4SD) Duration (yrs): 16.7 **INCLUSION CRITERIA** • People with mild to moderate plaque psoriasis • BSA < 30% **EXCLUSION CRITERIA** • Skin conditions interfering with assessment • Co-morbidities that put participant at risk • Severe psoriasis, including erythrodermic • Pregnancy or risk thereof • Lactation • Topical/UVB therapy within previous 2 wks • PUVA within previous 4 wks • Systemic therapy, beta blockers, or lithium within previous 8 wks
Interventions	• Calcipotriol 50 mcg/g ointment ON, plus clobetasol propionate 0.05% cream OM (2 to 4 wks), then calcipotriol ointment BD (to wk 12) (C1) • Calcitriol 3 mcg/g ointment ON, plus clobetasol propionate 0.05% cream OM (2 to 4 wks), then calcitriol ointment BD (to wk 12) (C2) In the initial phase, the participant applied dual therapy until achieving clearance or marked improvement or until 4 wks elapsed, then switched to monotherapy maintenance phase.
Outcomes	1. PASI, based on scores from 3 lesions, 1 each on trunk, and upper and lower limbs 2. Investigator's Assessment of Global Improvement (IAGI): 7-pt (worse to clear, rescaled 0 to 6) 3. Clinical success: IAGI > = marked improved 4. Relapse (maintenance phase): IAGI < = moderate improvement 5. Patient Assessment of Global Improvement: 7-pt (worse to clear) 6. Adverse events: cutaneous safety including signs and soreness (all scored 0 to 3); investigator assessment of global safety (poor, good, excellent); patient self report
Notes	Galderma Laboratories sponsored the trial.

Lahfa 2003 *(Continued)*

We sought unpublished data, but it was reported to be unavailable.

There was SD imputation (PASI).

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Unclear risk	The trial reported insufficient details.
Blinding (performance bias and detection bias) All outcomes	Unclear risk	The study was single-blind (investigator).
Randomisation method reported	Unclear risk	The trial did not report this.
Loss to follow up	Low risk	4.0%
Baseline assessments	Low risk	These were reported.
Baseline comparability demonstrated	Low risk	This was demonstrated.

Landi 1993

Methods	**DESIGN** Between-patient Delivery unclear **ALLOCATION** Random Method of randomisation: not stated Concealment: unclear **BLINDING** Unclear **WITHDRAWAL/DROPOUT** Described
Participants	N: 40 Treatment duration: 6 wks; FU: 10 wks LF: 0 (0%) BC: psoriasis comparable, demographics unclear Age: range = 17 to 84 Gender (per cent men): not stated Severity: PASI (mean) = 11.6 (range = 3.0 to 35.1) **INCLUSION CRITERIA** • Adult • Mild and moderate psoriasis **EXCLUSION CRITERIA**

Landi 1993 *(Continued)*

	• Not reported
Interventions	• Calcipotriol ointment 50 mcg/g BD (C) • Clobetasol propionate 0.05% ointment BD (CP)
Outcomes	1. PASI
Notes	Leo Pharmaceuticals sponsored the trial. Landi 1993 reported the findings of a single centre, 1 of 3 centres reported in Landi 1993 (N = 120).

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Unclear risk	The trial reported insufficient details.
Blinding (performance bias and detection bias) All outcomes	Unclear risk	The trial did not report this.
Randomisation method reported	Unclear risk	The trial did not report this.
Loss to follow up	Low risk	0.0%
Baseline assessments	Unclear risk	These were partially done.
Baseline comparability demonstrated	Unclear risk	This was partially demonstrated.

Lane 1983

Methods	**DESIGN** Between-patient Participant delivery **ALLOCATION** Random Method of randomisation: not reported Concealment: unclear **BLINDING** Double-blind (participant/investigator) **WITHDRAWAL/DROPOUT** Not described
Participants	N: 157 Treatment duration: 3 wks; FU: 3 wks LF: 18 (11.5%) BC: yes Age: 39.6 Gender (per cent men): 52.5% Severity: TSS (0 to 20) = 10.6

Lane 1983 *(Continued)*

	INCLUSION CRITERIA • History and physical finding compatible with psoriasis including scaling erythema, epidermal thickening, crusting, or both • All ages > 1 year • Stable disease. **EXCLUSION CRITERIA** • Recent topical or systemic corticosteroid treatment • Oral antihistamine • Antipruritic therapy, UV, or X-ray therapy or any medication affecting the study • Pregnant
Interventions	• Betamethasone dipropionate ointment 0.05% OD (B) • Diflorasone diacetate ointment 0.05% OD (D) • Placebo (vehicle) (P)
Outcomes	1. Severity (scaling; erythema; pruritis; thickening; crusting; overall condition) 2. Total Severity Score (0 to 20)
Notes	The trial did not report sponsorship. There was SD imputation (TSS).

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Unclear risk	The trial reported insufficient details.
Blinding (performance bias and detection bias) All outcomes	Low risk	The trial was double-blind (participant/investigator).
Randomisation method reported	Unclear risk	The trial did not report this.
Loss to follow up	Low risk	11.5%
Baseline assessments	Low risk	-
Baseline comparability demonstrated	Low risk	-

Langley 2011 (H)

Methods	**DESIGN** Between-patient Participant delivery **ALLOCATION** Random Method of randomisation: not stated (2:2:1) Concealment: adequate: treatments dispensed by non-study staff **BLINDING**

Langley 2011 (H) *(Continued)*

	Single-blind (investigator) **WITHDRAWAL/DROPOUT** Described
Participants	N: 458 Treatment duration: 8 wks; FU: 16 wks LF: 0 (0%) BC: yes Age: 51.6 (14SD) Gender (per cent men): 62.2% Ethnicity (per cent white): 93.9% Severity: mPASI = 9.39, range = 2.4 to 59.4; IGA moderate = 68.3%; IGA severe = 29.5%; IGA very severe = 2.2%; per cent BSA = 9.3 (8.2SD) Duration (yrs): 19.8 (13.3SD) **INCLUSION CRITERIA** • Participants with moderately severe plaque psoriasis involving trunk, limbs, or both • BSA > = 10% on arms, trunk, limbs, or a mixture of the aforementioned • Amendable to maximum weekly dose of 100 g of gel or 70 g of ointment **EXCLUSION CRITERIA** • Systemic biological therapy within previous 3 mths • Other systemic treatment within previous 4 wks • Concurrent oral vitamin D > 500 IU/day • UVA or grenz ray therapy within previous 4 wks • UVB within previous 2 wks • Pregnancy • Lactation
Interventions	• Tacalcitol ointment 4 mcg/g OD (T) • Calcipotriol gel 50 mcg/g plus betamethasone dipropionate gel 0.5 mg/g OD (C-B) • Placebo (gel vehicle) OD (P) Participants achieving clear IGA stopped treatment and restarted if psoriasis reappeared. There was follow up of responders only (IGA clear or almost clear).
Outcomes	1. Investigator's Global Assessment of Disease Severity: 6-pt (clear to very severe) 2. Treatment responder (controlled disease): IGA clear or almost clear at wk 8 3. mPASI (0 to 64.8) 4. PASI 50, PASI 75 5. Patient Global Assessment (PGA) of disease severity: 5-pt (clear to severe) 6. Adverse events 7. Relapse (treatment responders only): > = 50% reduction in PASI improvement achieved (wk0 to wk8) 8. Time to relapse 9. Rebound (treatment responders only): > 125% reduction in PASI at wk 0 10.Compliance (wk 2 to wk 6): self-report and medication usage 11.Adverse events

Langley 2011 (H) *(Continued)*

Notes	Leo Pharma A/S, Ballerup, Denmark, sponsored the trial. Participants could not be completely blinded to treatment allocation because of differences in formulation and packaging (bottles for gel vs. tubes for ointments). Atrophy was not assessed. The sponsor supplied unpublished data.

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Low risk	A designated third person performed allocation of the investigational products at all 18 centres.
Blinding (performance bias and detection bias) All outcomes	Unclear risk	The study was single-blind (investigator); it was not possible to blind participants to treatments because of differences in vehicle formulations.
Randomisation method reported	Unclear risk	The trial did not report this.
Loss to follow up	Low risk	0%
Baseline assessments	Low risk	These were reported.
Baseline comparability demonstrated	Low risk	This was demonstrated.

Langley 2011 (P)

Methods	**DESIGN** Between-patient Participant delivery **ALLOCATION** Random Method of randomisation: not stated (2:2:1) Concealment: adequate: treatments dispensed by non-study staff. **BLINDING** Single-blind (investigator) **WITHDRAWAL/DROPOUT** Described
Participants	N: 458 Treatment duration: 8 wks; FU: 16 wks LF: 0 (0%) BC: yes Age: 51.6 (14SD) Gender (per cent men): 62.2% Ethnicity (per cent white): 93.9% Severity: mPASI = 9.39, range = 2.4 to 59.4; IGA moderate = 68.3%; IGA severe = 29.5%; IGA very severe = 2.2%; per cent BSA = 9.3 (8.2SD) Duration (yrs): 19.8 (13.3SD) **INCLUSION CRITERIA**

Langley 2011 (P) *(Continued)*

- Participants with moderately severe plaque psoriasis involving trunk, limbs, or both
- BSA > = 10% on arms, trunk, limbs, or a mixture of the aforementioned
- Amendable to maximum weekly dose of 100 g of gel or 70 g of ointment

EXCLUSION CRITERIA

- Systemic biological therapy within previous 3 mths
- Other systemic treatment within previous 4 wks
- Concurrent oral vitamin D > 500 IU/day
- UVA or grenz ray therapy within previous 4 wks
- UVB within previous 2 wks
- Pregnancy
- Lactation

Interventions	• Tacalcitol ointment 4 mcg/g OD (T) • Calcipotriol gel 50 mcg/g plus betamethasone dipropionate gel 0.5 mg/g OD (C-B) • Placebo (gel vehicle) OD (P) Participants achieving clear IGA stopped treatment and restarted if psoriasis reappeared. There was follow up of responders only (IGA clear or almost clear).
Outcomes	1. Investigator's Global Assessment of Disease Severity: 6-pt (clear to very severe) 2. Treatment responder (controlled disease): IGA clear or almost clear at wk 8 3. mPASI (0 to 64.8) 4. PASI 50, PASI 75 5. Patient Global Assessment (PGA) of disease severity: 5-pt (clear to severe) 6. Adverse events 7. Relapse (treatment responders only): > = 50% reduction in PASI improvement achieved (wk0 to wk8) 8. Time to relapse 9. Rebound (treatment responders only): > 125% reduction in PASI at wk 0 10.Compliance (wk 2 to wk 6): self-report and medication usage 11.Adverse events
Notes	Leo Pharma A/S, Ballerup, Denmark, sponsored the trial. Participants could not be completely blinded to treatment allocation because of differences in formulation and packaging (bottles for gel vs. tubes for ointments). Atrophy was not assessed. The sponsor supplied unpublished data.

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Low risk	A designated third person performed allocation of the investigational products at all 18 centres.
Blinding (performance bias and detection bias) All outcomes	Unclear risk	The study was single-blind (investigator); it was not possible to blind participants to treatments because of differences in vehicle formulations.
Randomisation method reported	Unclear risk	The trial did not report this.

Langley 2011 (P) *(Continued)*

Loss to follow up	Low risk	0%
Baseline assessments	Low risk	These were reported.
Baseline comparability demonstrated	Low risk	This was demonstrated.

Langner 1992

Methods	**DESIGN** Within-patient Participant delivery **ALLOCATION** Random Method of randomisation: unclear Concealment: unclear **BLINDING** Double-blind (participant/investigator) **WITHDRAWAL/DROPOUT** Described
Participants	N: 29 Treatment duration: 6 wks; FU: 6 wks LF: 0 (0%) BC: yes Age: mean: 40.5 (range = 16-77) Gender (per cent men): 69.0% Severity: not reported **INCLUSION CRITERIA** • Severe chronic psoriasis • Symmetrical lesions • Adult • Outpatients **EXCLUSION CRITERIA** • Pregnancy or inadequate contraception
Interventions	• Calcitriol ointment 3 mcg/g BD (C) • Placebo (vehicle) (P)
Outcomes	1. Severity (erythema; pustules, desquamation, encrustation, vesiculation and pruritis) 2. Investigator Global Assessment (6-pt: worse to clear)
Notes	The trial did not report sponsorship. All participants received 2 weeks' pre-treatment with vehicle BD.
Risk of bias	

Langner 1992 *(Continued)*

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Unclear risk	The trial reported insufficient details.
Blinding (performance bias and detection bias) All outcomes	Low risk	The trial was double-blind (participant/investigator).
Randomisation method reported	Unclear risk	The trial did not report this.
Loss to follow up	Low risk	0.0%
Baseline assessments	Low risk	These were partially done.
Baseline comparability demonstrated	Low risk	This was demonstrated.

Langner 1993

Methods	**DESIGN** Within-patient Participant delivery **ALLOCATION** Random Method of randomisation: unclear Concealment: unclear **BLINDING** Double-blind (participant/investigator) **WITHDRAWAL/DROPOUT** Described
Participants	N: 32 Treatment duration: 6 wks; FU: 6 wks LF: 2 (6.3%) BC: yes Age: mean: 42.4 (range = 16 to 77) Gender (per cent men): 62.5% Severity: global severity score (0 to 4) = 3.5 **INCLUSION CRITERIA** • Bilateral • Symmetrical • Severe chronic plaque psoriasis • Outpatients. **EXCLUSION CRITERIA** • Pregnancy or inadequate contraception • Use of calcium

Langner 1993 *(Continued)*

	• Vitamin D or analogues • Calcium-containing antacids • Digitalis • Thiazide diuretics or glucocorticosteroids
Interventions	• Calcitriol ointment 15 mcg/g BD (C) • Placebo (vehicle) (P)
Outcomes	1. Severity (erythema; scaling; induration; pruritis) 2. PASI 3. Investigator Global Assessment (6-pt: worse to clear)
Notes	The trial did not report sponsorship. All participants received 2 weeks' pre-treatment with vehicle BD.

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Unclear risk	The trial reported insufficient details.
Blinding (performance bias and detection bias) All outcomes	Low risk	The trial was double-blind (participant/investigator).
Randomisation method reported	Unclear risk	The trial did not report this.
Loss to follow up	Low risk	6.3%
Baseline assessments	Low risk	-
Baseline comparability demonstrated	Low risk	-

Langner 2001 (H)

Methods	**DESIGN** Between-patient Participant delivery **ALLOCATION** Random Method of randomisation: unclear Concealment: unclear **BLINDING** Double-blind (participant/investigator) **WITHDRAWAL/DROPOUT** Described
Participants	N: 44 Treatment duration: 6 wks; FU: 6 wks (14 wks for responders) LF: 4 (9.1%)

Langner 2001 (H) *(Continued)*

	BC: not reported Age: not reported Gender (per cent men): 54.5% Severity: not reported **INCLUSION CRITERIA** • Adults with chronic plaque psoriasis • BSA = 20% **EXCLUSION CRITERIA** • Pregnancy • Inadequate contraception
Interventions	• Calcitriol ointment 3 mcg/g BD (C) • Betamethasone valerate ointment 0.1% BD (B)
Outcomes	1. IAGI (5-pt: worse to clearance)
Notes	The trial did not report sponsorship. All participants received 2 weeks' pre-treatment with vehicle BD.

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Unclear risk	The trial reported insufficient details.
Blinding (performance bias and detection bias) All outcomes	Low risk	The trial was double-blind (participant/investigator).
Randomisation method reported	Unclear risk	The trial did not report this.
Loss to follow up	Low risk	9.1%
Baseline assessments	Low risk	These were partially done.
Baseline comparability demonstrated	Unclear risk	The trial did not report this.

Langner 2001 (P)

Methods	**DESIGN** Between-patient Participant delivery **ALLOCATION** Random Method of randomisation: unclear Concealment: unclear **BLINDING** Double-blind (participant/investigator)

Langner 2001 (P) *(Continued)*

	WITHDRAWAL/DROPOUT Described
Participants	N: 44 Treatment duration: 6 wks; FU: 6 wks (14 wks for responders) LF: 4 (9.1%) BC: not reported Age: not reported Gender (per cent men): 54.5% Severity: not reported **INCLUSION CRITERIA** • Adults with chronic plaque psoriasis • BSA = 20% **EXCLUSION CRITERIA** • Pregnancy • Inadequate contraception
Interventions	• Calcitriol ointment 3 mcg/g BD (C) • Placebo ointment BD (P)
Outcomes	1. IAGI (5-pt: worse to clearance)
Notes	The trial did not report sponsorship. All participants received 2 weeks' pre-treatment with vehicle BD.

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Unclear risk	The trial reported insufficient details.
Blinding (performance bias and detection bias) All outcomes	Low risk	The trial was double-blind (participant/investigator).
Randomisation method reported	Unclear risk	The trial did not report this.
Loss to follow up	Low risk	9.1%
Baseline assessments	Low risk	These were partially done.
Baseline comparability demonstrated	Unclear risk	The trial did not report this.

Lassus 1991

Methods	**DESIGN** Between-patient Participant delivery **ALLOCATION** Random Method of randomisation: block randomisation Concealment: unclear **BLINDING** Double-blind (participant/investigator) **WITHDRAWAL/DROPOUT** Described
Participants	N: 50 Treatment duration: 12 wks; FU: 12 wks LF: 8 (16%) BC: yes Age: 42.8 (range = 22 to 50; N = 42) Gender (per cent men): 45.2% (N = 42) Severity: TSS (0 to 12) = 7.72 **INCLUSION CRITERIA** • Stable psoriasis of at least 1 years' duration • Mild to moderate plaque psoriasis • Nummular, discoid, or guttate psoriasis • Stable aged 18 to 50 • Localised lesions **EXCLUSION CRITERIA** • Pregnancy • Lactation • Antipsoriatic therapy within previous 2 wks • People declining to abstain from alcohol during treatment period
Interventions	• Oleum horwathiensis (Psoricur®) OD (O) • Placebo OD (P)
Outcomes	1. TSS (0 to 12) 2. Severity (scaling, pruritis, erythema, induration) 3. IAGI (5-pt: poor to healed)
Notes	The trial did not report sponsorship. There was SD imputation (TSS).

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Unclear risk	The trial reported insufficient details.

Lassus 1991 *(Continued)*

Blinding (performance bias and detection bias) All outcomes	Low risk	The trial was double-blind (participant/investigator).
Randomisation method reported	Low risk	Block randomisation was used.
Loss to follow up	Low risk	16.0%
Baseline assessments	Low risk	-
Baseline comparability demonstrated	Low risk	-

Lebwohl 2002

Methods	**DESIGN** Between-patient Participant delivery **ALLOCATION** Random Method of randomisation: not reported (but ratio 3:1 used) Concealment: unclear **BLINDING** Double-blind (participant/investigator) **WITHDRAWAL/DROPOUT** Described
Participants	N: 81 Treatment duration: 2 wks; FU: 4 wks LF: 5 (6.2%) BC: yes Age: not reported Gender (per cent men): not reported Severity: pruritis (0 to 4) = 2.11 **INCLUSION CRITERIA** • Mild to moderate plaque type psoriasis • Aged at least 18 • TSS (0 to 12) ≥ 3 • Target lesions in at least 1 of 5 anatomical regions • BSA ≤ 20% **EXCLUSION CRITERIA** • Investigational medication within previous 4 wks • Topical antipsoriatic treatment within previous 2 wks • Systemic antipsoriatic treatment within previous 4 wks • Concurrent UV treatment or sunbathing • Pregnancy

Lebwohl 2002 *(Continued)*

	• Lactation • Inadequate contraception • Men wishing to father children during the study • Concurrent drug or alcohol abuse
Interventions	• Clobetasol propionate foam 0.05% BD (maximum of 50 g/wk) (C) • Placebo foam BD (P)
Outcomes	1. IAGI (7-pt: worse to completely clear) 2. PAGI (7-pt: worse to completely clear) 3. Total Severity Score: erythema, scaling, thickness, pruritis (0 to 4) 4. Adverse events 5. Medicines consumption (compliance)
Notes	Connetics Corporation sponsored the trial. Only non-scalp sites were treated.

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Unclear risk	The trial reported insufficient details.
Blinding (performance bias and detection bias) All outcomes	Low risk	The trial was double-blind (participant/investigator).
Randomisation method reported	Unclear risk	The trial did not report this.
Loss to follow up	Low risk	6.2%
Baseline assessments	Low risk	These were partially done.
Baseline comparability demonstrated	Low risk	-

Lebwohl 2004

Methods	**DESIGN** Between-patient Participant delivery **ALLOCATION** Random Method of randomisation: not reported Concealment: unclear **BLINDING** Double-blind (participant/investigator) **WITHDRAWAL/DROPOUT** Described
Participants	N: 167 Treatment duration: 8 wks; FU: 8 wks

Lebwohl 2004 *(Continued)*

LF: 30 (18%)

BC: yes

Age: 48.0

Gender (per cent men): 58.7%

Severity: Static Severity Score (SSS) (0 to 6) (median) = 3 (range = 1.5 to 5.0); per cent with concurrent plaque-type lesions = 85%

INCLUSION CRITERIA

- Age limit unclear (stated as ≥ 2 and ≥ 16)
- Chronic plaque psoriasis affecting intertriginous and facial skin
- Disease stable or slowly worsening for ≥ 1 wk
- Target lesion of moderate erythema and TSS (0 to 12) ≥ 4

EXCLUSION CRITERIA

- Systemic therapy or phototherapy within previous 4 wks
- Topical therapy within previous 2 wks
- Inhaled/intranasal corticosteroids within previous 2 wks
- Other topical agents (excluding sunscreen) within previous 1 dy
- Recently diagnosed (< 6 mths) or recent exacerbation of inverse psoriasis
- Uncontrolled chronic co-morbidity
- Pregnancy
- Lactation
- Previous use of tacrolimus ointment for facial or intertriginous psoriasis

Interventions	• Tacrolimus ointment 0.1% BD • Placebo ointment BD
Outcomes	1. Inverse psoriasis severity score (Static Severity Score) (SSS) (6-pt: clear to very severe) 2. IAGI ('PGA') (7-pt: exacerbation to clear) 3. Signs (0 to 3 each) (erythema, induration, desquamation; overall severity) 4. Patient satisfaction (per cent agreeing with range of statements)
Notes	Fujisawa Healthcare Inc sponsored the trial. Loss to follow up was reported as 11/167. Non-study body sites received usual topical treatment. No adequate effectiveness data were reported or available from the sponsor. This was an inverse psoriasis trial.

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Unclear risk	The trial reported insufficient details.
Blinding (performance bias and detection bias) All outcomes	Low risk	The trial was double-blind (participant/investigator).
Randomisation method reported	Unclear risk	The trial did not report this.

Lebwohl 2004 *(Continued)*

Loss to follow up	Low risk	18.0%
Baseline assessments	Low risk	-
Baseline comparability demonstrated	Low risk	-

Lebwohl 2007

Methods	**DESIGN** Between-patient Participant delivery **ALLOCATION** Random Method of randomisation: not stated Concealment: unclear **BLINDING** Double-blind (participant/investigator) **WITHDRAWAL/DROPOUT** Not described
Participants	N: 418 Treatment duration: 8 wks; FU: 8 wks LF: 0 (0%) BC: NR separately (see notes) Age: NR Gender (per cent men): NR Severity: GSS (0 to 5) = 2.81 (0.40SD); DSS (0 to 12) (bony areas) = 6.4 (1.24SD); (non-bony areas) = 6.4 (1.33SD) **INCLUSION CRITERIA** • People aged > = 12 with mild to moderate plaque psoriasis • BSA < = 35% **EXCLUSION CRITERIA** • Not stated
Interventions	• Calcitriol 3 mcg/g ointment BD (C) • Placebo ointment BD (P)
Outcomes	1. Global Severity Score (GSS) on a 6-pt scale (0 = clear, 1 = almost clear, 2 = mild, 3 = moderate, 4 = severe, 5 = very severe) 2. Dermatological sum score (DSS) (0 to 12): reported separately for bony and non-bony areas 3. Investigator Assessment of Global Improvement (IAGI) on a 7-pt scale (clear to worse) 4. Subject Global Assessment (PAGI), 7-pt (clear to worse) 5. Routine clinical and safety laboratory parameters including calcium homeostasis (> 10% above upper limit of normal range)
Notes	Galderma R&D Inc, Princeton, New Jersey, sponsored the trial.

Lebwohl 2007 *(Continued)*

The main publication reports only pooled results and baseline statistics from 2 studies (Lebwohl 2007; Powers 2005).

The sponsor supplied unpublished data.

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Unclear risk	The trial reported insufficient details.
Blinding (performance bias and detection bias) All outcomes	Low risk	The trial was double-blind (participant/investigator).
Randomisation method reported	Unclear risk	The trial did not report this.
Loss to follow up	Low risk	0%
Baseline assessments	Unclear risk	The trial did not report these.
Baseline comparability demonstrated	Unclear risk	This was not demonstrated.

Lee 2007

Methods	**DESIGN** Between-patient Participant delivery **ALLOCATION** Random Method of randomisation: not stated Concealment: unclear **BLINDING** Single-blind (investigator) **WITHDRAWAL/DROPOUT** Described
Participants	N: 142 Treatment duration: 6 wks; FU: 14 wks LF: 11 (7.7%) BC: yes (clinical only) Age: NR Gender (per cent men): NR Severity: PASI = 3.75 (2.90SD) **INCLUSION CRITERIA** • People with mild to moderate psoriasis **EXCLUSION CRITERIA**

Lee 2007 *(Continued)*

	• NR
Interventions	• Calcitriol ointment BD (C) • Diflucortolone valerate OM, plus calcitriol ointment ON (C-D)
Outcomes	1. PASI (scale NR)
Notes	Sponsor: NR The trial was set in Korea.

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Unclear risk	The trial reported insufficient details.
Blinding (performance bias and detection bias) All outcomes	Unclear risk	The study was single-blind (investigator).
Randomisation method reported	Unclear risk	The trial did not report this.
Loss to follow up	Low risk	7.7%
Baseline assessments	Unclear risk	Clinical assessments were reported; demographics were unclear.
Baseline comparability demonstrated	Unclear risk	Only clinical comparability was demonstrated.

Lepaw 1978

Methods	**DESIGN** Within-patient Participant delivery **ALLOCATION** Random Method of randomisation: predetermined schedule using identical containers coded with participant number Concealment: unclear **BLINDING** Double-blind (participant/investigator) **WITHDRAWAL/DROPOUT** Described
Participants	N: 29 Treatment duration: 2 wks; FU: 2 wks LF: 2 (6.9%) BC: inadequately reported Age: 14 to 75 Gender (per cent men): 55.2%

Lepaw 1978 *(Continued)*

	Severity: not reported **INCLUSION CRITERIA** • Bilaterally similar psoriatic lesions of the scalp • Adults or adolescents **EXCLUSION CRITERIA** • Systemic therapy, topical scalp treatments
Interventions	• Halcinonide solution 0.1% TDS (H) • Placebo (vehicle) TDS (P)
Outcomes	1. Overall therapeutic response 2. Overall comparative response
Notes	The trial did not report sponsorship. This was a scalp trial.

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Unclear risk	The trial reported insufficient details.
Blinding (performance bias and detection bias) All outcomes	Low risk	The trial was double-blind (participant/investigator).
Randomisation method reported	Unclear risk	The trial did not report this.
Loss to follow up	Low risk	6.9%
Baseline assessments	Low risk	These were partially done.
Baseline comparability demonstrated	Unclear risk	The trial did not report this.

Levine 2010 (H)

Methods	**DESIGN** Within-patient Participant delivery **ALLOCATION** Random Method of randomisation: computer-generated randomisation table Concealment: adequate **BLINDING** Double-blind (participant/investigator) **WITHDRAWAL/DROPOUT** Described
Participants	N: 168

Levine 2010 (H) *(Continued)*

	Treatment duration: 12 wks; FU: 12 wks LF: 4 (2.4%) BC: stated, not demonstrated Age: not reported Gender (per cent men): not reported Severity: TLPSS = 6.69 (1.38 SD) **INCLUSION CRITERIA** • People aged 18 and over with moderate plaque psoriasis • Bilateral plaques or 2 plaques > = 5 cm distant on same side • 15 x 15 cm>plaque size > 2 x 2 cm **EXCLUSION CRITERIA** • BSA > 15% • Participants with only scalp, nail, flexural, palmoplantar, or pustular psoriasis • Participation in trial within previous 3 mths • Topical antipsoriatic therapy within previous 2 wks • Systemic antipsoriatic therapy within previous 1 mth • Use of systemic niacin or multivitamins within previous 2 wks • Concomitant use of carbamazepine or primidone • People starting or modifying treatment with betablockers within previous 1 mth • Significant hematologic, renal, or liver disease • Relevant psychiatric or medical illness or surgery • Hemoglobin < 10.0 g/dL, hematocrit < 30%, white blood cell count < 3000/mcg/L, platelets < 100,000/mcg/L, aspartate aminotransferase or alanine aminotransferase > 3 x upper limit of normal • Pregnancy
Interventions	Participants were randomised to 2 of 7 treatments: • calcipotriene 0.005% ointment BD (C) • placebo ointment BD (P)] • nicotinamide 1.4% BD (NI) • calcipotriene 0.005% ointment BD + nicotinamide 0.05% BD (NC005) • calcipotriene 0.005% ointment BD + nicotinamide 0.1% BD (NC010) • calcipotriene 0.005% ointment BD + nicotinamide 0.7% BD (NC070) • calcipotriene 0.005% ointment BD + nicotinamide 1.4% BD (NC140)

Outcomes	1. Total Local Psoriasis Severity Score (0 to 12): sum of erythema, plaque elevation, scaling (each scored 0 to 4)
	2. Efficacy end-point: per cent patients 'clear to almost clear' (TLPSS = 0 to 2):
	  • 'clear': no elevation above normal skin, no scaling, and no erythema
	  • 'almost clear': no elevation above normal skin, surface dryness with some white coloration, and slight to moderate red colouration

Notes	Dermipsor Ltd sponsored the trial. Compliance rates (medicine usage) were reported for each regimen. The trial author supplied unpublished data. As participants were randomised to 2 of 7 treatments, some comparisons were within-patient and others between-patient.

Levine 2010 (H) *(Continued)*

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Low risk	The participants, investigators, study site personnel, sponsor, and laboratories were unaware of the treatment assignments; throughout the study, the study investigator retained a set of code envelopes that were to be opened by the investigator only if deemed necessary after a serious adverse event.
Blinding (performance bias and detection bias) All outcomes	Low risk	The trial was double-blind (participant/investigator).
Randomisation method reported	Low risk	A computer-generated randomisation table was used.
Loss to follow up	Low risk	2.4%
Baseline assessments	Unclear risk	The trial did not report these.
Baseline comparability demonstrated	Unclear risk	Clinical comparability was stated (not demonstrated).

Levine 2010 (P)

Methods	**DESIGN** Within-patient Participant delivery **ALLOCATION** Random Method of randomisation: computer-generated randomisation table Concealment: adequate **BLINDING** Double-blind (participant/investigator) **WITHDRAWAL/DROPOUT** Described
Participants	N: 168 Treatment duration: 12 wks; FU: 12 wks LF: 4 (2.4%) BC: stated, not demonstrated Age: not reported Gender (per cent men): not reported Severity: TLPSS = 6.69 (1.38SD) **INCLUSION CRITERIA** • People aged 18 and over with moderate plaque psoriasis • Bilateral plaques or 2 plaques > = 5 cm distant on same side • 15 x 15 cm>plaque size > 2 x 2 cm **EXCLUSION CRITERIA** • BSA > 15% • Participants with only scalp, nail, flexural, palmoplantar, or pustular psoriasis • Participation in trial within previous 3 mths • Topical antipsoriatic therapy within previous 2 wks

Levine 2010 (P) *(Continued)*

- Systemic antipsoriatic therapy within previous 1 mth
- Use of systemic niacin or multivitamins within previous 2 wks
- Concomitant use of carbamazepine or primidone
- People starting or modifying treatment with betablockers within previous 1 mth
- Significant hematologic, renal, or liver disease
- Relevant psychiatric or medical illness or surgery
- Hemoglobin < 10.0 g/dL, hematocrit < 30%, white blood cell count < 3000/mcg/L, platelets < 100,000/mcg/L, aspartate aminotransferase or alanine aminotransferase > 3 x upper limit of normal
- Pregnancy

Interventions	Participants were randomised to 2 of 7 treatments: • calcipotriene 0.005% ointment BD (C) • placebo ointment BD (P)] • nicotinamide 1.4% BD (NI) • calcipotriene 0.005% ointment BD + nicotinamide 0.05% BD (NC005) • calcipotriene 0.005% ointment BD + nicotinamide 0.1% BD (NC010) • calcipotriene 0.005% ointment BD + nicotinamide 0.7% BD (NC070) • calcipotriene 0.005% ointment BD + nicotinamide 1.4% BD (NC140)
Outcomes	1. Total Local Psoriasis Severity Score (0 to 12): sum of erythema, plaque elevation, scaling (each scored 0 to 4) 2. Efficacy end-point: per cent patients 'clear to almost clear' (TLPSS = 0 to 2): • 'clear': no elevation above normal skin, no scaling, and no erythema • 'almost clear': no elevation above normal skin, surface dryness with some white coloration, and slight to moderate red colouration
Notes	Dermipsor Ltd sponsored the trial. Compliance rates (medicine usage) were reported for each regimen. The trial author supplied unpublished data. As participants were randomised to 2 of 7 treatments, some comparisons were within-patient and others between-patient.

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Low risk	The participants, investigators, study site personnel, sponsor, and laboratories were unaware of the treatment assignments; throughout the study, the study investigator retained a set of code envelopes that were to be opened by the investigator only if deemed necessary after a serious adverse event.
Blinding (performance bias and detection bias) All outcomes	Low risk	The trial was double-blind (participant/investigator).
Randomisation method reported	Low risk	A computer-generated randomisation table was used.
Loss to follow up	Low risk	2.4%
Baseline assessments	Unclear risk	The trial did not report these.

Levine 2010 (P) *(Continued)*

Baseline comparability demonstrated	Unclear risk	Clinical comparability was stated (not demonstrated).

Liao 2007

Methods	**DESIGN** Between-patient Participant delivery **ALLOCATION** Random Method of randomisation: not stated Concealment: unclear **BLINDING** Double-blind (participant/investigator) **WITHDRAWAL/DROPOUT** Described
Participants	N: 50 Treatment duration: 6 wks; FU: 6 wks LF: 1 (2.0%) BC: yes Age: 39.6 (12.8SD); range 21 to 69 Gender (per cent men): 73.5% Target lesion: face (89.8%); genitofemoral (10.2%) Severity: TAS (0 to 12) = 6.2 (3.32SD) **INCLUSION CRITERIA** • People aged 18 to 70 with chronic plaque psoriasis affecting facial and genitofemoral areas **EXCLUSION CRITERIA** • Topical therapies within previous 1 wk • UV therapy or sunbathing within previous 2 wks • Systemic therapy within previous 4 wks • Concurrent use of oral calcium or Vitamin D supplements, or lithium, beta-blockers, or ACE inhibitors
Interventions	• Calcitriol 3 mcg/g ointment BD (C) • Tacrolimus 0.3 mg/g ointment BD (T) No concomitant topical therapies or emollients were permitted. Dosing frequency could be reduced or medication discontinued depending on level of irritancy.
Outcomes	1. Target Area Score (TAS): 0 to 12 (erythema, plaque elevation, scaling) 2. Physician Global Assessment of improvement (PGA) on a 7-pt scale (worse to clear) 3. Safety: erythema (0 to 4), perilesional oedema (0 to 4), stinging/burning (0 to 4), hot sensation (0 to 4), folliculitis/acne (0 to 1)
Notes	Galderma, Taiwan, sponsored the trial.

Liao 2007 *(Continued)*

	Individual safety measures were reported, but the total number of participants experiencing any adverse event were not reported. The trial author supplied unpublished data.

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Unclear risk	The trial reported insufficient details.
Blinding (performance bias and detection bias) All outcomes	Low risk	The trial was double-blind (participant/investigator).
Randomisation method reported	Unclear risk	The trial did not report this.
Loss to follow up	Low risk	2.0%
Baseline assessments	Low risk	These were reported.
Baseline comparability demonstrated	Low risk	This was demonstrated.

Lin 2007

Methods	**DESIGN** Within-patient Participant delivery **ALLOCATION** Random Method of randomisation: not stated Concealment: unclear **BLINDING** Single-blind (investigator) **WITHDRAWAL/DROPOUT** Described
Participants	N: 14 Treatment duration: 8 wks; FU: 8 wks LF: 4 (28.6%) BC: yes Age: 35.8 (10.4SD), range = 21 to 54 Gender (per cent men): 78.6% Severity: PSI (0 to 12) = 9.9 (1.2SD); PASI = 11.7 (4.8SD), range = 5.5 to 19.2; per cent BSA = 13.6 (6.1SD), range = 3% to 20% Duration (yrs): 110.8 (9.4SD); range = 2 to 30 **INCLUSION CRITERIA**

Lin 2007 *(Continued)*

- Adult people with recalcitrant, bilateral chronic plaque psoriasis affecting 5% to 20% of BSA
- Plaques 3 to 20 cm diameter
- Disease duration > = 2 yrs
- Resistant to > = 1 topical therapy
- No other significant medical problem

EXCLUSION CRITERIA

- Systemic therapy within previous 30 days
- Topical therapy within previous 14 days
- Tests positive for HIV, hepatitis B, or hepatitis C
- Known sensitivity to Chinese herbs
- Pregnancy or risk thereof
- Lactation
- Clinically significant laboratory abnormality

Interventions	• Indigo naturalis 1.4% ointment,OD (I) • Placebo ointment (olive oil, yellow wax, petroleum jelly) OD (P)
Outcomes	1. Clearing per cent area of target lesions affected 2. Psoriasis severity Index (TSS, 0 to 12) 3. PASI (range not stated) 4. Safety (immunohistochemical analysis of skin biopsies and blood tests)
Notes	The sponsor was not reported. Assessments were conducted by 2 blinded investigators. A 3-month uncontrolled follow-study also conducted. The trial author supplied unpublished data.

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Unclear risk	The trial reported insufficient details.
Blinding (performance bias and detection bias) All outcomes	Unclear risk	The study was single-blind (investigator).
Randomisation method reported	Unclear risk	The trial did not report this.
Loss to follow up	High risk	28.6%
Baseline assessments	Unclear risk	These were reported.
Baseline comparability demonstrated	Unclear risk	This was demonstrated.

Lin 2008

Methods	**DESIGN** Within-patient Participant delivery **ALLOCATION** Random Method of randomisation: not stated Concealment: unclear **BLINDING** Single-blind (investigator) **WITHDRAWAL/DROPOUT** Described
Participants	N: 42 Treatment duration: 12 wks; FU: 12 wks LF: 0 (0%) BC: Yes Age: 34.6 (11.SD); range = 18 to 58 Gender (per cent men): 76.2% Severity: PASI (median) = 14.7; per cent BSA (median) = 18%; TSS (0 to 24) = 18.8 (3.03SD) Duration (yrs): 10 (median); range = 2 to 41 **INCLUSION CRITERIA** • People aged 18 to 75 with mild to moderate bilateral symmetric plaque psoriasis • Disease duration > = 2 yrs • Resistant to > = 2 topical therapies • Good general health (no abnormality in blood, renal, and liver function tests) **EXCLUSION CRITERIA** • BSA > 60% • Pustular or generalised erythrodermic psoriasis • Concomitant use of medications that could affect psoriasis • Systemic therapy within previous 30 days • UV therapy within previous 21 days • Topical therapy within previous 2 wks • Tests positive for HIV, hepatitis B, or hepatitis C • History of alcohol/drug misuse • History of hepatitis • Known sensitivity to Chinese herbs or vehicle ingredients • Pregnancy or risk thereof • Lactation • Trial participation within previous 30 days
Interventions	• Indigo naturalis 1.4% ointment OD (I) • Placebo ointment (olive oil, yellow wax, petroleum jelly) OD (P) Participants achieving clearance before study end point could stop treatment.
Outcomes	1. Global improvement (IAGI); 6-pt: worse to clearance 2. Signs (erythema, induration, scaling), each scored 0 (none) to 8 (very severe) 3. Total sum score (0 to 24)

Lin 2008 *(Continued)*

4. PASI (range unclear): baseline median used to explore response by group
5. Compliance (medication use)
6. Safety

Notes	The trial was supported by a grant: CMRPG33024 from Chang Gung Memorial Hospital. Participants were instructed to wash skin thoroughly before visits; assessments were based on photographs.

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Unclear risk	The trial reported insufficient details.
Blinding (performance bias and detection bias) All outcomes	Unclear risk	The study was single-blind (investigator).
Randomisation method reported	Unclear risk	The trial did not report this.
Loss to follow up	Low risk	0.0%
Baseline assessments	Unclear risk	These were reported.
Baseline comparability demonstrated	Unclear risk	This was demonstrated.

Lister 1997

Methods	**DESIGN** Between-patient Participant delivery **ALLOCATION** Random Method of randomisation: not stated Concealment: unclear **BLINDING** Single-blind (investigator) **WITHDRAWAL/DROPOUT** Described
Participants	N: 171 Treatment duration: 8 wks; FU: 16 wks LF: not reported BC: psoriasis comparable, demographics unclear Age: not stated Gender (per cent men): not stated Severity: TSS (scale NR) = 6.24

Lister 1997 *(Continued)*

	INCLUSION CRITERIA • Chronic plaque psoriasis **EXCLUSION CRITERIA** • Unclear
Interventions	• Dithranol cream 1 to 3% OD (D) • Calcipotriol BD (C)
Outcomes	1. Total Sign Score (erythema, scaling, induration) (scale NR) 2. Investigator and Patient Global Assessments (scales NR) 3. Relapse rates
Notes	Bioglan Laboratories sponsored the trial.

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Unclear risk	The trial reported insufficient detail.
Blinding (performance bias and detection bias) All outcomes	Low risk	The trial was single-blind (investigator).
Randomisation method reported	Unclear risk	The trial did not report this.
Loss to follow up	Unclear risk	The trial did not report this.
Baseline assessments	Low risk	These were partially done.
Baseline comparability demonstrated	Unclear risk	This was partially demonstrated.

Lowe 2005

Methods	**DESIGN** Between-patient Participant delivery **ALLOCATION** Random Method of randomisation: consecutive balanced blocks of 7 (3:3:1) Concealment: unclear **BLINDING** Single-blind (investigator); as cream and lotion were compared, not possible to blind patients **WITHDRAWAL/DROPOUT** Described
Participants	N: 192 Treatment duration: 4 wks; FU: 8 wks LF: 0 (0%)

Lowe 2005 *(Continued)*

	BC: yes Age: 48.65; range = 19 to 79 Gender (per cent men): 65.6% Ethnicity (per cent white): 82.8% Severity: DSS (0 to 12) = 7.60 (1.55SD) **INCLUSION CRITERIA** • People aged > = 18 with stable moderate to severe plaque psoriasis • DSS (0 to 12) > = 6 • Target lesion diameter > 3 cm, lesion not located on face, axillae, groin, scalp, hands, or feet **EXCLUSION CRITERIA** • Contravention of wash-out periods for topicals and systemics (duration not stated)
Interventions	• Clobetasol propionate lotion/cream BD (CP) • Placebo lotion BD (P) Participants were randomised to clobetasol propionate cream or lotion; results were aggregated for review purposes. Other affected areas could also be treated. There was a 4-wk treatment- free follow-up period.
Outcomes	1. Signs: erythema, plaque elevation, scaling, pruritus (0 (none) to 4 (very severe)) 2. Dermatological sum score (DSS) (erythema, plaque elevation, scaling): 0 to 12 3. Investigator's Assessment of Global improvement (IAGI): 7-pt (worse to clear) 4. Global severity score (GSS): dichotomised as success (GSS = 0, 0.5 or 1) or failure (GSS > = 2) 5. BSA
Notes	Galderma R&D, Sophia Antipolis, France, sponsored the trial. We sought unpublished data, but it was reported to be unavailable.

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Unclear risk	The trial reported insufficient details.
Blinding (performance bias and detection bias) All outcomes	Unclear risk	The study was single-blind (investigator); as the cream and lotion were compared, it was not possible to blind participants.
Randomisation method reported	Low risk	Participants allocated in consecutive balanced blocks of 7 using the following ratios: 3:3:1.
Loss to follow up	Low risk	0%
Baseline assessments	Low risk	These were reported.
Baseline comparability demonstrated	Low risk	This was demonstrated.

Luger 2008

Methods	**DESIGN** Between-patient Participant delivery **ALLOCATION** Random Method of randomisation: not stated Concealment: unclear **BLINDING** Double-blind (participant/investigator) **WITHDRAWAL/DROPOUT** Described
Participants	N: 869 Treatment duration: 52 wks; FU: 52 wks LF: 55 (6.3%) BC: yes Age: 48.7 (15.0SD), range = 18 to 86 Gender (per cent men): 44.0% Ethnicity (per cent white): 96.7% Severity: IGA moderate = 55.5%; IGA severe = 37.8%; IGA very severe = 6.7% Duration (yrs): 17.6 (14.2SD) **INCLUSION CRITERIA** • Hospital outpatients aged > = 18 with moderate to severe scalp psoriasis • Amendable to topical treatment with < = 100 g/wk • Psoriasis vulgaris on trunk or limbs; • Area of scalp affected > 10% • IGA at least moderate severity **EXCLUSION CRITERIA** • Use within previous 28 days of PUVA or grenz ray therapy • Systemics with a potential impact on scalp psoriasis, or biological therapies; UVB; topical therapies; calcium metabolism disorders associated with hypercalcaemia. Unclear if concurrent use permitted during the trial
Interventions	• Calcipotriol 50 mcg/g in scalp formulation (gel) OD PRN (C) • Calcipotriol gel 50 mcg/g plus betamethasone dipropionate "scalp formulation" (gel) 0.5 mg/g OD (C-B) Participants achieving clearance could stop treatment, but remained in the trial, and restart as needed. The regimen was intended to reflect usual clinical practice.
Outcomes	1. Adverse drug reactions 2. Adverse events associated with long-term corticosteroid use 3. Investigator's Global Assessment of disease severity (IGA) (6-pt: absence of disease (0) to very severe disease (5)) 4. Controlled disease: IGA < = 2

Luger 2008 *(Continued)*

	5. Compliance (self-report; failure to use treatment for any reason other than no treatment required) (tube weight also assessed)
Notes	Leo Pharma, Ballerup, Denmark,sponsored the trial. Adverse events were recorded by investigators and reviewed by an adjudication committee (Data Safety Monitoring Board) comprising of 3 dermatologists blinded to treatment assignment. The sponsor supplied unpublished data.

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Unclear risk	The trial reported insufficient details.
Blinding (performance bias and detection bias) All outcomes	Low risk	The trial was double-blind (participant/investigator).
Randomisation method reported	Unclear risk	This was not stated.
Loss to follow up	Low risk	6.3%
Baseline assessments	Low risk	These were reported.
Baseline comparability demonstrated	Low risk	This was demonstrated.

Maier 2004

Methods	**DESIGN** Between-patient Participant delivery **ALLOCATION** Random Method of randomisation: not stated Concealment: unclear **BLINDING** Double-blind (participant/investigator) **WITHDRAWAL/DROPOUT** Not described
Participants	N: 34 Treatment duration: 8 wks; FU: 8 wks LF: 10 (29.4%) BC: yes (clinical only) Age: NR Gender (per cent men): 55.9% Severity: mPASI = 6.3 (2.2SD)

Maier 2004 *(Continued)*

	INCLUSION CRITERIA • People with stable mild to moderate plaque psoriasis **EXCLUSION CRITERIA** • Concomitant antipsoriatic therapy or use within previous 2 wks
Interventions	• Herbal skincare products (Dr Michaels® cleansing gel, ointment, and skin conditioner) BD (H) • 3 fatty skin care products (not vehicle) BD (P)
Outcomes	1. mPASI (0 to 64.8)
Notes	The trial did not state the sponsor. This was an abstract only.

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Unclear risk	The trial reported insufficient details.
Blinding (performance bias and detection bias) All outcomes	Low risk	The trial was double-blind (participant/investigator).
Randomisation method reported	Unclear risk	The trial did not report this.
Loss to follow up	High risk	29.4%
Baseline assessments	Unclear risk	Clinical assessments were reported.
Baseline comparability demonstrated	Unclear risk	Clinical comparability was demonstrated.

Medansky 1987

Methods	**DESIGN** Between-patient Participant delivery **ALLOCATION** Random Method of randomisation: not reported Concealment: unclear **BLINDING** Double-blind (participant/investigator) **WITHDRAWAL/DROPOUT** Described
Participants	N: 121 Treatment duration: 3 wks; FU: 3 wks LF: 6 (5.0%)

Medansky 1987 *(Continued)*

BC: yes, except duration of disease (P = 0.04)

Age: 53.8 (range = 16 to 80)

Gender (per cent men): 67.8%

Severity: TSS (0 to 9) = 6.6

Duration (yrs): 17.9 (range = 1 to 52)

INCLUSION CRITERIA

- Aged ≥12; chronic plaque psoriasis, stable, or worsening
- Duration ≥ 1 year
- Total Sign Score ≥ 6

EXCLUSION CRITERIA

- Concomitant medication
- Recent systemic corticosteroids or antimetabolites
- Recent topical corticosteroids
- Pregnancy
- Lactation
- Those needing > 90 g/wk topical steroid
- Other forms of psoriasis

Interventions	• Mometasone furoate ointment 0.1% OD (M) • Vehicle OD (P)
Outcomes	1. Signs (erythema; induration; scaling) 2. Total Sign Score (0 to 9) 3. Investigator Global Assessment (6-pt: no change or worse to cleared or marked improvement)
Notes	The trial was supported in part by a grant from Schering Corporation. There was SD imputation (TSS).

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Unclear risk	The trial reported insufficient details.
Blinding (performance bias and detection bias) All outcomes	Low risk	The trial was double-blind (participant/investigator).
Randomisation method reported	Unclear risk	The trial did not report this.
Loss to follow up	Low risk	67.8%
Baseline assessments	Low risk	-
Baseline comparability demonstrated	Low risk	Baseline comparability was demonstrated (only significant difference: duration of disease).

Medansky 1996

Methods	**DESIGN** Within-patient Participant delivery **ALLOCATION** Random Method of randomisation: "schedule" Concealment: unclear **BLINDING** Double-blind (participant/assessor) **WITHDRAWAL/DROPOUT** Described
Participants	N: 134 Treatment duration: 3 wks; FU: 3 wks LF: 6 (4.5%) BC: unclear Age: 47 (range = 20 to 81) Gender (per cent men): not stated Severity: TSS (0 to 9) = 6.5; per cent unstable psoriasis = 28% **INCLUSION CRITERIA** • Mild-to-moderate symmetrical chronic plaque psoriasis • Adult • TSS (0 to 9) ≥ 6 **EXCLUSION CRITERIA** • Recent topical or systemic antipsoriatic therapy • Recent lithium, NSAIDs, or beta-blockers
Interventions	• Diflorasone diacetate ointment, 0.05% BD (D) • Calcipotriene ointment 0.005% BD (C)
Outcomes	1. Signs (erythema, scaling, induration) 2. Total Sign Score (0 to 9) 3. Physician overall evaluation (7 pt: worse to clear) 4. Physician comparative evaluation 5. Patient comparative evaluation
Notes	Dermik Laboratories Inc. sponsored the trial. Adverse events: itching and burning There was SD imputation (TSS/IAGI).

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Unclear risk	The trial reported insufficient details.
Blinding (performance bias and detection bias)	Low risk	The trial was double-blind (participant/assessor).

Medansky 1996 *(Continued)*
All outcomes

Randomisation method reported	Unclear risk	The trial did not report this.
Loss to follow up	Low risk	4.5%
Baseline assessments	Low risk	These were partially done.
Baseline comparability demonstrated	Unclear risk	The trial did not report this.

Menter 2009

Methods	**DESIGN** Between-patient Participant delivery **ALLOCATION** Random Method of randomisation: not reported Concealment: unclear **BLINDING** Open (blinding NS but product vehicles differ) **WITHDRAWAL/DROPOUT** Described
Participants	N: 122 Treatment duration: 4 wks; FU: 8 wks LF: 0 (0%) BC: yes Age: 46.5 (14.2SD) Gender (per cent men): 61.1% Duration (yrs): 16.4 (11.50SD) Severity: ODS = 3.06 (0.43SD) (participant demographics based on per-protocol sample). **INCLUSION CRITERIA** • People aged 18 to 80 with moderate to severe stable plaque psoriasis • BSA: 3 to 20% **EXCLUSION CRITERIA** • Known allergy to study ingredients • Psoriasis affecting scalp, face, or groin only • Area affected required weekly treatment with > 50 g CP spray or > 100 g C-BD ointment
Interventions	• Calcipotriol 50 mcg/g + betamethasone dipropionate 0.5 mg/g combination ointment OD (C-BD) • Clobetasol propionate 0.05% spray (CP)
Outcomes	1. Overall disease severity (ODS) on a 5-pt scale: clear (0), almost clear, mild, moderate, severe/very severe (4) 2. Based on erythema, scaling, and elevation 3. Investigator Global Assessment (IGA) on a 4-pt scale (0 to 3): clear (0), mild, moderate, severe (3). Based on per cent BSA affected (extent) rather than signs
Notes	Galderma Laboratories, LP, sponsored the trial.

Menter 2009 *(Continued)*

Atrophy was not assessed.

Telangiectasia was not assessed.

29 participants were 'non-compliant' with treatment, but intention-to-treat (ITT) analysis included all enrolled participants.

The sponsor supplied unpublished data.

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Unclear risk	The trial reported insufficient details.
Blinding (performance bias and detection bias) All outcomes	High risk	The trial was open (blinding not reported, but product vehicles differ).
Randomisation method reported	Unclear risk	The trial did not report this.
Loss to follow up	Low risk	0%
Baseline assessments	Low risk	These were reported.
Baseline comparability demonstrated	Low risk	This was demonstrated.

Molin 1997

Methods	**DESIGN** Between-patient Participant delivery **ALLOCATION** Random Method of randomisation: not stated Concealment: unclear **BLINDING** Double-blind (participant/assessor) **WITHDRAWAL/DROPOUT** Described
Participants	N: 421 Treatment duration: 8 wks; FU: 8 wks LF: 4 (1%) BC: Psoriasis comparable, demographics not reported Age: not stated Gender (per cent men): not stated Severity: no summary measure reported **INCLUSION CRITERIA**

Molin 1997 *(Continued)*

	• Adult outpatients • Mild-to-moderate stable and chronic plaque psoriasis of limbs and trunk **EXCLUSION CRITERIA** • None reported
Interventions	• Calcipotriol cream 50 mcg/g BD (C) • Betamethasone 17-valerate cream 1 mg/g BD (B)
Outcomes	1. PASI (0 to 64.8) 2. Severity scores 3. Investigator Global Assessment of response (5-pt: worse to cleared) 4. Patient Global Assessments of response (5-pt: worse to cleared)
Notes	Leo Pharmaceutical Products sponsored the trial.

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Unclear risk	The trial reported insufficient details.
Blinding (performance bias and detection bias) All outcomes	Low risk	The trial was double-blind (participant/assessor).
Randomisation method reported	Unclear risk	The trial did not report this.
Loss to follow up	Low risk	1.0%
Baseline assessments	Unclear risk	The trial did not report these.
Baseline comparability demonstrated	Unclear risk	This was partially demonstrated.

Monastirli 2000

Methods	**DESIGN** Between-patient Delivery unclear **ALLOCATION** Random Method of randomisation: not stated Concealment: unclear **BLINDING** Open **WITHDRAWAL/DROPOUT** Described
Participants	N: 70 Treatment duration: 10 wks; FU: 10 wks LF: not reported

Monastirli 2000 *(Continued)*

	BC: yes Age: 45.7 Gender (per cent men): 57.1% Severity: PASI = • D: 7.31 (1.79SD, N = 35) • C: 6.29 (1.63SD, N = 35) Duration (yrs): 17 **INCLUSION CRITERIA** • Inpatients with chronic plaque psoriasis **EXCLUSION CRITERIA** • Pregnancy • Lactation • Ineffective contraception • Systemic treatment within previous 2 mths • Hepatic or renal disease • Hypercalcaemia • Known hypersensitivity to study medications
Interventions	• Dithranol 2% 30 minutes OD (D) • Calcipotriol ointment 50 mcg/g BD (C)
Outcomes	1. PASI (excluding head)
Notes	The trial did not report sponsorship. Treatment was delivered in an inpatient setting.

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Unclear risk	The trial reported insufficient details.
Blinding (performance bias and detection bias) All outcomes	High risk	The trial was open.
Randomisation method reported	Unclear risk	The trial did not report this.
Loss to follow up	Unclear risk	The trial did not report this.
Baseline assessments	Low risk	-
Baseline comparability demonstrated	Low risk	-

Mortensen 1993b

Methods	**DESIGN** Between-patient Participant delivery **ALLOCATION** Random Method of randomisation: not reported Concealment: unclear **BLINDING** Double-blind (participant/investigator) **WITHDRAWAL/DROPOUT** Described
Participants	N: 34 Treatment duration: 3 wks; FU: 4 wks LF: 0 (0%) BC: psoriasis comparable, demographics inadequately reported. Age: 43 (range = 26 to 75) Gender (per cent men): 58.8% Severity: PASI = 12.2 **INCLUSION CRITERIA** • Stable plaque-type psoriasis • Adult outpatients • Normal hepatic and renal function **EXCLUSION CRITERIA** • Recent UV or other psoriasis treatments • Disease or medication influencing calcium or bone metabolism
Interventions	• Calcipotriol ointment 50 mcg/g BD (C) [max 100 g/wk] • Placebo (vehicle) (P)
Outcomes	1. PASI 2. Investigator Global Assessment: per cent improvement from baseline, based on PASI 3. Patient Global Assessment : per cent improvement from baseline, based on PASI
Notes	Leo Pharmaceuticals, Denmark Duration (yrs) sponsored the trial.

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Unclear risk	The trial reported insufficient details.
Blinding (performance bias and detection bias) All outcomes	Low risk	The trial was double-blind (participant/investigator).
Randomisation method reported	Unclear risk	The trial did not report this.

Mortensen 1993b *(Continued)*

Loss to follow up	Low risk	0.0%
Baseline assessments	Low risk	-
Baseline comparability demonstrated	Unclear risk	This was partially demonstrated.

Olsen 1991

Methods	**DESIGN** Between-patient Participant delivery **ALLOCATION** Random Method of randomisation: not reported Concealment: unclear **BLINDING** Double-blind (participant/investigator) **WITHDRAWAL/DROPOUT** Described
Participants	N: 378 Treatment duration: 2 wks; FU: 3 wks LF: 1 (0.3%) BC: yes Age: 46 (range = 18 to 88) Gender (per cent men): 45% Severity: 80% moderate (6 ≤ TSS < 7.5), 20% severe (TSS > 7.5) Duration (yr): 12.0 (9.7SD, N = 377); range = 0.4 to 55.0 **INCLUSION CRITERIA** • Moderate to severe scalp psoriasis (TSS (0 to 9) ≥ 6) • Stable or worsening • Adult **EXCLUSION CRITERIA** • Recent systemic, topical, or UV treatment for psoriasis.
Interventions	• Clobetasol propionate 0.05% BD (C) • Placebo (vehicle) (P)
Outcomes	1. Severity (erythema; induration; scaling, pruritis) 2. TSS (0 to12) 3. Investigator Global Assessment (6-pt: worse to cleared) 4. Patient Global Assessment (4-pt: poor to excellent)
Notes	In part, Glaxo Inc. sponsored the trial. This was a scalp trial. There was SD imputation (TSS).

Olsen 1991 *(Continued)*

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Unclear risk	The trial reported insufficient details.
Blinding (performance bias and detection bias) All outcomes	Low risk	The trial was double-blind (participant/investigator).
Randomisation method reported	Unclear risk	The trial did not report this.
Loss to follow up	Low risk	0.3%
Baseline assessments	Low risk	-
Baseline comparability demonstrated	Low risk	-

Olsen 1996 (1)

Methods	**DESIGN** Between-patient Participant delivery **ALLOCATION** Random Method of randomisation: not reported Concealment: unclear **BLINDING** Double-blind (participant/investigator) **WITHDRAWAL/DROPOUT** Described (for both trials together)
Participants	N: 181 Treatment duration: 4 wks; FU: 4 wks LF: 3 (1.7%) BC: yes Age: 49 (range = 15 to 76) Gender (per cent men): 68.0% Severity: per cent BSA affected = 12.0% (range = 1% to 80%); per cent BSA treated = 11% (range = 1% to 80%) Duration (yrs): 19 (range = 1 to 60)
Interventions	• Fluticasone propionate 0.005% ointment (F) (max 100 g/wk) • Placebo (vehicle) (P)
Outcomes	1. Investigator Global Assessment (6-pt: cleared to worse) 2. Severity (erythema; induration; scaling; pruritis) 3. Patient subjective assessment (treatment effect: 1 = excellent to 4 = poor)
Notes	The trial did not report sponsorship.

Risk of bias

Olsen 1996 (1) *(Continued)*

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Unclear risk	The trial reported insufficient details.
Blinding (performance bias and detection bias) All outcomes	Low risk	The trial was double-blind (participant/investigator).
Randomisation method reported	Unclear risk	The trial did not report this.
Loss to follow up	Low risk	1.7%
Baseline assessments	Low risk	-
Baseline comparability demonstrated	Low risk	-

Olsen 1996 (2)

Methods	**DESIGN** Between-patient Participant delivery **ALLOCATION** Random Method of randomisation: not reported Concealment: unclear **BLINDING** Double-blind (participant/investigator) **WITHDRAWAL/DROPOUT** Described (for both trials together)
Participants	N: 207 Treatment duration: 4 wks; FU: 4 wks LF: 2 (1.0%) BC: yes Age: 45 (range = 12 to 87) Gender (per cent men): 52.7% Severity: per cent BSA affected = 12.5% (range = 1% to 80%); per cent BSA treated = 12% (range = 1% to 80%) Duration (yrs): 16 (range = 0.8 to 52)
Interventions	• Fluticasone propionate 0.005% ointment (F) (max 100 g/wk) • Placebo (vehicle) (P)
Outcomes	1. Investigator Global Assessment (6-pt: cleared to worse) 2. Severity (erythema; induration; scaling; pruritis) 3. Patient subjective assessment (treatment effect: 1 = excellent to 4 = poor)
Notes	The trial did not report sponsorship.

Risk of bias

Bias	Authors' judgement	Support for judgement

Olsen 1996 (2) *(Continued)*

Allocation concealment (selection bias)	Unclear risk	The trial reported insufficient details.
Blinding (performance bias and detection bias) All outcomes	Low risk	The trial was double-blind (participant/investigator).
Randomisation method reported	Unclear risk	The trial did not report this.
Loss to follow up	Low risk	1.0%
Baseline assessments	Low risk	-
Baseline comparability demonstrated	Low risk	-

Oranje 1997

Methods	**DESIGN** Between-patient Patient/parent delivery **ALLOCATION** Random Method of randomisation: computer-generated random number table used by 7/14 centres to randomly select ≤ 3 participants Concealment: unclear **BLINDING** Double-blind (participant/investigator) **WITHDRAWAL/DROPOUT** Described
Participants	N: 77 Treatment duration: 8 wks; FU: 8 wks LF: 0 (0%) BC: yes Age: 10 (range = 2 to 14) Gender (per cent men): 46.8% Severity: not reported **INCLUSION CRITERIA** • Mild to moderate chronic plaque psoriasis • Children aged 2 to 14 **EXCLUSION CRITERIA** • Acute guttate, pustular, erythrodermic, or worsening psoriasis • Psoriasis mainly on the face, scalp, or diaper area • Systemic treatment • Recent phototherapy • Concurrent Vitamin D, calcium, or other intercurrent medication

Oranje 1997 *(Continued)*

	• Renal, hepatic, or osteoarthritic disease
Interventions	• Calcipotriol ointment 50 mcg/g BD (C) • Placebo (vehicle) (P)
Outcomes	1. PASI: severity (redness; thickness; scaliness, area) 2. Extent of disease 3. Investigator Global Assessment 4. Patient Global Assessment (by parent/guardian for those aged < 8) 5. Compliance
Notes	Leo Pharmaceutical Products, Denmark, sponsored the trial. The trial participants were children.

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Unclear risk	The trial reported insufficient details.
Blinding (performance bias and detection bias) All outcomes	Low risk	The trial was double-blind (participant/investigator).
Randomisation method reported	Low risk	Randomisation was computer-generated.
Loss to follow up	Low risk	0.0%
Baseline assessments	Low risk	These were partially done.
Baseline comparability demonstrated	Low risk	-

Ormerod 1997

Methods	**DESIGN** Within-patient Participant delivery **ALLOCATION** Random Method of randomisation: not reported Concealment: unclear **BLINDING** Double-blind (participant/investigator) **WITHDRAWAL/DROPOUT** Not described
Participants	N: 12 Treatment duration: 2 wks; FU: 2 wks LF: unclear BC: unclear

Ormerod 1997 *(Continued)*

	Age: not reported Gender (per cent men): not reported Severity: TSS (0 to 24) =12.2 **INCLUSION CRITERIA** • Bilaterally similar chronic • Stable plaque psoriasis. **EXCLUSION CRITERIA** • Recent systemic or UV therapy
Interventions	• Betamethasone valerate ointment 0.1% BD (B) • White soft paraffin BD (P)
Outcomes	1. Signs (erythema; elevation; scaling) 2. Total Sign Score (0 to 24)
Notes	Wyeth-Ayerst Research and Glaxo Dermatology sponsored the trial.

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Unclear risk	The trial reported insufficient details.
Blinding (performance bias and detection bias) All outcomes	Low risk	The trial was double-blind (participant/investigator).
Randomisation method reported	Unclear risk	The trial did not report this.
Loss to follow up	Unclear risk	The trial did not report this.
Baseline assessments	Low risk	These were partially done.
Baseline comparability demonstrated	Unclear risk	The trial did not report this.

Ormerod 2000

Methods	**DESIGN** Within-patient Participant delivery **ALLOCATION** Random Method of randomisation: not reported Concealment: unclear **BLINDING** Double-blind (participant/investigator) **WITHDRAWAL/DROPOUT** Described

Ormerod 2000 *(Continued)*

Participants	N: 17 Treatment duration: 4 wks; FU: 4 wks LF: 0 (0%) BC: not reported Age: not reported Gender (per cent men): not reported Severity: TSS (0 to 24) = 15.5 (SD: 3.7; N = 17) **INCLUSION CRITERIA** • Stable plaque psoriasis **EXCLUSION CRITERIA** • Pregnancy • Ineffective contraception • Lactation
Interventions	• NG-monomethyl-L-arginine (L-NMMA) cream 25% BD • NG-monomethyl-L-arginine (L-NMMA) cream 5% BD • Placebo (P)
Outcomes	1. TSS (elevation, erythema, scaling) (0 to 24)
Notes	The trial did not report sponsorship.

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Unclear risk	The trial reported insufficient details.
Blinding (performance bias and detection bias) All outcomes	Low risk	The trial was double-blind (participant/investigator).
Randomisation method reported	Unclear risk	The trial did not report this.
Loss to follow up	Low risk	0.0%
Baseline assessments	Low risk	These were partially done.
Baseline comparability demonstrated	Unclear risk	The trial did not report this.

Ormerod 2005

Methods	**DESIGN** Within-patient Participant delivery

Ormerod 2005 *(Continued)*

ALLOCATION
Random
Method of randomisation: randomised in blocks of 4 by the pharmacy department using 'Minitab'
Concealment: unclear
BLINDING
Double-blind (participant/investigator)
WITHDRAWAL/DROPOUT
Unclear

Participants	N: 24 Treatment duration: 12 wks; FU: 12 wks LF: 2 (8.3%) BC: yes Age: 47.5 (range = 28 to 78) Gender (per cent men): 75.0% Severity: TSS (0 to 24) = 17.0 (3.3SD, N = 22) **INCLUSION CRITERIA** • Chronic plaque psoriasis • Aged 18 and over • No significant co morbidity • Transminase levels within double normal upper limit **EXCLUSION CRITERIA** • Planned exposure to sunlight over trial duration • Pregnancy or risk thereof • Lactation; systemic or UV therapy within previous 4 wks • Topical therapy within previous 2 wks • Known allergy to macrolide drugs • Renal or hepatic disease • Renal malignancy within previous 5 yrs
Interventions	• Topical sirolimus 2.2% for 6 wks then 8% for a further 6 wks (S) • Placebo (P) Dosing frequency was not reported.
Outcomes	1. Total Sign Score (TSS) of target plaque (erythema, thickening, scaling) (0 to 24)
Notes	Wyeth Research, Philadelphia, sponsored the trial. No systemic adverse event was considered clinically significant. The daily dosing frequency was unclear.

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Unclear risk	The trial reported insufficient details.
Blinding (performance bias and detection bias)	Low risk	The trial was double-blind (participant/investigator).

Ormerod 2005 *(Continued)*
All outcomes

Randomisation method reported	Low risk	Block randomisation was used.
Loss to follow up	Low risk	9.3%
Baseline assessments	Low risk	-
Baseline comparability demonstrated	Low risk	-

Ortonne 1994

Methods	**DESIGN** Between-patient Participant delivery **ALLOCATION** Random Method of randomisation: participants allocated sequentially upon inclusion Concealment: unclear **BLINDING** Double-blind (participant/assessor) **WITHDRAWAL/DROPOUT** Described
Participants	N: 188 Treatment duration: 6 wks; FU: 6 wks LF: 32 (17.0%) BC: yes Age: 46.0 (range = 20 to 85) Gender (per cent men) 67.3% Severity: per cent BSA = 18.9%; PASI = 11.67; per cent unstable psoriasis = 40% Duration (yrs): 14.9 **INCLUSION CRITERIA** • Chronic plaque psoriasis • Stable or worsening • BSA 10% to 40% • PASI 1 to 30; outpatients **EXCLUSION CRITERIA** • Pregnancy • Lactation • Concurrent disease • Concomitant therapy • Hypersensitivity to Vitamin D or analogues • Planned exposure to sun

Ortonne 1994 *(Continued)*

Interventions	• Calcipotriol ointment BD (C) • Calcipotriol ointment OM, plus betamethasone dipropionate ointment ON (CB)
Outcomes	1. PASI 2. Investigator Global Assessment
Notes	Leo Pharmaceuticals sponsored the trial.

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Unclear risk	The trial reported insufficient details.
Blinding (performance bias and detection bias) All outcomes	Low risk	The trial was double-blind (participant/assessor).
Randomisation method reported	Low risk	Randomisation was sequential.
Loss to follow up	Low risk	17.0%
Baseline assessments	Low risk	-
Baseline comparability demonstrated	Low risk	-

Ortonne 2003

Methods	**DESIGN** Within-patient Participant delivery **ALLOCATION** Random Method of randomisation: computer-generated randomisation by blocks of 4 using RANUNI routine of the SAS system Concealment: unclear **BLINDING** Single-blind (investigator) **WITHDRAWAL/DROPOUT** Described
Participants	N: 75 Treatment duration: 6 wks; FU: 6 wks LF: 10 (13.3%) BC: yes, within-patient design but comparability of lesions at baseline not reported Age: 44.5 (14.5SD: range = 18.8 to 70.7) Gender (per cent men): 53% Severity: not reported

Ortonne 2003 *(Continued)*

	INCLUSION CRITERIA • People with stable chronic plaque psoriasis, localised on 'sensitive areas': face, hairline, retro-auricular, and flexural areas • Aged 18 to 70 • 1 to 4 bilateral lesions of similar severity **EXCLUSION CRITERIA** • Pregnancy or risk thereof • Lactation • Concomitant disease • Acute guttate, pustular, erythrodermic, or arthropathic psoriasis • History of hypercalcaemia, renal dysfunction • Calcium-based calculi • Conditions requiring systemic supplements of vitamin D or calcium • Previous topical therapy within previous 2 wks (4 wks for retinoids) • Previous systemic therapy within previous 4 wks (16 wks for retinoids)
Interventions	• Calcitriol ointment 3 mcg/g BD (C1) • Calcipotriol ointment 50 mcg/g BD (C2)
Outcomes	1. Investigator's Global Assessment of local safety for each lesion (3-pt: 0 = poor to 2 = excellent) 2. Mean of worst sign scores (0 to 9) (signs: perilesional erythema; perilesional oedema; stinging/burning) 3. Investigator's Global Assessment of Improvement (IAGI) (7-pt: worse to clear) 4. Patient's preference for tolerance, efficacy, and global preference (5-pt: right-hand side (RHS) > left-hand side (LHS): -2 to LHS > RHS: 2)
Notes	The trial did not report sponsorship, but 2 authors worked for Galderma, France This was an inverse psoriasis trial. There was SD imputation (TSS).

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Allocation concealment (selection bias)	Unclear risk	The trial reported insufficient details.
Blinding (performance bias and detection bias) All outcomes	Low risk	The trial was single-blind (investigator).
Randomisation method reported	Low risk	A computer-generated block list was used for randomisation.
Loss to follow up	Low risk	13.3%
Baseline assessments	Low risk	These were partially done.
Baseline comparability demonstrated	Unclear risk	This was partially demonstrated.

Ortonne 2004

Methods	**DESIGN** Between-patient Participant delivery **ALLOCATION** Random Method of randomisation: computer-generated randomisation schedule Concealment: unclear **BLINDING** Double-blind (participant/investigator) **WITHDRAWAL/DROPOUT** Described
Participants	N: 501 Treatment duration: 8 wks; FU: 8 wks LF: 21 (4.2%) BC: yes Age: 51.2 (15.0SD, N = 501) Gender (per cent men): 54.9% Severity: PASI = 9.8 (6.1SD, N = 501) Duration (yrs): 19.4 (14.6SD, N = 501) **INCLUSION CRITERIA** • Stable chronic plaque psoriasis amenable to topical treatment • Aged 18 and over **EXCLUSION CRITERIA** • Pregnancy or risk thereof • Lactation • Unstable psoriasis or other inflammatory diseases • Abnormality of calcium metabolism or hypercalcaemia • Systemic or phototherapy within previous 4 wks • Topical therapy within previous 2 wks • Other topical therapy for trunk or limbs during study period • Corticosteroid treatment of scalp (WHO: class IV) or facial area (WHO: class III/IV) during study period
Interventions	• TCP ointment ON for 4 wks then calcipotriol ointment 50 mcg/g ON for 4 wks (A) • Tacalcitol ointment 4 mcg/g ON for 8 wks (T) • TCP: calcipotriol 50 mcg/g, plus betamethasone dipropionate 0.5 mg/g ointment
Outcomes	1. PASI: mean % reduction 2. IAGI (6-pt: worse to clearance) 3. PAGI (6-pt: worse to clearance)
Notes	Leo Pharmaceutical Products sponsored the trial.

Risk of bias

Bias	Authors' judgement	Support for judgement

Ortonne 2004 *(Continued)*

Allocation concealment (selection bias)	Unclear risk	The trial reported insufficient details.
Blinding (performance bias and detection bias) All outcomes	Low risk	The trial was double-blind (participant/investigator).
Randomisation method reported	Low risk	Randomisation was computer-generated.
Loss to follow up	Low risk	4.2%
Baseline assessments	Low risk	-
Baseline comparability demonstrated	Low risk	-

Ortonne 2006

Methods	**DESIGN** Between-patient Participant delivery **ALLOCATION** Random Method of randomisation: generated by sponsor; stratified by centre (N = 16); Concealment: unclear **BLINDING** Single-blind (investigator); as cream and gel were compared, it was not possible to blind participants **WITHDRAWAL/DROPOUT** Described
Participants	N: 124 Treatment duration: 12 wks; FU: 14 wks LF: 0 (0%) BC: yes Age: 48.2 (14.8SD); range = 18 to 82 Gender (per cent men): 68.5% Ethnicity (per cent white): 96.0% Severity: per cent BSA = 6.3 ((2.2SD), range = 1% to 10%; LPSI (0 to 12) = 7.2 (1.7SD), range = 4 to 12; PASI (range NS) = 7.1 (3.7SD), range = 1.4 to 21.8 Duration (yrs): 18.9 (13.9SD); range = 0.7 to 69.3 **INCLUSION CRITERIA** • People aged > = 18 with mild to moderate stable plaque psoriasis • Per cent BSA < = 10% • Target lesion on extremities or trunk between 40 and 200 cm^2 • LPSI > = 5 **EXCLUSION CRITERIA**

Ortonne 2006 *(Continued)*

	• Intranasal or inhaled corticosteroids, systemic, and topic corticosteroids, phototherapy, topical antipsoriatic therapies • Immunosuppriessive drugs, chemotherapy agents, systemic drugs with potential to alter tacrolimus concentrations, lithium, beta blockers, antimalarials, other medicated topical agents
Interventions	• Calcipotriol 0.005% ointment BD (C) • Tacrolimus 0.3% gel BD or 0.5% tacrolimus cream BD (T) There were10 to 14 hours between applications; lesions were treated for 7 days following clearance. Participants were randomised to tacrolimus cream or gel; results were aggregated for review purposes.
Outcomes	1. Local Psoriasis Severity Index (LPSI) (erythema, induration, scaling): 0 to 12 2. Physician assessment of clinical response of target lesion: IAGI: 5-pt = 0 (worse) to 4 (much better) 3. Subject's assessment of clinical response of target lesion: PAGI: 5-pt = 0 (worse) to 4 (much better) 4. Compliance (median daily medication usage) 5. Cosmetic acceptability (participant) 6. Adverse events and clinical laboratory evaluations
Notes	Fujisawa GmbH, Munich, Germany, sponsored the trial. Vissers 2008 (secondary reference under Ortonne 2006) reports immunohistochemistry findings for subgroup (N = 18).

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Unclear risk	The trial reported insufficient details.
Blinding (performance bias and detection bias) All outcomes	Unclear risk	The study was single-blind (investigator); as the cream and gel were compared, it was not possible to blind participants.
Randomisation method reported	Low risk	Randomisation was generated by the sponsor and stratified by centre.
Loss to follow up	Low risk	0%
Baseline assessments	Low risk	These were reported.
Baseline comparability demonstrated	Low risk	This was demonstrated.

Ortonne 2010

Methods	**DESIGN** Between-patient Participant delivery **ALLOCATION** Random Method of randomisation: pre-planned computer-generated schedule Concealment: unclear **BLINDING** Double-blind (participant/investigator)

Ortonne 2010 *(Continued)*

	WITHDRAWAL/DROPOUT Described
Participants	N: 408 Treatment duration: 8 wks; FU: 8 wks LF: 9 (2.2%) BC: yes Age: 45.6; range = 18 to 86 Gender (per cent men): 54.7% Ethnicity (per cent white): 97.8% Severity: PASI = 9.6, range = 0.9 to 32.7; IGA moderate = 68.6% Duration (yrs): 17.7; range = 0 to 70 **INCLUSION CRITERIA** • People aged > = 18 with chronic plaque psoriasis amenable to topical treatment • % face affected >10% • % 1 of more body areas affected > = 10% • IGA at least mild **EXCLUSION CRITERIA** • Pregnancy or risk thereof • Lactation • Unstable forms of psoriasis in treatment areas • Other skin condition that could affect assessment • PUVA or systemic therapy within previous 4 wks • UVB or topical therapy on trunk, limbs, or face within previous 2 wks • Treatment of scalp psoriasis with very potent (WHO group IV) corticosteroids or vitamin D analogues • Known or suspected abnormality in calcium homeostasis
Interventions	• Calcipotriol 25 mcg/g ointment OD (C25) • Calcipotriol 25 mcg/g ointment plus hydrocortisone 10 mg/g ointment, OD (C25H) • Calcipotriol 50 mcg/g ointment OD (C50) • Calcipotriol 50 mcg/g ointment plus hydrocortisone 10 mg/g ointment OD (C50H)
Outcomes	Outcomes were assessed for the face and body overall and for the face only: 1. PASI (per cent change from baseline to EOT): face = 0 to 3.6; face + body = 0 to 68.4 [1] 2. Investigator's Global Assessment of Disease Severity (IGA): 6-pt = absence of disease to very severe disease 3. Adverse events 4. Compliance (self-report)
Notes	Leo Pharma A/S sponsored the trial. The sponsor supplied unpublished data.

Risk of bias

Bias	Authors' judgement	Support for judgement

Ortonne 2010 *(Continued)*

Allocation concealment (selection bias)	Unclear risk	The trial reported insufficient details.
Blinding (performance bias and detection bias) All outcomes	Low risk	The trial was double-blind (participant/investigator).
Randomisation method reported	Low risk	A preplanned computer-generated schedule was used.
Loss to follow up	Low risk	2.2%
Baseline assessments	Low risk	These were reported.
Baseline comparability demonstrated	Low risk	This was demonstrated.

Papakostantinou 2005

Methods	**DESIGN** Between-patient Participant delivery **ALLOCATION** Random Method of randomisation: not stated Concealment: unclear **BLINDING** Double-blind (participant/investigator) **WITHDRAWAL/DROPOUT** Described
Participants	N: 22 Treatment duration: 2 wks; FU: 2 wks LF: 0 (0%) BC: no Age: 41.3 (3.94SD) Gender (per cent men): 45.5% Severity: NS **INCLUSION CRITERIA** • People with mild or moderate plaque psoriasis • PASI (0 to 72) < = 10 • Elbow lesions for treatment > = 5 cm diameter **EXCLUSION CRITERIA** • Antipsoriatic therapy within previous 4 wks
Interventions	• Theophylline 1% ointment BD (T) • Vehicle ointment (20% transcutol, 10% oleic acid) BD (P)

Papakostantinou 2005 *(Continued)*

Outcomes	1. PASI (0 to 72)
Notes	The sponsor was not stated.

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Unclear risk	The trial reported insufficient details (abstract only).
Blinding (performance bias and detection bias) All outcomes	Low risk	The trial was double-blind (participant/investigator).
Randomisation method reported	Unclear risk	The trial did not report this.
Loss to follow up	Low risk	0%
Baseline assessments	Unclear risk	The trial did not report this (but this was a within-patient study, so demographics will be comparable by definition).
Baseline comparability demonstrated	Unclear risk	This was not demonstrated (see comment above).

Papp 2003 (H)

Methods	**DESIGN** Between-patient Participant delivery **ALLOCATION** Random Method of randomisation: computer-generated random code Concealment: adequate **BLINDING** Double-blind (participant/assessor) **WITHDRAWAL/DROPOUT** Described
Participants	N: 1043 Treatment duration: 4 wks; FU: 4 wks LF: 15 (1.4%) BC: yes Age: 47.1 Gender (per cent men): 58.4% Severity: mean PASI = 10.8 (range = 1 to 36) Duration: 18.7 years **INCLUSION CRITERIA**

Papp 2003 (H) *(Continued)*

- Chronic plaque psoriasis
- Aged at least 18
- BSA ≥10%

EXCLUSION CRITERIA

- Other types of psoriasis or skin diseases
- Hypercalcaemia
- Systemic antipsoriatic treatment or UV therapy within previous 6 wks
- Topical antipsoriatic therapy within previous 2 wks
- Other concomitant medication that might affect psoriasis
- Contraindications for corticosteroid treatment
- Planned exposure to UV light
- Pregnancy
- Lactation

Interventions	• Calcipotriol 50 mcg/g + betamethasone dipropionate 0.5 mg/g combination ointment BD (D) • Calcipotriol 50 mcg/g in combination vehicle ointment BD (C) • Betamethasone dipropionate 0.5 mg/g in combination vehicle ointment BD (B) • Placebo (combination vehicle) ointment BD (P)
Outcomes	1. PASI (head excluded) 2. Total Severity Score (9-pt, absent to very severe) 3. IAGI (6-pt: worse to clearance) 4. PAGI (6-pt: worse to clearance)
Notes	Leo Pharmaceuticals sponsored the trial.

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Low risk	Treatments were assigned by computer-generated code and assigned chronologically at each centre.
Blinding (performance bias and detection bias) All outcomes	Low risk	The trial was double-blind (participant/investigator). Treatments were identifiable only by a code number.
Randomisation method reported	Low risk	Randomisation was computer-generated. (3:3:3:1)
Loss to follow up	Low risk	1.4%
Baseline assessments	Low risk	-
Baseline comparability demonstrated	Low risk	-

Papp 2003 (P)

Methods	**DESIGN** Between-patient Participant delivery

Papp 2003 (P) *(Continued)*

ALLOCATION
Random
Method of randomisation: computer-generated random code
Concealment: adequate
BLINDING
Double-blind (participant/investigator)
WITHDRAWAL/DROPOUT
Described

Participants	N: 1043 Treatment duration: 4 wks; FU: 4 wks LF: 15 (1.4%) BC: yes Age: 47.1 Gender (per cent men): 58.4% Severity: mean PASI = 10.8 (range = 1 to 36) Duration: 18.7 years **INCLUSION CRITERIA** • Chronic plaque psoriasis • Aged at least 18 • BSA ≥10% **EXCLUSION CRITERIA** • Other types of psoriasis or skin diseases • Hypercalcaemia • Systemic antipsoriatic treatment or UV therapy within previous 6 wks • Topical antipsoriatic therapy within previous 2 wks • Other concomitant medication that might affect psoriasis • Contraindications for corticosteroid treatment • Planned exposure to UV light • Pregnancy • Lactation
Interventions	• Calcipotriol 50 mcg/g + betamethasone dipropionate 0.5 mg/g combination ointment BD (D) • Calcipotriol 50 mcg/g in combination vehicle ointment BD (C) • Betamethasone dipropionate 0.5 mg/g in combination vehicle ointment BD (B) • Placebo (combination vehicle) ointment BD (P)
Outcomes	1. PASI (head excluded) 2. Total Severity Score (9-pt, absent to very severe) 3. IAGI (6-pt: worse to clearance) 4. PAGI (6-pt: worse to clearance)
Notes	Leo Pharmaceuticals sponsored the trial.

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Low risk	Treatments were assigned by computer-generated code and assigned chronologically at each centre.
Blinding (performance bias and detection bias)	Low risk	The trial was double-blind (participant/investigator), and treatments were identifiable only by a code number.

Papp 2003 (P) *(Continued)*
All outcomes

Randomisation method reported	Low risk	Randomisation was computer-generated. (3:3:3:1)
Loss to follow up	Low risk	1.4%
Baseline assessments	Low risk	-
Baseline comparability demonstrated	Low risk	-

Pariser 1996

Methods	**DESIGN** Between-patient Participant delivery **ALLOCATION** Random Method of randomisation: not reported Concealment: unclear **BLINDING** Double-blind (participant/assessor) **WITHDRAWAL/DROPOUT** Not described
Participants	N: 235 Treatment duration: 8 wks; FU: 8 wks LF: Unclear BC: psoriasis comparable, demographics not reported. Age: 45.1 (range = 18 to 86) Gender (per cent men): not reported Severity: TSS (0 to 9) = 4.75 **INCLUSION CRITERIA** • Stable plaque-type psoriasis; otherwise healthy, non-pregnant people • At least 4/9 for plaque elevation • BSA range = 5% to 20% **EXCLUSION CRITERIA** • None reported
Interventions	• Calcipotriene ointment 0.005% OD (C) • Placebo (vehicle) (P)
Outcomes	1. Severity (scaling; erythema; plaque elevation) 2. TSS (0 to 9) 3. Investigator Global Assessment (10-pt)
Notes	Bristol-Myers Squibb Pharmaceutical Research Institute sponsored the trial.

Pariser 1996 *(Continued)*

There was SD imputation (TSS).

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Unclear risk	The trial reported insufficient details.
Blinding (performance bias and detection bias) All outcomes	Low risk	The trial was double-blind (participant/assessor).
Randomisation method reported	Unclear risk	The trial did not report this.
Loss to follow up	Unclear risk	The trial did not report this.
Baseline assessments	Low risk	These were partially done.
Baseline comparability demonstrated	Unclear risk	This was partially demonstrated.

Pauporte 2004

Methods	**DESIGN** Between-patient Participant delivery **ALLOCATION** Random Method of randomisation: not reported Concealment: unclear **BLINDING** Double-blind (participant/investigator) **WITHDRAWAL/DROPOUT** Described
Participants	N: 89 Treatment duration: 3 wks; FU: 4 wks LF: 4 (4.5%) BC: yes Age: 46 (15SD) Gender (per cent men): 44.8% Severity: TSS (0 to 9) = 7.15 **INCLUSION CRITERIA** • Moderate to severe scalp psoriasis, stable, or slowly exacerbating > 1 wk • Aged ≥12 • Good general health • Scalp involvement ≥ 20% • TSS (0 to 9) ≥ 6

Pauporte 2004 *(Continued)*

	EXCLUSION CRITERIA • Pregnancy or risk thereof • Lactation • People requiring topical or systemic treatments that could affect psoriasis • Systemic corticosteroids within previous 4 wks • Topical therapies within previous 1 wk • Concomitant use of other scalp therapies
Interventions	• Fluocinolone acetonide 0.01% topical oil (Derma-Smoothe/FS), plus occlusion ON or for at least 4 hours (F) • Placebo oil, plus occlusion ON or for at least 4 hours (P) Participants washed their hair with a non-medicated shampoo after treatment.
Outcomes	1. Total Severity Score (0 to 9) (erythema, thickening, scaling) 2. Investigator's Assessment of Global Improvement (IAGI) (7-pt: cleared to exacerbation)
Notes	The trial did not report sponsorship, but the corresponding author worked for Hill Dermaceuticals Inc, US. To be eligible for inclusion in the efficacy analysis, participants were permitted to deviate from the treatment plan < = 2 consecutive days and < = 4/10 days. No case of skin atrophy or telangiectasia were reported. This was a scalp trial.

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Unclear risk	The trial reported insufficient details.
Blinding (performance bias and detection bias) All outcomes	Low risk	The trial was double-blind (participant/investigator).
Randomisation method reported	Unclear risk	The trial did not report this.
Loss to follow up	Low risk	4.5%
Baseline assessments	Low risk	-
Baseline comparability demonstrated	Low risk	-

Perez 1996

Methods	**DESIGN** Within-patient Participant delivery **ALLOCATION** Random Method of randomisation: not reported Concealment: unclear **BLINDING**

Perez 1996 *(Continued)*

	Double-blind (participant/investigator) **WITHDRAWAL/DROPOUT** Described
Participants	N: 84 Treatment duration: 10 wks: FU: 52 wks LF: 0 (0%) BC: yes Age: 46 (range = 19 to 76) Gender (per cent men): 65.5% Severity: TSS (0 to 9) = 7.6 (range = 5 to 9) **INCLUSION CRITERIA** • Stable plaque or erythrodermic psoriasis • Unsatisfactory response to at least 1 previous treatment (topical steroids/UVB/PUVA/MTX) • Adult • BSA ≥10% **EXCLUSION CRITERIA** • Pregnant, nursing, or inadequate contraception • Hepatic or renal impairment • Recent systemic therapy or phototherapy or topical medications (excluding emollients)
Interventions	• Calcitriol 1.5 mcg/g OD (C) • Placebo (vehicle) (P)
Outcomes	• Severity (erythema; plaque thickness; scaling) • Total Severity Score (0 to 9) • Investigator Global Assessment (5-pt, worse to excellent improvement) • PASI (reported only for participants participating in follow-up study)
Notes	The NIH General Clinical Research Center supported the trial. There was also an uncontrolled follow up study (N = 22) involving large-area administration of calcitriol; 12-month results were based on results from 6 participants.

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Unclear risk	The trial reported insufficient details.
Blinding (performance bias and detection bias) All outcomes	Low risk	The trial was double-blind (participant/investigator).
Randomisation method reported	Unclear risk	The trial did not report this.
Loss to follow up	Low risk	0.0%

Perez 1996 *(Continued)*

Baseline assessments	Low risk	-
Baseline comparability demonstrated	Low risk	-

Pinheiro 1997

Methods	**DESIGN** Between-patient Participant delivery **ALLOCATION** Random Method of randomisation: not reported Concealment: unclear **BLINDING** Open **WITHDRAWAL/DROPOUT** Described
Participants	N: 132 Treatment duration: 8 wks; FU: 8 wks LF: 10 (7.6%) BC: yes Age: 48.2 (range = 17 to 90) Gender (per cent men): 59.1% Severity: per cent severe = 13.6% Duration (yrs): 16.9 (range = 0.5 to 60) **INCLUSION CRITERIA** • Chronic plaque psoriasis • Adult • BSA ≥100 cm^2 **EXCLUSION CRITERIA** • Hypersensitivity to trial medications • Concomitant treatment with Vitamin D/calcium/other relevant agent • Pregnancy • Risk of pregnancy • Lactation • Unable to comply with protocol
Interventions	• Calcipotriol ointment 50 mcg/g BD (C) • Coal tar 5%/allantoin 2%/hydrocortisone cream 0.5% BD (T)
Outcomes	1. Signs (redness; thickness; scaliness) 2. Total Sign Score (0 to 12) 3. Investigator Global Assessment (5-pt: worse to cleared) 4. Area of affected skin (area scales)

Pinheiro 1997 *(Continued)*

	5. Patient evaluation of overall response (VAS)
Notes	Leo Pharmaceuticals sponsored the trial. There was SD imputation (TSS).

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Unclear risk	The trial reported insufficient details.
Blinding (performance bias and detection bias) All outcomes	High risk	The trial was open.
Randomisation method reported	Unclear risk	The trial did not report this.
Loss to follow up	Low risk	7.6%
Baseline assessments	Low risk	-
Baseline comparability demonstrated	Low risk	-

Poulin 2010

Methods	**DESIGN** Between-patient Participant delivery **ALLOCATION** Random Method of randomisation: not stated Concealment: unclear **BLINDING** Double-blind (participant/investigator) **WITHDRAWAL/DROPOUT** Described
Participants	N: 217 Treatment duration: 6 mths; FU: 6 mths LF: 45 (20.7%) BC: yes Age: 50.4; range = 18 to 82 Gender (per cent men): 44.7% Ethnicity (per cent white): 91.2% Severity: GSS = 0 (clear): 10.1%; GSS = 0 (very mild): 33.7%; GSS = 0 (mild): 56.2%; < 20% scalp affected = 76.5%; mPASI = 4.2 (4.2SD) **INCLUSION CRITERIA** • People aged > = 18 with moderate to severe scalp psoriasis (GSS = 3 or 4) eligible for initial phase (4 wks) • Responders (GSS < = 2) eligible for maintenance phase (6 mths) • Topical and systemic wash-out periods required but not specified

Poulin 2010 *(Continued)*

	EXCLUSION CRITERIA • Pregnancy or risk thereof • Lactation • Use of superpotent steroids on body • Body psoriasis requiring systemic therapy.

Interventions	• Open-label initial treatment phase with clobetasol propionate 0.05% shampoo OD for up to 4 wks (N = 288), then participants with GSS < = 2 were randomised to maintenance therapy:
	  • clobetasol propionate 0.05% shampoo, 2 x/wk for 6 mths (CP)
	  • placebo (vehicle) shampoo, 2 x/wk for 6 mths (P)
	• Participants evaluated every 4 wks for relapse (GSS > 2): relapses received clobetasol propionate 0.05% shampoo OD for 4 wks
	  • GSS < = 2: participants re-initiated maintenance therapy
	  • GSS > 2: participants exited the study

Outcomes	1. Global Severity Score (GSS) (6-pt: 0 = clear to 5 = very severe) 2. Extent of disease (6-pt, 0 (none) to 5 (80% to 100%)) (investigator) 3. Signs (investigator): erythema, scaling, thickness (each scored 0 to 4) 4. MPASI (0 to 7.2) 5. Per cent with rebound at first relapse (mPASI > = 125% of baseline score) 6. Pruritis (subject) (0 to 3) 7. No. relapses 8. Atrophy (0 to 2) 9. Telangiectasia (0 to 2) 10.Burning (0 to 2) 11.adverse events 12.HPA axis activity 13.Patient satisfaction
Notes	Galderma Laboratories, LP, sponsored the trial. The trial (JDT) reported findings for a subset with moderate scalp psoriasis. The sponsor supplied unpublished safety data. No useable efficacy data were available.

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Unclear risk	The trial reported insufficient details.
Blinding (performance bias and detection bias) All outcomes	Low risk	The trial was double-blind (participant/investigator).
Randomisation method reported	Unclear risk	The trial did not report this.
Loss to follow up	Unclear risk	20.7%
Baseline assessments	Low risk	These were reported (clinical and demographic).
Baseline comparability demonstrated	Low risk	This was demonstrated.

Powers 2005

Methods	**DESIGN** Between-patient Participant delivery **ALLOCATION** Random Method of randomisation: unclear Concealment: unclear **BLINDING** Double-blind (participant/investigator) **WITHDRAWAL/DROPOUT** Not described
Participants	N: 421 Treatment duration: 8 wks; FU: 8 wks LF: 0 (0%) BC: yes (clinically), demographics NR (abstract) Age: NR Gender (per cent men): NR Per cent white: NR Severity: GSS (0 to 5) = 2.71 (0.45SD) **INCLUSION CRITERIA** • People aged > = 12 with mild to moderate plaque psoriasis • BSA < = 35% **EXCLUSION CRITERIA** • Not reported
Interventions	• Calcitriol 3 mcg/g ointment BD (C) • Placebo ointment BD (P) Max 30 g/day
Outcomes	1. Global Severity Score (GSS) (6-pt: 0 = none to 5 = very severe), dichotomised as success (clear/almost clear) and failure 2. Signs: erythema, scaling, thickness (each scored 0 = absent to 4 = severe) 3. Dermatological Sum Score (DSS) (0 to 12) 4. Pruritus (0 to 4) 5. Investigator Global Improvement score (7-pt: worse to clear) 6. Subject Global Improvement score (7-pt: worse to clear) 7. Routine clinical and safety laboratory parameters including calcium homeostasis (> 10% above upper limit of normal range)
Notes	Galderma Laboratories, LP, sponsored the trial. The sponsor supplied unpublished data. This was an abstract only.

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Unclear risk	The trial reported insufficient details.

Powers 2005 *(Continued)*

Blinding (performance bias and detection bias) All outcomes	Low risk	The trial was double-blind (participant/investigator).
Randomisation method reported	Unclear risk	The trial did not report this.
Loss to follow up	Low risk	0%
Baseline assessments	Unclear risk	Clinical assessments were reported (demographic characteristics was unclear).
Baseline comparability demonstrated	Unclear risk	Clinical comparability was demonstrated (demographic comparability was unclear).

Reygagne 2005

Methods	**DESIGN** Between-patient Participant delivery **ALLOCATION** Random Method of randomisation: computer-generated randomisation list Concealment: unclear **BLINDING** Single-blind (investigator) **WITHDRAWAL/DROPOUT** Described
Participants	N: 151 Treatment duration: 4 wks; FU: 4 wks LF: 0 (0%) BC: yes Age: 45.3 (17.1SD)(range = 10 to 89) Gender (per cent men): 47.0% Per cent white: 98.7% Severity: TSS (0 to 9) = 4.90 (1.74SD); GSS (0 to 5) = 1.50 (0.60SD) Per cent scalp affected: 45% (SD28%) **INCLUSION CRITERIA** • People aged at least 12 with moderate to severe scalp psoriasis (GSS (0 to 5) > = 3 • Affected area on scalp > = 2 cm^2 **EXCLUSION CRITERIA** • Very severe scalp psoriasis requiring systemic treatment • Known allergy to study medications • Immuno-compromised • History of adverse response to topical or systemic steroid therapy • Use of concomitant antipsoriatic therapy, betablockers, lithium, antimalarials or NSAIDs
Interventions	• calcipotriol 0.005% solution BD (C) • clobetasol propionate 0.05% shampoo OD (CP)
Outcomes	1. Global Severity Score (GSS) (6-pt: 0 = none to 5 = very severe)

Reygagne 2005 *(Continued)*

2. Total Severity Score (10-pt: 0 = none to 9 = severe)
3. Pruritus (0 to 3)
4. Per cent scalp area affected
5. Investigator's Global Assessment of Improvement (7-pt: worse to cleared)
6. Subject's Global Assessment of Improvement (7-pt: worse to cleared)
7. Atrophy, telangiectasia; burning sensation (scalp/neck/face) (0 to 3), burning/stinging sensation (eyes) (0 to 3)
8. Adverse events

Notes	Galderma Laboratories, LP, sponsored the trial. The sponsor supplied unpublished data.

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Unclear risk	The trial reported insufficient details.
Blinding (performance bias and detection bias) All outcomes	Unclear risk	The study was single-blind (investigator).
Randomisation method reported	Low risk	A computer-generated randomisation list was used.
Loss to follow up	Low risk	0%
Baseline assessments	Low risk	These were reported.
Baseline comparability demonstrated	Low risk	This was demonstrated.

Ruzicka 1998

Methods	**DESIGN** Between-patient Participant delivery **ALLOCATION** Random Method of randomisation: not stated Concealment: unclear **BLINDING** Double-blind (participant/assessor) **WITHDRAWAL/DROPOUT** Described
Participants	N: 178 Treatment duration: 2 + 4 wks; FU: 14 wks LF: 7 (3.9%) BC: psoriasis comparable, demographics not reported Age: 42 (range = 18 to 80)

Ruzicka 1998 *(Continued)*

	Gender (per cent men): 55.6% Severity: PASI = 6.0 **INCLUSION CRITERIA** • Adults • Chronic plaque-type psoriasis • BSA ≥ 30% • Calcium levels, renal, and liver function within normal range **EXCLUSION CRITERIA** • Pregnancy • Lactation • Recent systemic or UV therapy
Interventions	1. Calcipotriol 0.005% ointment BD 6 weeks (C) 2. Calcipotriol 0.005% ointment BD 2 weeks, then calcipotriol ointment 0.005% OM plus Betamethasone valerate ointment ON 4 weeks (CB)
Outcomes	1. PASI 2. Investigator Global Assessment (6-pt: deterioration to complete healing) 3. Patient evaluation of overall response (5-pt: scale NR)
Notes	The trial did not state sponsorship. Schering AG employed 1 author.

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Unclear risk	The trial reported insufficient details.
Blinding (performance bias and detection bias) All outcomes	Low risk	The trial was double-blind (participant/investigator).
Randomisation method reported	Unclear risk	The trial did not report this.
Loss to follow up	Low risk	3.9%
Baseline assessments	Low risk	These were partially done.
Baseline comparability demonstrated	Unclear risk	This was partially demonstrated.

Salmhofer 2000

Methods	**DESIGN** Within-patient Participant delivery **ALLOCATION** Random

Salmhofer 2000 *(Continued)*

	Method of randomisation: not reported Concealment: NR **BLINDING** Double-blind (participant/assessor) **WITHDRAWAL/DROPOUT** Described
Participants	N: 63 Treatment duration: 4 wks; FU: 8 wks LF: 5 (7.9%) BC: yes Age: 47 (15.4SD, range = 19 to 83) Gender (per cent men): 54.0% Severity: PASI = 5.5 (2.65SD) Duration (months): 141 (124SD) **INCLUSION CRITERIA** • Stable chronic plaque psoriasis • Aged over 19 • Symmetrical lesions **EXCLUSION CRITERIA** • Other types of psoriasis • BSA affected > 30% • Concurrent systemic antipsoriatic therapy • Pregnancy • Lactation • Concurrent infectious disease • Other concurrent dematoses • Hypercalcaemia • Severe hepatic/renal disease
Interventions	• Calcipotriol ointment 5 mcg/g BD (C) • Calcipotriol ointment 5 mcg/g OM plus diflucortolone valerate ointment 0.1%, ON (D)
Outcomes	1. PASI 2. IAGI (7-pt: extreme deterioration to complete healing) 3. PAGI (7-pt: extreme deterioration to complete healing)
Notes	Schering Wien GmbH sponsored the trial.

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Unclear risk	The trial reported insufficient details.
Blinding (performance bias and detection bias)	Low risk	The trial was double-blind (participant/assessor).

Salmhofer 2000 *(Continued)*
All outcomes

Randomisation method reported	Unclear risk	The trial did not report this.
Loss to follow up	Low risk	7.9%
Baseline assessments	Low risk	-
Baseline comparability demonstrated	Low risk	-

Sanchez 2001

Methods	**DESIGN** Between-patient Participant delivery **ALLOCATION** Random Method of randomisation: not reported Concealment: unclear **BLINDING** Unclear **WITHDRAWAL/DROPOUT** Described
Participants	N: 28 Treatment duration: 8 wks; FU: 8 wks LF: 3 (10.7%) BC: yes Age: 49.5 (range = 22 to 73) Gender (per cent men): 50% Severity: PASI = 7.7 (range = 4 to 10) **INCLUSION CRITERIA** • People with plaque type psoriasis **EXCLUSION CRITERIA** • Systemic treatment within previous 4 wks • Topical treatment within previous 2 wks • Known hypersensitivity to sulphides • Hypothyroidism • Lactation
Interventions	• Propylthiouracil cream 5% TD • Calcipotriol ointment 50 mcg/g BD
Outcomes	1. PASI
Notes	The trial did not report sponsorship.

Sanchez 2001 *(Continued)*

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Unclear risk	The trial reported insufficient details.
Blinding (performance bias and detection bias) All outcomes	Unclear risk	The trial did not report this.
Randomisation method reported	Unclear risk	The trial did not report this.
Loss to follow up	Low risk	10.7%
Baseline assessments	Low risk	-
Baseline comparability demonstrated	Low risk	-

Santoianni 2001

Methods	**DESIGN** Between-patient Participant delivery **ALLOCATION** Random Method of randomisation: computer-generated list using block randomisation; pharmacy-dispensed treatments in identical tubes Concealment: unclear **BLINDING** Double-blind (participant/investigator) **WITHDRAWAL/DROPOUT** Described
Participants	N: 85 Treatment duration: 3 wks; FU: 3 wks LF: 4 (4.7%) BC: clinical only Age: 51.9 (range = 18.8 to 88.5) Gender (per cent men): 55.3% Severity: PASI = 6.2 **INCLUSION CRITERIA** • Outpatients with disseminated keratotic plaque psoriasis • Aged over 18 **EXCLUSION CRITERIA** • Not reported

Santoianni 2001 *(Continued)*

Interventions	• Betamethasone 17-valerate 21-acetate plus tretinoine plus salicylic acid OD • Placebo OD
Outcomes	1. PASI 2. IAGI (5-pt: worse to cured) 3. PAGI (5-pt: no change to excellent) 4. Adverse events
Notes	IDI Farmaceuticia SpA sponsored the trial.

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Unclear risk	The trial reported insufficient details.
Blinding (performance bias and detection bias) All outcomes	Low risk	The trial was double-blind (participant/investigator).
Randomisation method reported	Low risk	Randomisation was computer-generated.
Loss to follow up	Low risk	4.7%
Baseline assessments	Low risk	-
Baseline comparability demonstrated	Unclear risk	This was partially demonstrated.

Saraceno 2007

Methods	**DESIGN** Between-patient Participant delivery **ALLOCATION** Random Method of randomisation: computer-generated randomisation schedule; boxes dispensed sequentially Concealment: inadequate **BLINDING** Open **WITHDRAWAL/DROPOUT** Described
Participants	N: 150 Treatment duration: 12 wks; FU: 12 wks LF: 3 (2.0%) BC: yes Age: 47.7 (16.5SD); range = 18 to 83 Gender (per cent men): 66.0%

Saraceno 2007 *(Continued)*

	Severity: per cent BSA = 18.6 (7.6SD), range 2 to 30; PASI = 9.2 (4.8SD), range = 1.6 to 33.0 Duration (yrs): 13.8 (13.4SD); range = 0 to 60.1 **INCLUSION CRITERIA** • People aged > = 18 with mild to moderate plaque psoriasis **EXCLUSION CRITERIA** • Topical therapy within previous 2 wks • Systemic therapy within previous 4 wks • Severe forms of plaque psoriasis • Guttate, erythrodermic, and pustular psoriasis • Cutaneous atrophy • Suspected abnormality in calcium homeostasis • Pregnancy • Lactation
Interventions	• Calcipotriol 50 mcg/g cream BD (C) • Calcipotriol 50 mcg/g plus betamethasone dipropionate 0.5 mg/g formulation (4 weeks) OD then calcipotriol 50 mcg/g cream (8 weeks) BD (C-B)
Outcomes	1. PASI (scale NR) 2. Skindex-29: burden of symptoms; social functioning; quality of life
Notes	Prodotti Formenti Srl, Milano, Italy, sponsored the trial.

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	High risk	Consecutive coded treatment boxes were assigned to participants in a 1:1 ratio. It was unclear if boxes were of identical appearance.
Blinding (performance bias and detection bias) All outcomes	High risk	The trial was open.
Randomisation method reported	Low risk	A computer-generated randomisation schedule was used.
Loss to follow up	Low risk	2.0%
Baseline assessments	Low risk	These were reported (clinical and demographic).
Baseline comparability demonstrated	Low risk	This was demonstrated (clinical and demographic).

Scarpa 1994

Methods	**DESIGN** Between-patient Delivery unclear **ALLOCATION** Random

Scarpa 1994 *(Continued)*

	Method of randomisation: not reported Concealment: unclear **BLINDING** Blinding unclear **WITHDRAWAL/DROPOUT** Not described
Participants	N: 160 Treatment duration: 6 wks; FU: 10 wks LF: not reported BC: demographics comparable, severity not reported Age: 50 Gender (per cent men): 68.1% Severity: not reported **INCLUSION CRITERIA** • Plaque-type psoriasis **EXCLUSION CRITERIA** • Not reported
Interventions	• Calcipotriol ointment 50 mg/g BD (C) • Betamethasone dipropionate ointment 0.05% + salicylic acid 3% BD (B)
Outcomes	1. Investigator Global Assessment (5-pt: null to excellent) 2. Patient's overall acceptance (5-pt: null to excellent)
Notes	The trial did not report sponsorship.

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Unclear risk	The trial reported insufficient details.
Blinding (performance bias and detection bias) All outcomes	Unclear risk	The trial did not report this.
Randomisation method reported	Unclear risk	The trial did not report this.
Loss to follow up	Unclear risk	The trial did not report this.
Baseline assessments	Unclear risk	These were partially done.
Baseline comparability demonstrated	Unclear risk	This was partially demonstrated.

Scarpa 1996

Methods	**DESIGN** Within-patient Delivery unclear **ALLOCATION** Random Method of randomisation: block randomisation (6 participants) Concealment: unclear **BLINDING** Double-blind (participant/investigator) **WITHDRAWAL/DROPOUT** Described
Participants	N: 76 Treatment duration: 6 wks; FU: 8 wks LF: 13 (17.1%) BC: yes Age: not reported Gender (per cent men): not reported Severity: TSS (0 to 12) = 7.92 **INCLUSION CRITERIA** • Chronic plaque psoriasis **EXCLUSION CRITERIA** • Concomitant medications (except emollients, tar shampoo, and salicylic acid) • Topical or systemic steroids • Calcium or vitamin D intake • Antipsoriatic medications
Interventions	• Tacalcitol ointment 4 mcg/g OD (T) • Betamethasone-17-valerate ointment 0.1% OD (B)
Outcomes	1. Severity (erythema; thickness; scaling) 2. Total Severity Score (0 to 12) 3. Comparison of lesions, based on difference in TSS 4. Investigator Global Assessment (6-pt: worsening to healing) 5. Patient assessment of difference
Notes	The trial did not report sponsorship. There was SD imputation (TSS).

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Unclear risk	The trial reported insufficient details.
Blinding (performance bias and detection bias) All outcomes	Low risk	The trial was double-blind (participant/investigator).

Scarpa 1996 *(Continued)*

Randomisation method reported	Low risk	Block randomisation was used.
Loss to follow up	Low risk	17.1%
Baseline assessments	Low risk	These were partially done.
Baseline comparability demonstrated	Low risk	-

Scarpa 1997

Methods	**DESIGN** Within-patient Participant delivery **ALLOCATION** Random Method of randomisation: not reported; tubes labelled left or right and with participant ID number and tube ID number Concealment: unclear **BLINDING** Double-blind (participant/investigator) **WITHDRAWAL/DROPOUT** Described
Participants	N: 157 Treatment duration: 6 wks; FU: 7 wks LF: 23 (14.6%) BC: yes Age: 49 (15SD; N = 134) Gender (per cent men): 65.6% (N = 157) Severity: TSS (0 to 12) = 7.7 **INCLUSION CRITERIA** • Stable chronic plaque psoriasis • Symmetrical lesions • In- and outpatients **EXCLUSION CRITERIA** • Pregnancy • Lactation • Inadequate contraception • Recent systemic, light, or topical therapy • Severe renal failure • Liver and cardiac dysfunction • Hypercalcemia • Hyperphosphoremia • AIDS • Drug addiction

Scarpa 1997 *(Continued)*

Interventions	• Tacalcitol ointment 4 mcg/g OD (T) • Placebo (vehicle) OD (P)
Outcomes	1. Signs: scaling; erythema; scaling 2. TSS (0 to 12) 3. Patient compliance (tube count; tube contents)
Notes	The trial did not report sponsorship, but Istituto Gentili SpA provided medications and appeared to have undertaken the randomisation. There was SD imputation (TSS).

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Unclear risk	The trial reported insufficient details.
Blinding (performance bias and detection bias) All outcomes	Low risk	The trial was double-blind (participant/investigator).
Randomisation method reported	Unclear risk	The trial did not report this.
Loss to follow up	Low risk	14.6%
Baseline assessments	Low risk	-
Baseline comparability demonstrated	Low risk	-

Sears 1997

Methods	**DESIGN** Between-patient Participant delivery **ALLOCATION** Random Method of randomisation: not reported Concealment: unclear **BLINDING** Double-blind (participant/investigator) **WITHDRAWAL/DROPOUT** Described
Participants	N: 190 participants Treatment duration: 3 wks; FU: 3 wks LF: 21 (11%) BC: yes Age: 44 (range = 19 to 73) Gender (per cent men): 47.9%

Sears 1997 *(Continued)*

	Severity: TSS (0 to 9) = 6.0 Duration (yrs): 17 (range = 1 to 56) **INCLUSION CRITERIA** • Mild or moderate psoriasis not spontaneously remitting • Adults aged 18 to 70 • Total Sign Score 3 to 8 **EXCLUSION CRITERIA** • Acute systemic illness • Hypothamic-pituitary-adrenal system disorder, severe hepatic or renal disorder • Psoriatic infection • Lactation, pregnancy, or inadequate contraception • Recent use of any corticosteroid, long-acting antihistamines, retinoids • Drugs exacerbating or influencing psoriasis • Antimetabolic therapy • PUVA • ACE inhibitor • Intolerant of topical corticosteroids or study medication
Interventions	• Hydrocortisone buteprate 0.1% cream BD (H) • Placebo (vehicle) (P)
Outcomes	1. Signs (erythema; skin thickening; scaling) 2. Total Sign Score (0 to 9) 3. Pruritis 4. Investigator and patient evaluations of efficacy (4-pt: poor to excellent) 5. Investigator Global Assessment (7-pt: exacerbation to cleared) 6. Compliance (actual vs. expected usage)
Notes	The trial did not report sponsorship.

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Unclear risk	The trial reported insufficient details.
Blinding (performance bias and detection bias) All outcomes	Unclear risk	The trial was double-blind (participant/investigator).
Randomisation method reported	Unclear risk	The trial did not report this.
Loss to follow up	Low risk	11%
Baseline assessments	Low risk	These were reported.
Baseline comparability demonstrated	Low risk	-

Seidenari 1997 (H)

Methods	**DESIGN** Within-patient Participant delivery **ALLOCATION** Random Method of randomisation: not reported Concealment: unclear **BLINDING** Double-blind (participant/assessor) **WITHDRAWAL/DROPOUT** Described
Participants	N: 14 Treatment duration: 6 wks; FU: 8 wks LF: 3 (21.4%) BC: yes Age: 46 (range 23 to 69, N = 26) Gender (per cent men): 46.2% (N = 26) Severity: TSS = 6.31 (1.25SD, N = 11) **INCLUSION CRITERIA** • Symmetrical, stable psoriatic plaques • Adult • Inpatient or outpatients **EXCLUSION CRITERIA** • Recent topical, UV, or systemic therapy • Inadequate contraception
Interventions	• Tacalcitol ointment 4 mcg/g OD (T) • Betamethasone valerate ointment 0.1% OD (B)
Outcomes	1. Signs: erythema; thickening; scaling 2. Total Sign Score (0 to 12)
Notes	Demographic characteristics were summarised over both studies, placebo and active controls (N = 26).

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Unclear risk	The trial reported insufficient details.
Blinding (performance bias and detection bias) All outcomes	Low risk	The trial was double-blind (participant/assessor).
Randomisation method reported	Unclear risk	The trial did not report this.

Seidenari 1997 (H) *(Continued)*

Loss to follow up	Unclear risk	21.4%
Baseline assessments	Low risk	These were reported.
Baseline comparability demonstrated	Low risk	-

Seidenari 1997 (P)

Methods	**DESIGN** Within-patient Participant delivery **ALLOCATION** Random Method of randomisation: not reported Concealment: unclear **BLINDING** Double-blind (participant/assessor) **WITHDRAWAL/DROPOUT** Described
Participants	N: 12 Treatment duration: 6 wks; FU: 8 wks LF: 1 (8%) BC: yes Age: 46 (range 23 to 69, N = 26) Gender (per cent men): 46.2% (N = 26) Severity: TSS = 6.50 (0.76SD, N = 11) **INCLUSION CRITERIA** • Symmetrical, stable psoriatic plaques • Adult • Inpatient or outpatients **EXCLUSION CRITERIA** • Recent topical, UV, or systemic therapy • Inadequate contraception
Interventions	• Tacalcitol ointment 4 mcg/g OD (T) • Placebo (vehicle) (P)
Outcomes	1. Signs: erythema; thickening; scaling 2. Total Sign Score (0 to 12)
Notes	Demographic characteristics were summarised over both studies, placebo and active controls (N = 26).

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Allocation concealment (selection bias)	Unclear risk	The trial reported insufficient details.

Seidenari 1997 (P) *(Continued)*

Blinding (performance bias and detection bias) All outcomes	Low risk	The trial was double-blind (participant/assessor).
Randomisation method reported	Unclear risk	The trial did not report this.
Loss to follow up	Low risk	8.0%
Baseline assessments	Low risk	These were reported.
Baseline comparability demonstrated	Low risk	-

Shuttleworth 1998

Methods	**DESIGN** Between-patient Participant delivery **ALLOCATION** Random Method of randomisation: predetermined randomisation schedule in blocks of 10 Concealment: unclear **BLINDING** Double-blind (participant/investigator) **WITHDRAWAL/DROPOUT** Described
Participants	N: 40 Treatment duration: 4 wks; FU: 4 wks LF: 3 (7.5%) BC: yes Age: 41.4 (12.0SD) Gender (per cent men):60.0% Severity: investigator's overall assessment (0 to 9) = 4.85; patient's overall assessment (0 to 4) = 2.43 **INCLUSION CRITERIA** • Scalp psoriasis • Aged 18 to 70 **EXCLUSION CRITERIA** • Pregnancy • Lactation • Inadequate contraception • Known hypersensitivity to study medication • Participation in other study within previous month • Concurrent systemic medication likely to affect psoriasis • Photosensitivity; PUVA within previous 2 wks • 'helmet' (diffuse) psoriasis

Shuttleworth 1998 *(Continued)*

	• Concurrent topical antipsoriatics • Eye disease
Interventions	• Ciclopirox olamine shampoo 1.5% 3 times/wk • Placebo shampoo 3 times/wk
Outcomes	1. IAGI (7-pt: very much worse to completely cleared) 2. Area affected 3. Investigator's overall assessment (extent of scalp psoriasis) (10-pt: normal to ≥ 75% scaling) 4. Scaling (0 to 4.5) 5. Pruritis 6. Patient overall assessment (5-pt: poor to excellent) 7. Adverse events
Notes	Stiefel Laboratories sponsored the trial. The study was underpowered to detect a statistically significant difference due to recruitment difficulties. This was a scalp trial.

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Unclear risk	The trial reported insufficient details.
Blinding (performance bias and detection bias) All outcomes	Low risk	The trial was double-blind (participant/investigator).
Randomisation method reported	Low risk	Block randomisation was used.
Loss to follow up	Low risk	7.5%
Baseline assessments	Low risk	-
Baseline comparability demonstrated	Low risk	-

Staberg 1989

Methods	**DESIGN** Within-patient Delivery unclear **ALLOCATION** Random Method of randomisation: not reported Concealment: unclear **BLINDING** Double-blind (participant/investigator) **WITHDRAWAL/DROPOUT** Described
Participants	N: 10

Staberg 1989 *(Continued)*

	Treatment duration: 6 wks; FU: 6 wks LF: 1 (10%) BC: yes Age: 50 (26 to 76) Gender (per cent men): not reported Severity: TSS (0 to 9) = 7.3 **INCLUSION CRITERIA** • Symmetrical chronic plaque psoriasis • Inpatients • Adult **EXCLUSION CRITERIA** • None reported
Interventions	• Calcipotriol cream 1200 mcg/g BD (C) • Placebo cream (P)
Outcomes	1. Signs: infiltration; erythema; scaling 2. Total Sign Score (0 to 9)
Notes	Leo Pharmaceutical Products supplied the drugs and undertook the statistical analysis.

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Unclear risk	The trial reported insufficient details.
Blinding (performance bias and detection bias) All outcomes	Low risk	The trial was double-blind (participant/investigator).
Randomisation method reported	Unclear risk	The trial did not report this.
Loss to follow up	Low risk	10.0%
Baseline assessments	Low risk	These were partially done.
Baseline comparability demonstrated	Low risk	-

Stein 2001

Methods	**DESIGN** Within-patient Participant delivery **ALLOCATION** Random

Stein 2001 *(Continued)*

	Method of randomisation: investigator undertook randomisation Concealment: inadequate **BLINDING** Double-blind (participant/investigator) **WITHDRAWAL/DROPOUT** Described
Participants	N: 40 Treatment duration: 12 wks; FU: 12 wks LF: 3 (7.5%) BC: unclear Age: range = 20 to 70 + Gender (per cent men): not reported Severity: TSS (elbows) (0 to 12) = 7.0 **INCLUSION CRITERIA** • Mild to moderate symmetrical plaque psoriasis • Aged at least 18 **EXCLUSION CRITERIA** • Systemic treatment within previous 4 wks • Topical treatment within previous 2 wks • Investigational medication within previous 4 wks
Interventions	• Betamethasone valerate foam 0.12% (Luxiq®) BD (B) • Placebo foam BD (P)
Outcomes	1. IAGI (7-pt: worse to completely clear) 2. Composite severity score (sum of change scores in erythema, scaling, thickness) (0 to 12) 3. Pruritis 4. BSA involvement 5. Compliance (weight of containers)
Notes	The Connetics Corporation sponsored the trial. There was SD imputation (IAGI).

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	High risk	Allocation concealment was inadequate: The investigator undertook randomisation.
Blinding (performance bias and detection bias) All outcomes	Unclear risk	The trial was double-blind (participant/investigator).
Randomisation method reported	Unclear risk	The trial did not report this.
Loss to follow up	Low risk	7.5%

Stein 2001 *(Continued)*

Baseline assessments	Low risk	These were partially done.
Baseline comparability demonstrated	Unclear risk	The trial did not report this.

Stuecker 2001

Methods	**DESIGN** Within-patient Participant delivery **ALLOCATION** Random Method of randomisation: not reported Concealment: unclear **BLINDING** Blinding unclear **WITHDRAWAL/DROPOUT** Described
Participants	N: 13 Treatment duration: 12 wks; FU: 12 wks LF: 2 (15.4%) BC: yes Age: 52.9 (12.2SD, range = 38 to 67) Gender (per cent men): 76.9% Severity: PASI = 9.11 (4.88SD, range = 2.20 to 18.70) Duration: 20.8 (12.7SD) **INCLUSION CRITERIA** • Stable psoriasis vulgaris • Aged 18 to 70 **EXCLUSION CRITERIA** • Topical treatment within previous wk • Modification of systemic treatment within previous 3 mths • Pototherapy within previous 6 wks • Known hypersensitivity to study medications • Avocado oil allergy • BSA ≥ 60%
Interventions	• Calcipotriol cream BD • Vitamin B_{12} cream (with avocado oil) BD
Outcomes	1. PASI (modified to exclude head and neck; each side given weighting of 50%) 2. IAGI (4-pt: poor to very good) 3. PAGI (4-pt: poor to very good) 4. Tolerability

Stuecker 2001 *(Continued)*

Notes	Regeneratio Pharma AG sponsored the trial.

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Unclear risk	The trial reported insufficient details.
Blinding (performance bias and detection bias) All outcomes	Unclear risk	The trial did not report this.
Randomisation method reported	Unclear risk	The trial did not report this.
Loss to follow up	Low risk	15.4%
Baseline assessments	Low risk	-
Baseline comparability demonstrated	Low risk	-

Stutz 1996

Methods	**DESIGN** Within-patient Participant delivery **ALLOCATION** Random Method of randomisation: computer-generated randomisation code to allocate sides Concealment: adequate **BLINDING** Double-blind (participant/investigator) **WITHDRAWAL/DROPOUT** Not described
Participants	N: 15 Treatment duration: 3 wks; FU: 3 wks LF: 2 (13.3%) BC: not reported Age: range = 21 to 68 Gender (per cent men): The trial did not report this. Severity: TSS (scale not reported) = 2.8 (0.3SD) **INCLUSION CRITERIA** • Mild plaque psoriasis **EXCLUSION CRITERIA** • Prescription treatments within previous 2 wks

Stutz 1996 *(Continued)*

Interventions	• Polymyxin B cream 200,000 U/g TD • Placebo cream TD
Outcomes	1. Total severity 2. Erythema, scaling, thickness
Notes	Babcock Dermatologic Endowment and the alumni of the Department of Dermatology, University of Michigan Medical Center, MI, sponsored the trial.

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Low risk	Body sites were selected then assigned a computer-generated randomisation code that was concealed from both investigators and participants.
Blinding (performance bias and detection bias) All outcomes	Low risk	The trial was double-blind (participant/investigator).
Randomisation method reported	Low risk	Randomisation was computer-generated.
Loss to follow up	Low risk	13.3%
Baseline assessments	Low risk	These were partially done.
Baseline comparability demonstrated	Unclear risk	The trial did not report this.

Sudilovsky 1981

Methods	**DESIGN** Within-patient Participant delivery **ALLOCATION** Random Method of randomisation: identical tubes allocated by random numbers table Concealment: adequate **BLINDING** Double-blind (participant/investigator) **WITHDRAWAL/DROPOUT** Described
Participants	N: 78 (57% psoriasis) Treatment duration: 3 wks; FU: 3 wks LF: 0% BC: Inadequately reported Age: not reported Gender (per cent men): not reported Severity: not reported

Sudilovsky 1981 *(Continued)*

	INCLUSION CRITERIA • Bilateral lesions of similar severity and duration **EXCLUSION CRITERIA** • Recent corticosteroid medication • History of poor response to corticosteroids • Concomitant local or systemic therapy that could affect psoriasis
Interventions	• Halcinonide cream 0.1% OD + vehicle cream BD (H) • Placebo (vehicle) treatment durations (P)
Outcomes	1. Comparative therapeutic response (3-pt: equal response to markedly superior response) 2. Absolute therapeutic response (4-pt: poor (< 25% improvement) to excellent (75% to 100% improvement)) 3. Investigator Global Assessment: reflects comparative and absolute responses (methodology unclear)
Notes	The Squibb Institute for Medical Research sponsored the trial. Part of a larger study involving participants with atopic dermatitis and trialling other dosages; aggregated demographics were reported.

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Low risk	The part of the study (I or II) and side of the body chosen for treatment were concealed from investigators and determined by random numbers table.
Blinding (performance bias and detection bias) All outcomes	Low risk	The trial was double-blind (participant/investigator).
Randomisation method reported	Unclear risk	The trial did not report this.
Loss to follow up	Low risk	0.0%
Baseline assessments	Unclear risk	The trial did not report these.
Baseline comparability demonstrated	Unclear risk	The trial did not report this.

Sutton 2001

Methods	**DESIGN** Within-patient Participant delivery **ALLOCATION** Random Method of randomisation: not reported Concealment: unclear **BLINDING** Double-blind (participant/investigator) **WITHDRAWAL/DROPOUT** Described

Sutton 2001 *(Continued)*

Participants	N: 53 participants Treatment duration: 8 wks; FU: 12 wks LF: 5 (9.4%) BC: yes Age: range = 26 to 67 Gender (per cent men): 58.5% Severity: duration (yrs) = 2 to 50 **INCLUSION CRITERIA** • Psoriasis • Good general health **EXCLUSION CRITERIA** • Women of childbearing potential • Systemic retinoids within previous 6 mths • NSAIDs, cytostatic agents, or folic acid-containing vitamin preparations within previous mth • Topical or UV treatments within previous 2 wks
Interventions	• Methotrexate gel (Azone®) 1% OD • Placebo gel OD
Outcomes	1. IAGI (6-pt: worse to cleared) 2. Total Severity Score (erythema, thickness, scaling, pruritis) (0 to 20) 3. Adverse events
Notes	Cato Research Ltd and Durham Pharmaceuticals LLC, NC, sponsored the trial. They treated lesions < = 20% BSA.

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Unclear risk	The trial reported insufficient details.
Blinding (performance bias and detection bias) All outcomes	Low risk	The trial was double-blind (participant/investigator).
Randomisation method reported	Unclear risk	The trial did not report this.
Loss to follow up	Low risk	9.4%
Baseline assessments	Low risk	These were partially done.
Baseline comparability demonstrated	Low risk	-

Syed 1996

Methods	**DESIGN** Between-patient Participant delivery **ALLOCATION** Random Method of randomisation: not reported Concealment: unclear **BLINDING** Double-blind (participant/investigator) **WITHDRAWAL/DROPOUT** Described
Participants	N: 60 Treatment duration: 4 wks; FU: 52 wks LF: 0 (0%) BC: yes Age: 25.6 (range = 18 to 50) Gender (per cent men): 60.0% Severity: PASI = 9.3 (range = 4.8 to 16.7) Duration (yrs): 8.5 (range = 1 to 21) **INCLUSION CRITERIA** • Mild-to-moderate chronic plaque-type psoriasis **EXCLUSION CRITERIA** • Pregnancy • Lactation • Cytotoxic drugs • Beta-blockers • Recent systemic medication, UV therapy • Epilepsy
Interventions	• Aloe vera extract 0.5% hydrophilic cream TDS (5 days/wk) • Placebo cream TDS (5 days/wk)
Outcomes	1. PASI 2. Cure rate 3. Significant clearing
Notes	The trial did not report sponsorship. Concomitant water soluble emollients were permitted. SDs were imputed (PASI).

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Unclear risk	The trial reported insufficient details.

Syed 1996 *(Continued)*

Blinding (performance bias and detection bias) All outcomes	Low risk	The trial was double-blind (participant/investigator).
Randomisation method reported	Unclear risk	The trial did not report this.
Loss to follow up	Low risk	0.0%
Baseline assessments	Low risk	-
Baseline comparability demonstrated	Low risk	-

Syed 2001b

Methods	**DESIGN** Between-patient Participant delivery **ALLOCATION** Random Method of randomisation: not reported Concealment: unclear **BLINDING** Double-blind (participant/investigator) **WITHDRAWAL/DROPOUT** Described
Participants	N: 60 participants Treatment duration: 4 wks; FU: 8 wks LF: 0 (0%) BC: yes Age: 29.3 (range = 18 to 70) Gender (per cent men): 61.7% Severity: PASI = 9.8 (range = 5.3 to 17.5) Duration (yrs): 9.6 (range = 1 to 24) **INCLUSION CRITERIA** • Chronic, mild to moderate, plaque type psoriasis • Outpatients • PASI > 4 or BSA > 20% **EXCLUSION CRITERIA** • Topical or systemic corticosteroids or cytotoxic drugs or beta-blockers or phototherapy within previous 3 mths • Pregnancy • Lactation • Alcoholic problems • Concurrent renal, hepatic, or haematological abnormalities

Syed 2001b *(Continued)*

Interventions	• Methotrexate gel (Azone ®) 0.25% BD (5 days/wk) • Placebo gel BD (5 days/wk)
Outcomes	1. PASI 2. Plaques cleared 3. Adverse events 4. Compliance (≤ 40 topical applications during 4-wk period)
Notes	The trial did not report sponsorship. SDs were imputation (PASI).

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Unclear risk	The trial reported insufficient details.
Blinding (performance bias and detection bias) All outcomes	Low risk	The trial was double-blind (participant/investigator).
Randomisation method reported	Unclear risk	The trial did not report this.
Loss to follow up	Low risk	0.0%
Baseline assessments	Low risk	-
Baseline comparability demonstrated	Low risk	-

Tham 1994

Methods	**DESIGN** Within-patient Participant delivery **ALLOCATION** Random Method of randomisation: computer-generated random numbers Concealment: unclear **BLINDING** Single-blind (investigator) **WITHDRAWAL/DROPOUT** Described
Participants	N: 30 Treatment duration: 6 wks; FU: 6 wks LF: 3 (10%) BC: yes Age: 40 (range = 20 to 74) Gender (per cent men): 56.7%

Tham 1994 *(Continued)*

	Ethnicity: Chinese (70.0%), Indian (16.7%), Malay (10.0%), and Sikh (3.3%) Severity: PASI = 6.65 Duration (years): 9.7 (range = 2 to 20) **INCLUSION CRITERIA** • Stable symmetrical chronic plaque-type psoriasis • Adult **EXCLUSION CRITERIA** • Recent systemic or UV therapy • Hypercalcaemia • High calcium or vitamin D intake • Impaired renal or hepatic function • Previous poor response to tar • Concomitant medications
Interventions	• Calcipotriol ointment 50 mcg/g BD (C) • White soft paraffin OM plus coal tar solution BP in aqueous cream 15% ON (T)
Outcomes	1. PASI (modified to exclude head) 2. Severity (erythema; infiltration; desquamation) 3. Investigator Global Assessment (5-pt: worse to cleared) 4. Patient Global Assessment (5-pt: worse to cleared)
Notes	Leo Pharmaceutical Products sponsored the trial.

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Unclear risk	The trial reported insufficient details.
Blinding (performance bias and detection bias) All outcomes	Low risk	The trial was single-blind (investigator).
Randomisation method reported	Low risk	Randomisation was computer-generated.
Loss to follow up	Low risk	10.0%
Baseline assessments	Low risk	-
Baseline comparability demonstrated	Low risk	-

Tyring 2010

Methods	**DESIGN** Between-patient Participant delivery

Tyring 2010 *(Continued)*

ALLOCATION
Random
Method of randomisation: computer-generated schedule (3:1), stratified by ethnicity;
Concealment: adequate
BLINDING
Double-blind (participant/investigator)
WITHDRAWAL/DROPOUT
Described

Participants	N: 177 Treatment duration: 8 wks; FU: 52 wks LF: 0 (0%) (at 8 wks) BC: yes Age: 44.7 (range = 18 to 76) Gender (per cent men): 63.3% Ethnicity: per cent white = 0%; per cent Hispanic/Latino: 56%; per cent black/African American = 44% Severity: scalp IGA (moderate) = 80.2%; scalp IGA (severe/very severe) = 19.8%; TSS (0 to 12) = 6.3, range = 4 to 11 Duration (yrs): 10.8, range = 1 to 50 **INCLUSION CRITERIA** • People aged > = 18 with plaque psoriasis affecting the scalp and limbs/trunk • > = 10% scalp affected • IGA scalp psoriasis at least moderate • Ethnicity: Hispanic/Latino/black/African American **EXCLUSION CRITERIA** • Topical or UV therapy within previous 2 wks • Biological within previous 12 wks • Systemic therapies within previous 4 wks • Erythrodermic, exfoliative, or pustular psoriasis • Skin infections • Skin diseases confounding evaluation of psoriasis • Calcium metabolic disorder or hypercalcaemia • Pregnancy • Lactation
Interventions	• Calcipotriene 50 mcg/g plus betamethasone 0.5 mg/g scalp formulation (gel) OD (C-B) • Placebo gel OD (P) (8 wks) then C-B (44 wks) Maximum of 40 g/wk. Treatment was stopped if scalp psoriasis cleared. Concurrent (scalp) antipsoriatics and 'chemical treatments of the hair' were not permitted. All participants received C-B ointment for trunk/limbs.
Outcomes	1. Investigator Global Assessment of Disease Severity (IGA): 6-pt = clear (0) to very severe (5). Based on written definitions for plaque thickness, scaling, and erythema. 2. Success: IGA < = 1

Tyring 2010 *(Continued)*

	3. Signs (investigator assessment): plaque thickness, scaling and erythema (each scored 0 (none) to 4 (very severe). 4. Total Sign Score (0 to 12) 5. Response criteria: TSS < = 1; PGA < = 1 6. Signs (each): absent 7. Patient Global Assessment of Disease Severity (PGA): 6-pt = clear (0) to very severe (5). Based overall severity and impact on daily life 8. Adverse events 9. Blood pressure 10. Laboratory tests: serum calcium, albumin, blood urea nitrogen, creatinine. 11. Compliance (medication usage)
Notes	Leo Pharma A/S sponsored the trial This was part of a 52-wk study: Following 8 wks of double-blind treatment, all participants received C-B scalp formulation for 44 wks. Data were reported only for the 8-wk end point. The sponsor supplied unpublished data.

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Low risk	Participants were assigned the next consecutive randomisation number available at the site for his/her ethnic category.
Blinding (performance bias and detection bias) All outcomes	Unclear risk	The trial was double-blind (participant/investigator).
Randomisation method reported	Unclear risk	Randomisation was preplanned according to a computer-generated randomisation schedule in a ratio of 3:1, stratified by ethnicity.
Loss to follow up	Unclear risk	0%
Baseline assessments	Low risk	These were reported.
Baseline comparability demonstrated	Unclear risk	This was partially demonstrated (reported means, but not standard, deviations; proportions reported).

Tzung 2005

Methods	**DESIGN** Within-patient Participant delivery **ALLOCATION** Random Method of randomisation: not stated Concealment: unclear **BLINDING** Single-blind (investigator) **WITHDRAWAL/DROPOUT** Described
Participants	N: 23

Tzung 2005 *(Continued)*

	Treatment duration: 12 wks; FU: 16 wks LF: 4 (17.4%) BC: yes Age: 60.2; range = 12 to 80 Gender (per cent men): 91.3% Severity: Signs = mean baseline scores ranged from 2.1 to 2.3 (SD range = 0.71 to 0.80) **INCLUSION CRITERIA** • People with plaque psoriasis attending study centre (veteran's hospital) • Ethnicity: Chinese • Target lesions of at least moderate severity **EXCLUSION CRITERIA** • Topical within previous 2 wks • Oral systemic therapies within previous 6 wks • Phototherapy or sun exposure within previous 4 wks • Unstable psoriasis • Pregnancy • Lactation • Uncontrolled systemic disease
Interventions	• Calcipotriol 0.005% ointment BD (C) • Tazarotene 0.1% gel ON placebo petrolatum ointment OM (T)
Outcomes	1. Adverse events 2. Scaling, plaque elevation, erythema (8 pt: 0 = none to 4 = very severe; 0.5 increments) 3. Patient Assessment of Overall Improvement (PAGI): 5-pt = deterioration to excellent improvement (> 75%)
Notes	The trial did not state the sponsor. The number of adverse events was described, but the number of participants experiencing ADRs was not reported.

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Unclear risk	The trial reported insufficient details.
Blinding (performance bias and detection bias) All outcomes	Unclear risk	The study was single-blind (investigator).
Randomisation method reported	Unclear risk	The trial did not report this.
Loss to follow up	Unclear risk	17.4%
Baseline assessments	Low risk	Clinical assessments were reported (within-patient study, so demographics comparable).

Tzung 2005 *(Continued)*

Baseline comparability demonstrated	Low risk	Clinical comparability was demonstrated.

Vali 2005

Methods	**DESIGN** Within-patient Participant delivery **ALLOCATION** Random Method of randomisation: flip of coin Concealment: unclear **BLINDING** Double-blind (participant/investigator) **WITHDRAWAL/DROPOUT** Described
Participants	N: 42 Treatment duration: 8 wks; FU: 8 wks LF: 3 (7.1%) BC: yes Age: 32 (12.22SD) Gender (per cent men): 66.7% Severity: PASI = 10.86 (5.15SD) **INCLUSION CRITERIA** • People with symmetrical plaque psoriasis • BSA < 20% **EXCLUSION CRITERIA** • Systemic or topical antipsoriatic therapy within previous 4 wks • Pregnancy • Lactation • Use of medications that could affect course of psoriasis
Interventions	• Topical caffeine 10% in Plastibase® TD (C) • Placebo (Plastibase®) TD (P)
Outcomes	1. modified PASI ('regional PASI'): range unclear 2. Adverse events
Notes	The trial did not state the sponsor.

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Unclear risk	The trial reported insufficient details.

Vali 2005 *(Continued)*

Blinding (performance bias and detection bias) All outcomes	Low risk	The trial was double-blind (participant/investigator).
Randomisation method reported	Low risk	Randomisation was by the flip of a coin.
Loss to follow up	Low risk	7.1%
Baseline assessments	Low risk	These were reported.
Baseline comparability demonstrated	Low risk	This was demonstrated.

Van de Kerkhof 1989

Methods	**DESIGN** Within-patient Participant delivery **ALLOCATION** Random Method of randomisation: not reported Concealment: adequate **BLINDING** Double-blind (participant/investigator) **WITHDRAWAL/DROPOUT** Described
Participants	N: 10 Treatment duration: 4 wks; FU: 4 wks LF: 0 (0%) BC: yes Age: range = 28 to 72 Gender (per cent men): 70% Severity: TSS (0 to 9) = 7.2 **INCLUSION CRITERIA** • People with symmetrical chronic stable plaque psoriasis **EXCLUSION CRITERIA** • Topical antipsoriatic therapy within previous 2 wks • Systemic antipsoriatic therapy within previous 1 mth • BSA affected < = 15%
Interventions	• Calcitriol solution 2 mcg/ml BD (C) • Placebo (vehicle) (P)
Outcomes	1. Severity (erythema; thickness; scaling) 2. TSS (0 to 9)

Van de Kerkhof 1989 *(Continued)*

Notes	The trial did not report sponsorship, but Hoffmann-La Roche, Switzerland , employed 1 of the authors. The authors stated that allocation was concealed to the investigator, but provided no justification. Treatment was given at subtherapeutic dose. There was SD imputation (TSS).

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Low risk	A randomisation code was generated centrally and concealed from the investigator until after trial completion.
Blinding (performance bias and detection bias) All outcomes	Low risk	The trial was double-blind (participant/investigator).
Randomisation method reported	Unclear risk	The trial did not report this.
Loss to follow up	Low risk	0.0%
Baseline assessments	Low risk	These were partially done.
Baseline comparability demonstrated	Low risk	-

Van de Kerkhof 1996a

Methods	**DESIGN** Within-patient Participant delivery **ALLOCATION** Random Method of randomisation: not reported Concealment: unclear **BLINDING** Double-blind (participant/investigator) **WITHDRAWAL/DROPOUT** Described
Participants	N: 122 Treatment duration: 8 wks; FU: 12 wks LF: 19 (15.6%) BC: inadequately reported Age: 44.8 (13.69SD) Gender (per cent men): 62.3% Severity: BSA = 5.6% Duration (mths): 233.5 (175.9SD) **INCLUSION CRITERIA**

Van de Kerkhof 1996a *(Continued)*

- Stable plaque psoriasis
- Not localised on the scalp
- BSA: 5.6%
- Score ≥ 2 for erythema and desquamation and Score sum > 5
- White adults and adolescents

EXCLUSION CRITERIA

- Increased serum calcium or serum phosphate level
- Recent systemic or topical antipsoriatic treatment
- Serious disease
- Known allergy to study medication
- Recent participation in another clinical trial
- Expected poor compliance
- Calcium supplements
- Drugs influencing calcium metabolism
- Corticosteroids
- Barbiturates
- Phenytoin
- NSAIDs
- Pregnancy

Interventions	• Tacalcitol 4 mcg/g OD (T) • Placebo (vehicle) (P)
Outcomes	1. Signs: erythema; infiltration; desquamation 2. Total Sign Score (0 to 12) 3. Severity 4. Preference assessment 5. Area of test lesions 6. Investigator Global Assessment (4-pt: poor to very good) 7. Patient Global Assessment (4-pt: poor to very good) 8. Assessment of benefit 9. Post-treatment relapse
Notes	Hermal Kurt Herrmann sponsored the trial. Maximum treatment area: 10% BSA There was SD imputation (TSS).

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Unclear risk	The trial reported insufficient details.
Blinding (performance bias and detection bias) All outcomes	Low risk	The trial was double-blind (participant/investigator).
Randomisation method reported	Unclear risk	The trial did not report this.
Loss to follow up	Low risk	15.6%

Van de Kerkhof 1996a *(Continued)*

Baseline assessments	Low risk	-
Baseline comparability demonstrated	Unclear risk	The trial did not report this.

Van de Kerkhof 2002a

Methods	**DESIGN** Between-patient Participant delivery **ALLOCATION** Random Method of randomisation: not reported Concealment: unclear **BLINDING** Open **WITHDRAWAL/DROPOUT** Described
Participants	N: 88 participants Treatment duration: 4 wks; FU: 5 wks LF: 7 (8.0%) BC: yes Age: not reported Gender (per cent men): not reported Severity: PASI = 16.9 (range = 4.3 to 48.0) **INCLUSION CRITERIA** • Inpatients or outpatients • Aged 18 or over; chronic plaque psoriasis • Scalp involvement **EXCLUSION CRITERIA** • Other forms of psoriasis • Systemic antipsoriatic treatment within previous 6 wks • UV treatment within previous 6 wks • Impaired renal or hepatic function • History of urolithiasis or hypercalciurea • Arthritis • Immobilisation • Hypo- or hyperthyroidism • Heavy exposure to sunlight • Pregnancy • Lactation • Planning of pregnancy
Interventions	• Calcipotriol ointment 50 mcg/g (80 to 100 g/wk) and calcipotriol scalp solution 50 mg/ml (30 to 50 ml/wk) (C)

Van de Kerkhof 2002a *(Continued)*

- Dithranol/tar regimen (D)

Outcomes	1. PASI (scalp assessed separately) 2. TSS (SCALP: erythema, thickness, scaling) (0 to 12) 3. IAGI (6-pt: worse to clearance) 4. PAGI (6-pt: worse to clearance) 5. Adverse events
Notes	Leo Pharmaceutical Products sponsored the trial. The trial included inpatients. The trial reported medication quantities used: "patients complied well". 'High dose' calcipotriol was given (above recommended dosage). IAGI/PAGI: combined scalp/body TSS: scalp only PASI: body only

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Unclear risk	The trial reported insufficient details.
Blinding (performance bias and detection bias) All outcomes	High risk	The trial was open.
Randomisation method reported	Unclear risk	The trial did not report this.
Loss to follow up	Low risk	8.0%
Baseline assessments	Low risk	These were partially done.
Baseline comparability demonstrated	Low risk	-

Van de Kerkhof 2006

Methods	**DESIGN** Between-patient Nurse and participant delivery **ALLOCATION** Random Method of randomisation: computer-generated system using telephone response Concealment: adequate **BLINDING** Open **WITHDRAWAL/DROPOUT** Described
Participants	N: 106

Van de Kerkhof 2006 *(Continued)*

Treatment duration: 12 wks; FU: 12 wks

LF: 0 (0%)

BC: yes

Age (mean): 51.2; range = 25 to 83

Gender (per cent men): 59/100 (reported by de Korte 2008 - this is a secondary reference under Van de Kerkhof 2006); 6 participants missing)

Ethnicity: NR

Severity: mPASI (mean) = 9.9, range = 2.7 to 27.0

INCLUSION CRITERIA

- Outpatients aged > = 18 with plaque psoriasis involving arms, trunk, legs, or a combination of the aforementioned
- Condition amendable to topical treatment
- Target area treatable with < = 100 g calcipotriol/wk
- PASI extent score > = 2 (i.e. BSA (body region) > = 10%)
- Willing/able to comply with study protocol

EXCLUSION CRITERIA

- Acute guttate, generalised pustular, or erythrodermic exfoliative psoriasis
- Atopic dermatitis, seborrhoeic dermatitis, or other inflammatory skin diseases
- Systemic antipsoriatic therapy (including corticosteroids) or phototherapy within previous 6 wks
- Topical antipsoriatic therapy (body) within previous 2 wks
- Planned changes in concurrent medication that could affect psoriasis (e.g. beta-blockers, lithium, etc)
- Pregnancy or risk thereof
- Lactation
- Known or suspected hypercalcaemia
- Hypersensitivity to components of study medication
- Treatment with an investigational drug within previous 3 mths
- Current participation in other clinical trial
- Planned exposure to excessive levels of sun/UV radiation
- Known treatment resistance to study medication

Interventions

- Calcipotriol 50 mcg/g ointment BD (C)
- Short-contact dithranol cream (dose titration from 0.1% to 5%; application time 15 to 45 mins) OD; class II or III corticosteroids for treatment of severe skin irritation (D)
  - wk1: 5 (daily) visits to outpatient clinic
  - wk2 onwards: twice-weekly visits PRN

Participants intolerant of 0.1% dithranol used 0.05% dose.

Cases of extensive hyperkeratosis, scales of participants in both treatment groups could be removed with salicylic acid (5%) in petrolatum before wk 0.

Participants achieving clearance exited the study.

Outcomes

PRIMARY OUTCOMES

1. mPASI (scalp excluded)

SECONDARY OUTCOMES

1. IAGI: Investigator's overall assessment of treatment response: 6-pt (worse to clearance)

Van de Kerkhof 2006 *(Continued)*

	2. PAGI: Patient's overall assessment of treatment response: 6-pt (worse to clearance) 3. Quality of life 4. Adverse events 5. Compliance (per cent using study medication as prescribed)
Notes	Leo Pharma sponsored the trial. Secondary response criteria did not demonstrate a statistically significant difference between treatments. The sponsor supplied unpublished data.

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Low risk	The treatment was assignment using a telephone voice response system, to ensure that the investigators' decision to randomise the participant preceded knowledge of the randomised treatment.
Blinding (performance bias and detection bias) All outcomes	High risk	The trial was open.
Randomisation method reported	Low risk	Randomisation was through a computer-generated system using telephone response.
Loss to follow up	Low risk	0%
Baseline assessments	Low risk	These were reported.
Baseline comparability demonstrated	Unclear risk	This was partially demonstrated (de Korte 2008). There were significantly more men in the dithranol group (72% versus 46%). However, de Korte does not provide data on 6 participants. If all these participants are assumed to be of the gender that minimises between group differences, the difference is almost statistically significant at the 5% level (= 0.0502; Fisher's exact test). This may indicate a flawed randomisation process, or it may be chance. The primary reference does not report variance around mean PASI baseline estimates, so comparability was unclear.

Van de Kerkhof 2009

Methods	**DESIGN** Between-patient Participant delivery **ALLOCATION** Random Method of randomisation: computer-generated schedule (1:2:2) Concealment: unclear **BLINDING** Double-blind (participant/investigator) **WITHDRAWAL/DROPOUT** Described
Participants	N: 1417 Treatment duration: 8 wks; FU: 8 wks

Van de Kerkhof 2009 *(Continued)*

	LF: 2 (0.1%) BC: yes Age: 48.3 (16.4SD); range = 18 to 92 Gender (per cent men): 44.8% Ethnicity (per cent white): 97.2% Severity: IGA (0 to 5) = 3.32 (0.71SD), range = 2 to 5; TSS (0 to 12) = 6.8 (1.8SD) Duration (yrs): 15.9 (13.4SD) **INCLUSION CRITERIA** • People aged > = 18 with scalp psoriasis involving > 10% of the scalp, amenable to treatment with < = 100 g medication/wk **EXCLUSION CRITERIA** • Concomitant topical scalp therapy (except medicated shampoos and emollients) • Planned initiation of/changes to concomitant medication that could affect scalp psoriasis • Use of topical treatment of the face, trunk or limbs with very potent (WHO group IV) corticosteroids or UVB within previous 2 wks • PUVA or grenz ray therapy, planned exposure to the sun, systemic therapy within previous 4 wks • Biological therapy within previous 6 mths • Erythrodermic, exfoliative, or pustular psoriasis • Presence of viral lesions, fungal, or bacterial skin infections, parasitic infections, or atrophic skin on the scalp, known/suspected abnormality of calcium homeostasis associated with clinically significant hypercalcaemia • Severe renal insufficiency • Severe hepatic disorders
Interventions	• Calcipotriol 50 mcg/g gel OD (C) • Betamethasone dipropionate 0.5 mg/g gel OD (B) • Calcipotriol 50 mcg/g plus betamethasone dipropionate 0. 5 mg/g gel (scalp formulation) OD (C-B) Participants achieving IGA = 0 could stop medication during the study.
Outcomes	1. Investigator's Global Assessment of severity of scalp psoriasis (IGA); 6-pt (0 = absence of disease to 5 = very severe disease) 2. Responder: IGA absence or very mild 3. Total Sign Score (erythema, thickness, scaliness): 13-pt (0 to 12) 4. Patient assessment of overall response: 7-pt (worse to clear) 5. Adverse events (local) 6. Laboratory tests for calcium and albumin. 7. Compliance (self report and weight medication used)
Notes	Leo Pharma A/S, Ballerup, Denmark, sponsored the trial. The sponsor supplied unpublished data.

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Unclear risk	The trial reported insufficient details.

Van de Kerkhof 2009 *(Continued)*

Blinding (performance bias and detection bias) All outcomes	Low risk	The trial was double-blind (participant/investigator).
Randomisation method reported	Low risk	A computer-generated randomisation schedule was used (1:2:2).
Loss to follow up	Low risk	0.1%
Baseline assessments	Low risk	These were reported.
Baseline comparability demonstrated	Low risk	This was demonstrated.

Van der Vleuten 1995

Methods	**DESIGN** Within-patient Delivery unclear **ALLOCATION** Random Method of randomisation: not reported Concealment: unclear **BLINDING** Open **WITHDRAWAL/DROPOUT** Described
Participants	N: 10 Treatment duration: 2 wks; FU: 2 wks LF: 0 (0%) BC: inadequately reported Age: range = 20 to 72 Gender (per cent men): 40% Severity: PASI (modified) = 17.1 (2.1SEM) Duration (yrs): 3 to 53 **INCLUSION CRITERIA** • Adult • Inpatient • Severe, disabling psoriasis • Resistant to topical therapy **EXCLUSION CRITERIA** • Recent or concomitant oral antipsoriatic therapy, no topical or systemic treatments except corticosteroids for the scalp and face
Interventions	• Calcipotriol ointment 50 mcg/g BD • Dithranol in paste or petroleum 0.05% to 4%, 24-hour application on alternate days

Van der Vleuten 1995 *(Continued)*

Outcomes	1. PASI (excludes scalp)
Notes	The trial did not report sponsorship. Treatment was delivered in an inpatient setting.

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Unclear risk	The trial reported insufficient details.
Blinding (performance bias and detection bias) All outcomes	High risk	The trial was open.
Randomisation method reported	Unclear risk	The trial did not report this.
Loss to follow up	Low risk	0.0%
Baseline assessments	Low risk	These were partially done.
Baseline comparability demonstrated	Unclear risk	The trial did not report this.

Vanderploeg 1976

Methods	**DESIGN** Between-patient Participant delivery **ALLOCATION** Random Method of randomisation: identical tubes allocated by sequential admission number, corresponding to a standard randomisation schedule using a double-blind code Concealment: adequate **BLINDING** Double-blind (participant/investigator) **WITHDRAWAL/DROPOUT** Described
Participants	N: 36 Treatment duration: 3 wks; FU: 3 wks LF: 3 of 36 (8.3%) BC: yes Age: 45.7 (range = 10 to 66; N = 33) Gender (per cent men): 48.5% (N = 33) Severity: TSS (0 to 20) = 9.9 **INCLUSION CRITERIA** • Psoriasis or atopic dermatitis

Vanderploeg 1976 *(Continued)*

	EXCLUSION CRITERIA • Recent systemic or topical steroids • Concomitant medications
Interventions	• Betamethasone dipropionate ointment 0.05% BD (B) • Vehicle BD (P)
Outcomes	1. Signs: scale; erythema; pruritis; thickness; crusting 2. Total Sign Score (0 to 20) 3. Investigator Global Assessment (5 pt: exacerbation to excellent improvement)
Notes	The trial did not report sponsorship. This was part of a larger trial that included participants with atopic dermatitis (50% psoriasis). There was SD imputation (TSS).

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Low risk	The sequential trial admission number corresponded to the randomisation schedule; the randomisation code was 'double blind'.
Blinding (performance bias and detection bias) All outcomes	Low risk	The trial was double-blind (participant/investigator).
Randomisation method reported	Low risk	Randomisation was sequential.
Loss to follow up	Low risk	8.3%
Baseline assessments	Low risk	-
Baseline comparability demonstrated	Low risk	-

Veien 1997

Methods	**DESIGN** Between-patient Participant delivery **ALLOCATION** Random Method of randomisation: block Concealment: unclear **BLINDING** Double-blind (participant/investigator) **WITHDRAWAL/DROPOUT** Described
Participants	N: 287 Treatment duration: 8 wks; FU: 12 wks LF: 0 (0%)

Veien 1997 *(Continued)*

	BC: psoriasis comparable, demographics inadequately reported Age: 45.0 Gender (per cent men): 53.7% Severity: BSA = 7.9% (range = 1% to 75%); TSS (0 to 12) = 7.59 **INCLUSION CRITERIA** • Adult • Stable plaque psoriasis • TSS > 5 • Erythema ≥ 2, scaling ≥ 2 **EXCLUSION CRITERIA** • Pregnancy • Lactation • High serum calcium, serum phosphate, serum creatinine • Unresponsive to calcipotriol • Intolerant to study ingredients • Serious co-morbidity
Interventions	• Tacalcitol ointment 4 mcg/g OD plus Tacalcitol vehicle OD (T) • Calcipotriol ointment 50 mcg/g BD (C)
Outcomes	1. Severity: erythema; infiltration; scaling; pruritus 2. Total Sign Score (TSS): 0 to12 3. Investigator Global Assessment (6-pt: worse to clear) 4. Patient Global Assessment (scale "virtually identical" to IAGI; details not reported) 5. Patient evaluation of global usefulness (VAS) 6. Patient evaluation of cosmetic acceptability 7. Quantity of medication used 8. Rebound (aggravation equal to or worse than pre-treatment severity)
Notes	Nycomed Pharma sponsored the trial.

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Allocation concealment (selection bias)	Unclear risk	The trial reported insufficient details.
Blinding (performance bias and detection bias) All outcomes	Low risk	The trial was double-blind (participant/investigator).
Randomisation method reported	Low risk	Block randomisation was used.
Loss to follow up	Low risk	0.0%
Baseline assessments	Low risk	-

Veien 1997 *(Continued)*

Baseline comparability demonstrated	Unclear risk	The trial did not report this.

Vladimirov 1994

Methods	**DESIGN** Between-patient Participant delivery **ALLOCATION** Random Method of randomisation: not reported Concealment: unclear **BLINDING** Double-blind (participant/investigator) **WITHDRAWAL/DROPOUT** Not described
Participants	N: 60 Treatment duration: 6 wks; FU: 6 wks LF: 0 (0%) BC: inadequately reported Age: range = 18 to 70 Gender (per cent men): not reported Severity: PASI = 2.92 Duration (yrs): range = 0.2 to 30 **INCLUSION CRITERIA** • Adult • Mild to moderate psoriasis **EXCLUSION CRITERIA** • None reported
Interventions	• Calcipotriol cream 50 mcg/g BD (C) • Betamethasone17-valerate ointment 0.1% BD (B)
Outcomes	1. PASI (range unclear) 2. Investigator Global Assessment (scale NR)
Notes	Leo Pharmaceuticals sponsored the trial. There was SD imputation (PASI).

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Unclear risk	The trial reported insufficient details.

Vladimirov 1994 *(Continued)*

Blinding (performance bias and detection bias) All outcomes	Low risk	The trial was double-blind (participant/investigator).
Randomisation method reported	Unclear risk	The trial did not report this.
Loss to follow up	Low risk	0.0%
Baseline assessments	Low risk	These were partially done.
Baseline comparability demonstrated	Unclear risk	The trial did not report this.

Volden 1992

Methods	**DESIGN** Within-patient Participant delivery **ALLOCATION** Random Method of randomisation: not reported Concealment: unclear **BLINDING** Double-blind (participant/investigator) **WITHDRAWAL/DROPOUT** Described
Participants	N: 10 Treatment duration: 4 wks; FU: 4 wks LF: 1 (10%) BC: yes Age: not reported Gender (per cent men): not reported Severity: BSA = 5% to 15% Duration (mean years): 20 **INCLUSION CRITERIA** • Symmetrical plaque-type psoriasis • Adult outpatients **EXCLUSION CRITERIA** • Recent active treatment for psoriasis
Interventions	• Dithranol 1% in petrolatum (D) • Placebo (vehicle) (P)
Outcomes	1. Signs: erythema; infiltration; scaling 2. Total Sign Score (0 to 12)

Volden 1992 *(Continued)*

Notes	The trial did not report sponsorship, but Hydro Pharma, Swedenone, employed 1 of the authors.

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Unclear risk	The trial reported insufficient details.
Blinding (performance bias and detection bias) All outcomes	Low risk	The trial was double-blind (participant/investigator).
Randomisation method reported	Unclear risk	The trial did not report this.
Loss to follow up	Low risk	10.0%
Baseline assessments	Low risk	These were partially done.
Baseline comparability demonstrated	Low risk	-

Wall 1998

Methods	**DESIGN** Between-patient Participant delivery **ALLOCATION** Random Method of randomisation: not reported Concealment: unclear **BLINDING** Open **WITHDRAWAL/DROPOUT** Not described
Participants	N: 306 Treatment duration: 3 mths LF: 28 (7.2%) BC: yes Age: 46.7 Gender (per cent men): 47.1% Severity: duration (yrs) = 18.7 Signs and extent reported, but not by summary measure **INCLUSION CRITERIA** • Adult • Stable mild-to-moderate chronic plaque psoriasis • BSA ≥100 cm^2 but < 40%

Wall 1998 *(Continued)*

	• Recent GP visit **EXCLUSION CRITERIA** • Acute guttate or pustular psoriasis • Psoriasis of scalp or face only • Recent topical or systemic antipsoriatic therapy • Pregnancy • Lactation; concomitant vitamin D or calcium intake • Hypersensitivity to study medication • Unlikely to comply with protocol
Interventions	• Calcipotriol ointment 50 mcg/g BD (C) • Dithranol 0.1 to 2% OD (D)

Outcomes	1. Investigator assessment of overall clinical response (5-pt: worse to clear)
	2. Patient assessment of overall clinical response (5-pt: worse to clear)
	3. Quality of Life:
	  • Psoriasis Disability Index (PDI)
	  • Sickness Impact Profile (SIP)

Notes	Leo Pharmaceuticals sponsored the trial.

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Unclear risk	The trial reported insufficient details.
Blinding (performance bias and detection bias) All outcomes	High risk	The trial was open.
Randomisation method reported	Unclear risk	The trial did not report this.
Loss to follow up	Low risk	7.2%
Baseline assessments	Low risk	These were partially done.
Baseline comparability demonstrated	Low risk	-

Weinstein 1996

Methods	**DESIGN** Between-patient Participant delivery **ALLOCATION** Random Method of randomisation: not reported Concealment: unclear **BLINDING** Double-blind (participant/investigator)

Weinstein 1996 *(Continued)*

	WITHDRAWAL/DROPOUT Described
Participants	N: 324 Treatment duration: 12 wks; FU: 24 wks LF: 6 (1.9%) BC: yes Age: 46.8 (range = 12 to 83) Gender (per cent men): 67% Severity: per cent BSA = 6.9 (5.2SD); TSS (0 to 12) = 7.3 Duration (yrs): 17.5 (12.7SD) **INCLUSION CRITERIA** • Stable plaque psoriasis • BSA ≤ 20% • 2 target lesions with plaque elevation ≥ 2 and ≥ 2 cm in diameter: 1 on elbow/knee and 1 on trunk/limbs **EXCLUSION CRITERIA** • Pustular or exfoliative psoriasis • Sensitivity to study medication • Other confounding skin conditions • Recent use of tar shampoos • Topical/systemic/light therapies • Topical corticosteroids/UVB • PUVA/systemic therapy • Oral retinoids • Uncontrolled systemic disease • Pregnant • Lactating • Inadequate contraception
Interventions	• Tazarotene gel 0.1% OD • Tazarotene gel 0.05% OD • Placebo (vehicle) (P)
Outcomes	1. Signs: plaque elevation; scaling; erythema 2. Total Sign Score (0 to 12) 3. Per cent clearance 4. Patient assessment of cosmetic acceptability
Notes	Allergan Inc. sponsored the trial. The authors stated that concealment of treatment allocation was achieved for participants and clinicians, as tubes were identical. There was SD imputation (TSS).

Risk of bias

Bias	Authors' judgement	Support for judgement

Weinstein 1996 *(Continued)*

Allocation concealment (selection bias)	Unclear risk	The trial reported insufficient details.
Blinding (performance bias and detection bias) All outcomes	Low risk	The trial was double-blind (participant/investigator).
Randomisation method reported	Unclear risk	The trial did not report this.
Loss to follow up	Low risk	1.9%
Baseline assessments	Low risk	-
Baseline comparability demonstrated	Low risk	-

Weinstein 2003

Methods	**DESIGN** Between-patient Participant delivery **ALLOCATION** Random Method of randomisation: randomised in blocks of 6 Concealment: unclear **BLINDING** Double-blind (participant/investigator) **WITHDRAWAL/DROPOUT** Described
Participants	N: 1303 Treatment duration: 12 wks; FU: 24 wks LF: 411 (31.5%) BC: yes Age: 48.2 (range = 18 to 84) Gender (per cent men): 62.6% Severity: OLA (0 to 5) (mean) = 3.6; BSA affected (mean) = 10.5% Duration (mean yrs): 18.4 **INCLUSION CRITERIA** • Aged ≥18 • BSA ≥ 2%; OLA (0 to 5) ≥ 3 • Acceptable blood or urinary test results **EXCLUSION CRITERIA** • Pregnancy or risk thereof • Lactation • UV or topical therapies within previous 2 wks

Weinstein 2003 *(Continued)*

	• PUVA or systemic therapies within previous 4 wks • Oral retinoid therapy within previous 8 wks • Expected prolonged exposure to UV light
Interventions	• Tazarotene cream 0.05% OD (T1) • Tazarotene cream 0.1% OD (T2) • Placebo (P)
Outcomes	1. Overall lesion assessment (OLA) (0 = none to 5 = very severe), as applied to all treated lesions 2. Clinical success (OLA ≤ 2 at 12 wks) 3. Effectiveness (improvement in OLA from baseline of ≥ 15% relative to placebo improvement score) 4. Overall plaque elevation, scaling and erythema (each scored 0 = none to 4 = severe) 5. Overall global response to treatment (7-pt: completely cleared to worsened) 6. Target lesion response (7-pt: completely cleared to worsened)
Notes	Allergan Inc. sponsored the trial. The paper reported 2 trials; only study A reported follow-up data after 12 weeks (N = 108).

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Unclear risk	The trial reported insufficient details.
Blinding (performance bias and detection bias) All outcomes	Low risk	The trial was double-blind (participant/investigator).
Randomisation method reported	Low risk	Block randomisation was used.
Loss to follow up	High risk	31.5%
Baseline assessments	Low risk	-
Baseline comparability demonstrated	Low risk	-

White 2006 (H)

Methods	**DESIGN** Between-patient Participant delivery **ALLOCATION** Random Method of randomisation: computer-generated schedule Concealment: unclear **BLINDING** Open (acute phase and maintenance phase for CB-W); double-blind (participant/investigator) (maintenance phase for CB-C and CB-P) **WITHDRAWAL/DROPOUT** Described
Participants	N: 1136

White 2006 (H) *(Continued)*

	Treatment duration: 12 wks; FU: 12 wks LF: 0 (0%) BC: yes Age: 50.7; range = 18 to 89 Gender (per cent men): 60.7% Ethnicity (per cent white): 96.9% Severity: per cent BSA = 12.1%; mPASI = 8.9 (3.8SD), range = 2.4 to 30.9; IGA moderate = 76%; IGA severe = 24% Duration (yrs): 0 to 75 **INCLUSION CRITERIA** • People aged > = 18 with plaque psoriasis affecting at least 10% arms, 10% trunk, 10% legs, or a combination of the aforementioned • IGA at least moderate **EXCLUSION CRITERIA** • Erythrodermic, exfoliative, pustular, or guttate psoriasis • Skin infections • Other confounding inflammatory skin disease • Calcium metabolic disorder • Pregnancy • Lactation • Concurrent antipsoriatic therapy
Interventions	• Calcipotriol 50 mcg/g plus betamethasone dipropionate 0.5 mg/g ointment OD (4 wks), then calcipotriol cream 50 mcg/g OD [8 wks] (CB-C) • Calcipotriol 50 mcg/g plus betamethasone dipropionate 0.5 mg/g ointment OD (4 wks), then calcipotriol cream 50 mcg/g OD weekdays, CB ointment OD weekends (8 wks) (CB-W) • Calcipotriol 50 mcg/g plus betamethasone dipropionate 0.5 mg/g ointment OD (4 wks), then placebo cream (calcipotriol vehicle), OD (8 wks) (CB-P)] Use < = 100 g/wk
Outcomes	1. mPASI (0 to 64.8) - per cent change from baseline: rebound: > 125% of baseline; relapse: > 50% reduction in maximum improvement from baseline 2. Investigator's Assessment of disease severity (IGA); 6-pt (absent to very severe) 3. Patient's assessment of overall response (PAGI); 7-pt (worse to clear) 4. Adverse events 5. Compliance (medication usage; self-reported compliance)
Notes	Leo Pharma A/S sponsored the trial. Atrophy was not assessed.

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Unclear risk	The trial reported insufficient details.

White 2006 (H) *(Continued)*

Blinding (performance bias and detection bias) All outcomes	High risk	The trial was open in the acute phase and maintenance phase for CB-W and double-blind (participant/investigator) in the maintenance phase for CB-C and CB-P. It was not possible to blind the alternating group (CB-W), as the vehicles were different.
Randomisation method reported	Low risk	A preplanned computer-generated randomisation schedule was used (1:1:1).
Loss to follow up	Low risk	0%
Baseline assessments	Low risk	These were reported.
Baseline comparability demonstrated	Unclear risk	This was partially demonstrated (reported means, but not standard, deviations; proportions reported).

White 2006 (P)

Methods	**DESIGN** Between-patient Participant delivery **ALLOCATION** Random Method of randomisation: computer-generated schedule Concealment: unclear **BLINDING** Open (acute phase and maintenance phase for CB-W); double-blind (participant/investigator) (maintenance phase for CB-C and CB-P) **WITHDRAWAL/DROPOUT** Described
Participants	N: 1136 Treatment duration: 12 wks; FU: 12 wks LF: 0 (0%) BC: yes Age: 50.7; range = 18 to 89 Gender (per cent men): 60.7% Ethnicity (per cent white): 96.9% Severity: per cent BSA = 12.1%; mPASI = 8.9 (3.8SD), range = 2.4 to 30.9; IGA moderate = 76%; IGA severe = 24% Duration (yrs): 0 to 75 **INCLUSION CRITERIA** • People aged > = 18 with plaque psoriasis affecting at least 10% arms, 10% trunk, 10% legs, or a combination of the aforementioned • IGA at least moderate **EXCLUSION CRITERIA** • Erythrodermic, exfoliative, pustular, or guttate psoriasis • Skin infections

White 2006 (P) *(Continued)*

	• Other confounding inflammatory skin disease • Calcium metabolic disorder • Pregnancy • Lactation • Concurrent antipsoriatic therapy
Interventions	• Calcipotriol 50 mcg/g plus betamethasone dipropionate 0.5 mg/g ointment OD (4 wks), then calcipotriol cream 50 mcg/g OD [8 wks] (CB-C) • Calcipotriol 50 mcg/g plus betamethasone dipropionate 0.5 mg/g ointment OD (4 wks), then calcipotriol cream 50 mcg/g OD weekdays, CB ointment OD weekends (8 wks) (CB-W) • Calcipotriol 50 mcg/g plus betamethasone dipropionate 0.5 mg/g ointment OD (4 wks), then placebo cream (calcipotriol vehicle), OD (8 wks) (CB-P)] Use < = 100 g/wk
Outcomes	1. mPASI (0 to 64.8) - per cent change from baseline: rebound: > 125% of baseline; relapse: > 50% reduction in maximum improvement from baseline 2. Investigator's Assessment of disease severity (IGA); 6-pt (absent to very severe) 3. Patient's assessment of overall response (PAGI); 7-pt (worse to clear) 4. Adverse events 5. Compliance (medication usage; self-reported compliance)
Notes	Leo Pharma A/S sponsored the trial. Atrophy was not assessed.

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Unclear risk	The trial reported insufficient details.
Blinding (performance bias and detection bias) All outcomes	High risk	The trial was open in the acute phase and maintenance phase for CB-W and double-blind (participant/investigator) in the maintenance phase for CB-C and CB-P. It was not possible to blind the alternating group (CB-W), as the vehicles were different.
Randomisation method reported	Low risk	A preplanned computer-generated randomisation schedule was used (1:1:1).
Loss to follow up	Low risk	0%
Baseline assessments	Low risk	These were reported.
Baseline comparability demonstrated	Unclear risk	This was partially demonstrated (reported means, but not standard, deviations; proportions reported).

Wolska 1995

Methods	**DESIGN** Within-patient Participant delivery **ALLOCATION** Random

Wolska 1995 *(Continued)*

	Method of randomisation: not reported Concealment: unclear **BLINDING** Double-blind (participant/investigator) **WITHDRAWAL/DROPOUT** Described
Participants	N: 52 Treatment duration: 4 wks; FU: 4 wks LF: 12 (23.1%) BC: yes Age: 44.7 (range = 18 to 77; N = 40) Gender (per cent men): 70%; N = 40 Severity: TSS (0 to 9) (median) = 7.1 (range = 6.0 to 9.0) **INCLUSION CRITERIA** • Plaque type psoriasis • At least 2 symmetrical lesions, excluding those on neck, head, feet, and hands • TSS ≥ 6 • Between-plaque TSS scores ≤ 1 • Lesions clinically stable ≥ 1wk **EXCLUSION CRITERIA** • Topical antipsoriatic treatment (tar/dithranol/steroids) within previous 2 wks • Systemic antipsoriatic treatment (steroids/retinoids/methotrexate/cyclosporin) within previous 4 wks • UV treatment within previous 4 wks • Pregnancy • Lactation; • Inadequate contraception • Impaired renal or hepatic function
Interventions	• Platelet aggregation activating factor (PAF) (Ro 24 to 0238) 10% solution BD • Placebo solution BD
Outcomes	1. TSS (erythema, desquamation, infiltration) (0 to 9) 2. IAGI (6-pt: marked worsening to total clearing) 3. Adverse events
Notes	The trial did not report sponsorship. Inpatients PLS CAN YOU PUT THIS IN A SENTENCE?]

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Unclear risk	The trial reported insufficient details.
Blinding (performance bias and detection bias)	Low risk	The trial was double-blind (participant/investigator).

Wolska 1995 *(Continued)*
All outcomes

Randomisation method reported	Unclear risk	The trial did not report this.
Loss to follow up	Unclear risk	23.1%
Baseline assessments	Low risk	-
Baseline comparability demonstrated	Low risk	-

Wortzel 1975 (1)

Methods	**DESIGN** Between-patient Delivery unclear **ALLOCATION** Random Method of randomisation: sequential admission number Concealment: adequate **BLINDING** Double-blind (participant/physician) **WITHDRAWAL/DROPOUT** Not described
Participants	N: 76 Treatment duration: 3 wks; FU: 3 wks LF: 0 (0%) BC: not reported Age: not reported Gender (per cent men): not reported Severity: not reported **INCLUSION CRITERIA** • Moderately severe to very severe psoriasis and atopic dermatitis • Outpatients **EXCLUSION CRITERIA** • Not reported
Interventions	• Betamethasone dipropionate ointment 0.05 BD (B) • Placebo BD (P)
Outcomes	1. IAGI (5-pt: worse to excellent) 2. Physician opinion of drug effect (scale unclear, results not reported)
Notes	Leo Pharmaceuticals sponsored the trial.
Risk of bias	

Wortzel 1975 (1) *(Continued)*

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Low risk	The sequential trial admission number corresponded to a treatment unit on a randomisation schedule.
Blinding (performance bias and detection bias) All outcomes	Low risk	The trial was double-blind (participant/physician).
Randomisation method reported	Low risk	Randomisation was sequential.
Loss to follow up	Low risk	0.0%
Baseline assessments	Unclear risk	The trial did not report these.
Baseline comparability demonstrated	Unclear risk	The trial did not report this.

Wortzel 1975 (2)

Methods	**DESIGN** Between-patient Delivery unclear **ALLOCATION** Random Method of randomisation: sequential admission number Concealment: adequate **BLINDING** Double-blind (participant/physician) **WITHDRAWAL/DROPOUT** Not described
Participants	N: 9 Treatment duration: 3 wks; FU: 3 wks LF: 0 (0%) BC: The trial did not report this. Age: not reported Gender (per cent men): not reported Severity: not reported **INCLUSION CRITERIA** • Moderately severe to very severe psoriasis and atopic dermatitis • Inpatients **EXCLUSION CRITERIA** • Not reported
Interventions	• Betamethasone dipropionate ointment 0.05 BD (B) • Placebo BD (P)

Wortzel 1975 (2) *(Continued)*

Outcomes	1. IAGI (5-pt: worse to excellent) 2. Physician opinion of drug effect (scale unclear, results not reported)
Notes	The trial did not report sponsorship. Concomitant water soluble emollients were permitted. There was SD imputation (PASI).

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Low risk	The sequential trial admission number corresponded to a treatment unit on a randomisation schedule.
Blinding (performance bias and detection bias) All outcomes	Low risk	The trial was double-blind (participant/physician).
Randomisation method reported	Low risk	Randomisation was sequential.
Loss to follow up	Low risk	0.0%
Baseline assessments	Unclear risk	The trial did not report these.
Baseline comparability demonstrated	Unclear risk	The trial did not report this.

Wozel 2001

Methods	**DESIGN** Between-patient Participant delivery **ALLOCATION** Random Method of randomisation: not reported Concealment: unclear **BLINDING** Double-blind (unclear) **WITHDRAWAL/DROPOUT** Described
Participants	N: 38 Treatment duration: 2 wks; FU: 6 wks LF: 0 (0%) BC: yes (statistical significance not reported) Age: not reported Gender (per cent men): not reported Severity: not reported **INCLUSION CRITERIA**

Wozel 2001 *(Continued)*

	• Chronic plaque psoriasis **EXCLUSION CRITERIA** • Not reported
Interventions	• Calcipotriol ointment OM plus fluocinolone acetonide ointment 0.025% ON (CF) • Calcipotriol ointment OM plus vehicle ointment ON (CP) • 4 weeks' maintenance for both groups with calcipotriol ointment BD
Outcomes	1. PASI
Notes	The trial did not report sponsorship.

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Unclear risk	The trial reported insufficient detail.
Blinding (performance bias and detection bias) All outcomes	Low risk	The trial was double-blind (it was unclear who was blinded).
Randomisation method reported	Unclear risk	The trial did not report this.
Loss to follow up	Low risk	0.0%
Baseline assessments	Unclear risk	The trial did not report these.
Baseline comparability demonstrated	Low risk	-

Yang 2009

Methods	**DESIGN** Between-patient Participant delivery **ALLOCATION** Random Method of randomisation: not stated Concealment: unclear **BLINDING** Not stated **WITHDRAWAL/DROPOUT** Described
Participants	N: 76 Treatment duration: 6 wks; FU: 6 wks LF: 0 (0%) BC: yes Age: range = 18 to 65

Yang 2009 *(Continued)*

	Gender (per cent men): 68.4% Severity: PASI = 14.3 (5.5SD), range = 4.2 to 19.6 Duration (yrs): range = 0.5 to 34 **INCLUSION CRITERIA** • People aged 18 to 65 with plaque psoriasis affecting limbs and body • PASI < 25 **EXCLUSION CRITERIA** • Systemic antipsoriatic therapy within previous 4 wks • Topical therapy within previous 2 wks • Use of corticosteroids or vitamin D3 derivatives • Concurrent infection • Pregnancy • Heart, liver, kidney, or mental disorder • Known sensitivity to study medication • External injury
Interventions	• Calcipotriol cream BD (C) • Halometasone cream (OM), calcipotriol cream (ON) (2 wks); calcipotriol cream BD (weekdays), halometasone cream BD (weekends) (2 wks); calcipotriol cream BD (2 wks) (CH) Treatments were stopped when 90% improvement achieved.
Outcomes	1. mPASI (0 to 64.8) 2. Improvement score (based on change in PASI score x 100%) (IAGI): • Complete recovery: > 90% • Marked improvement: 60% to 89% • Some improvement: 25% to 59% • No effect: <25%
Notes	The trial did not state the sponsor. There was 1 case of skin atrophy in the monotherapy group. We received translation support for data extraction.

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Unclear risk	The trial reported insufficient details.
Blinding (performance bias and detection bias) All outcomes	Unclear risk	The trial did not report this.
Randomisation method reported	Unclear risk	The trial did not report this.
Loss to follow up	Low risk	0%
Baseline assessments	Low risk	These were reported.

Yang 2009 *(Continued)*

Baseline comparability demonstrated	Low risk	This was demonstrated.

Zonneveld 1998 (H)

Methods	**DESIGN** Between-patient Delivery unclear **ALLOCATION** Random Method of randomisation: not reported Concealment: unclear **BLINDING** Double-blind (but unmatched regimens) (participant/assessor) **WITHDRAWAL/DROPOUT** Not described
Participants	N: 70 Treatment duration: 6 wks; FU: 6 wks LF: not reported BC: Yes (clinical); demographics not reported Age: not reported Gender (per cent men): not reported Severity: median LPSI ranged from 7.0 (C;T) to 8.0 (P) **INCLUSION CRITERIA** • Chronic plaque psoriasis • LPSI ≥ 6 **EXCLUSION CRITERIA** • Not reported
Interventions	• Calcipotriol ointment 0.005% BD (C) • Tacrolimus ointment 0.3% OD (T) • Placebo ointment BD (P)
Outcomes	1. Local psoriasis severity index (scale NR)
Notes	The study was double-blind (but unmatched regimens). Fujisawa GmbH sponsored the trial. There was SD imputation (TSS).

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Unclear risk	The trial reported insufficient details.

Zonneveld 1998 (H) *(Continued)*

Blinding (performance bias and detection bias) All outcomes	Low risk	The trial was double-blind (but unmatched regimens) (participant/assessor).
Randomisation method reported	Unclear risk	The trial did not report this.
Loss to follow up	Unclear risk	The trial did not report this.
Baseline assessments	Low risk	These were partially done.
Baseline comparability demonstrated	Unclear risk	This was partially demonstrated.

Zonneveld 1998 (P)

Methods	**DESIGN** Between-patient Delivery unclear **ALLOCATION** Random Method of randomisation: not reported Concealment: unclear **BLINDING** Double-blind (but unmatched regimens) (participant/assessor) **WITHDRAWAL/DROPOUT** Not described
Participants	N: 70 Treatment duration: 6 wks; FU: 6 wks LF: not reported BC: yes (clinical), demographics not reported Age: not reported Gender (per cent men): not reported Severity: median LPSI ranged from 7.0 (C;T) to 8.0 (P) **INCLUSION CRITERIA** • Chronic plaque psoriasis • LPSI ≥ 6 **EXCLUSION CRITERIA** • Not reported
Interventions	• Calcipotriol ointment 0.005% BD (C) • Tacrolimus ointment 0.3% OD (T) • Placebo ointment BD (P)
Outcomes	1. Local psoriasis severity index (scale NR)
Notes	The study was double-blind (but unmatched regimens).

Zonneveld 1998 (P) *(Continued)*

Fujisawa GmbH sponsored the trial.
There was SD imputation (TSS).

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Unclear risk	The trial reported insufficient details.
Blinding (performance bias and detection bias) All outcomes	Low risk	The trial was double-blind (but unmatched regimens) (participant/assessor).
Randomisation method reported	Unclear risk	The trial did not report this.
Loss to follow up	Unclear risk	The trial did not report this.
Baseline assessments	Low risk	-
Baseline comparability demonstrated	Unclear risk	This was partially demonstrated.

Characteristics of excluded studies *[ordered by study ID]*

Study	Reason for exclusion
Agrawal 2010	The study did not provide a comparison of interest (compared acitretin gel in 2 formulations).
Akerman 2009	The trialists did not report or make available adequate data.
Ambroziak 2002	The study compared steroid against no treatment (rather than against placebo).
Baadsgaard 1995	The study was within-patient, but did not adopt clear left-right design and assessed multiple plaques for each participant.
Baran 1999	The trialists did not report or make available adequate data.
Bianchi 2003	The study compared steroid against no treatment (rather than against placebo).
Brodell 2011a	The sponsor did not report or make available adequate data.
Buder 2010	The study assessed multiple plaques for each participant (7 per participant).
Callen 1996	The trialists or sponsor did not report or make available adequate data.
Cannavo 2003	This was a nail psoriasis trial, which was removed in the 2011 update.
Carroll 2005	The comparator was not strictly placebo (salicylic acid in vehicle).
De Jong 1999	The comparator was not strictly placebo (urea in vehicle).
Elias 1994	It was unclear if it was a valid randomised controlled trial.

Study	Reason for exclusion
Esposito 2009	The study did not provide a comparison of interest.
Friedrich 2004	The sponsors did not report or make available adequate data.
Hsia 2010	The study did not assess patient outcomes/tolerability
Insa 2009	The study did not assess patient outcomes/tolerability.
Iraji 2010	The trialists did not report or make available adequate data.
Ito 2005	The study was not randomised.
Jansen 1986	No adequate data were reported.
Kaur 2004	The study was not randomised.
Kleyn 2005	The study did not provide a comparison of interest.
Kragballe 1989	Participants were randomised to the 2 substudies, but within the substudies, treatments were applied without randomisation.
Kragballe 1994	This was a dose-ranging study of an unlicensed product not subsequently marketed.
Lebwohl 1998b	The study did not provide a simple comparison against a vitamin D_3 derivative treatment.
Lebwohl 2001	The trialists or sponsor did not report or make available adequate data.
Levin 2003	The trialists or sponsor did not report or make available adequate data.
Meyrat 1996	The study did not provide a comparison of interest.
Palazon 2005	The study did not provide a comparison of interest.
Reygagne 2002a	The trialists or sponsor did not report or make available adequate data.
Rhemus 2006	The study did not provide a comparison of interest (product unlicensed).
Ruzicka 2004	The trialists or sponsor did not report or make available adequate data.
Sander 1998	The study did not provide a simple comparison against a vitamin D_3 derivative treatment.
Saraswat 2007	The study did not provide a simple comparison against a vitamin D_3 derivative treatment.
Scher 2001	This was a nail psoriasis trial, which was removed in the 2011 update.
Sefton 1984	The trialists or sponsor did not report or make available adequate data.
Sharma 2003	The study used concomitant UV light.
Syed 2001a	The trialists did not report or make available adequate data.
Tokura 2004	No translation was available.
Tosti 1998	This was a nail psoriasis trial, which was removed in the 2011 update.

Study	Reason for exclusion
Tzaneva 2003	The study used concomitant UV light.
van de Kerkhof 1996b	The trialists did not report or make available adequate data.
Vena 2005	The study was not a randomised controlled trial.

Characteristics of studies awaiting assessment *[ordered by study ID]*

Bissonnette 2011

Methods	**DESIGN** Between-patient Participant delivery **ALLOCATION** Random Method of randomisation: computer-generated code Concealment: unclear **BLINDING** Double-blind (participant/investigator) **WITHDRAWAL/DROPOUT** Described
Participants	N: 61 Treatment duration: 12 wks; FU: 12 wks LF: 0 (0%) BC: yes Age: 50.6 (22 to 65) Gender (per cent men): 83.6% Severity: PGA = 3.3 (0.6SD); PASI = 6.0 (2.5SD); BSA = 3.2% (2.0SD) **INCLUSION CRITERIA** • Participants aged 18 to 65 with mild to moderate plaque psoriasis • BSA: 1% to 15% • PGA: 2 to 4 • Good general health **EXCLUSION CRITERIA** • Concomitant serious illness/medical condition • Systemic therapy within previous 12 to 24 wks (depending on drug) • Phototherapy within previous 4 wks • Topical antipsoriatic therapy within previous 2 wks • Other non-plaque forms of psoriasis
Interventions	• 1% WBI-1001 in a cream formulation twice daily • Placebo vehicle twice daily
Outcomes	1. Physician's Global Assessment (PGA), 6-pt (0 = clear to 5 = very severe) 2. Body surface area (BSA)

Bissonnette 2011 *(Continued)*

	3. Psoriasis Area and Severity Index (PASI)
Notes	Welichem Biotech Inc. sponsored the trial.

Callis Duffin 2010

Methods	**DESIGN** Between-patient Participant delivery **ALLOCATION** Random Method of randomisation: not stated Concealment: unclear **BLINDING** Double-blind (participant/investigator) **WITHDRAWAL/DROPOUT** Not described
Participants	N: 200 Treatment duration: 12 wks; FU: 12 wks LF: NS BC: NS Age: NS Gender (per cent men): NS Severity: NS **INCLUSION CRITERIA** • Participants aged 18 to 75 with mild to moderate plaque psoriasis • BSA: 2% to 20% **EXCLUSION CRITERIA** • Lesions solely involving intertriginious areas, the scalp, or the face • Pustular psoriasis or erythroderma • Concurrent systemic therapy, topical agents, or UVB therapy within 2 weeks of the first dose of study medication • Systemic triazole antifungals except fluconazole
Interventions	• INCB018424: Ruxolitinib phosphate cream QD • Placebo cream QD
Outcomes	1. Total Lesion Score (sum of erythema, scaling, and thickness; points NS) 2. PASI
Notes	Incyte Corporation sponsored the trial.

Calzavara-Pinton 2011

Methods	**DESIGN** Within-patient Participant delivery **ALLOCATION** Random Method of randomisation: not stated

Calzavara-Pinton 2011 *(Continued)*

	Concealment: unclear **BLINDING** Single-blind (investigator/outcome assessor) **WITHDRAWAL/DROPOUT** Described
Participants	N: 20 Treatment duration: 8 wks; FU: 16 wks LF: 2 (10%) BC: yes Age: 40.2 (range = 19 to 68) Gender (per cent men): 40% Severity: PSI = median 8 (IQR = 7 to 9.25) **INCLUSION CRITERIA** • Participants with mild plaque psoriasis • Symmetrical plaques **EXCLUSION CRITERIA** • Not stated
Interventions	• Budesonide 0.25 mg/g cream OM plus tacalcitol 4 mcg/g ointment ON • Calcipotriol 50 mcg/g and betamethasone dipropionate 0.5 mg/g once daily
Outcomes	1. Psoriasis Severity Index (erythema + infiltration + scaling) (0 to 12) 2. VAS (adverse events; itching): 0 to 10 3. Patient preference and satisfaction (better/equal/worse)
Notes	The sponsor was not stated.

Henry 2011

Methods	**DESIGN** Within-patient Participant delivery **ALLOCATION** Random Method of randomisation: not stated Concealment: unclear **BLINDING** Single-blind (investigator) **WITHDRAWAL** Described
Participants	N: 13 Treatment duration: 4 wks; FU: 4 wks LF: 3 (23.0%) BC: NS

Henry 2011 *(Continued)*

	Age: NS Gender (per cent men): NS Severity: NS **INCLUSION CRITERIA** • Participants with mild to moderate plaque psoriasis **EXCLUSION CRITERIA** • NS
Interventions	• Clobetasol propionate spray followed by calcitriol ointment twice daily • Calcitriol ointment followed by clobetasol propionate spray twice daily
Outcomes	1. Signs: erythema, induration, scaling
Notes	Galderma sponsored the trial. This was an abstract only.

Katoh 2003

Methods	**DESIGN** Between-patient Participant delivery **ALLOCATION** Random Method of randomisation: not stated Concealment: unclear **BLINDING** Not stated **WITHDRAWAL/DROPOUT** Described
Participants	N: 61 Treatment duration: 12 wks; FU: 12 wks LF: 2 (3%) BC: yes Age: 49.2 (14.3SD) Gender (per cent men): 34% Severity: PASI = 12.9 (5.3SD) Ethnicity: Japanese **INCLUSION CRITERIA** • Participants with stable plaque psoriasis **EXCLUSION CRITERIA** • Participants requiring systemic therapy or use of any antipsoriatic treatment within previous 4 wks

Katoh 2003 *(Continued)*

Interventions	• Calcipotriol 0.005% ointment once daily • Combination treatment with calcipotriol 0.004% and 0.01% clobetasol propionate ointment once daily Treatments were applied after bathing. Participants achieving 50% reduction in baseline PASI then used calcipotriol once daily for a further 12 weeks.
Outcomes	1. Eruption score of trunk involvement: sum of erythema, scaling, and induration (0 to 12) 2. PASI
Notes	The Japanese Ministry of Education, Science, Sports, and Culture sponsored the trial.

Matheson 2011

Methods	**DESIGN** Between-patient Participant delivery **ALLOCATION** Random Method of randomisation: not stated Concealment: unclear **BLINDING** Open **WITHDRAWAL/DROPOUT** Not described
Participants	N: 32 Treatment duration: 2 wks; FU: 2 wks LF: NS BC: no Age: NS Gender (per cent men): NS Severity: NS **INCLUSION CRITERIA** • Participants aged ≥12 with mild to moderate plaque psoriasis **EXCLUSION CRITERIA** • Not stated
Interventions	• Calcipotriol ointment 0.005% twice daily • Calcipotriol foam 0.005% twice daily
Outcomes	1. Safety: adverse events; serum calcium
Notes	Stiefel, a GSK company, sponsored the trial.

Paulsen 2005

Methods	**DESIGN** Within-patient Participant delivery **ALLOCATION** Random Method of randomisation: not stated Concealment: unclear **BLINDING** Double-blind (participant/investigator) **WITHDRAWAL/DROPOUT** Described
Participants	N: 41 Treatment duration: 4 wks; FU: 12 wks LF: 1 (2%) BC: yes Age (median): 44 (23 to 77) Gender (per cent men): 65% Severity: duration (yrs; median) = 15 (range = 2 to 60) **INCLUSION CRITERIA** • Participants aged ≥18 with stable mild to moderate plaque psoriasis • Test plaques similar within each participant (TSS ≤ 1), TSS ≤ 8 **EXCLUSION CRITERIA** • Concurrent use of topical steroids or vitamin D or emollients containing aloe vera • Pregnancy • Systemic or photo therapy within previous 2 mths • Topical antipsoriatic therapy within previous 2 wks • Known allergy to gel • Severe concomitant disease • Use of specific drugs
Interventions	• Aloe vera gel twice daily • Placebo gel twice daily
Outcomes	1. PASI 2. Local PASI (TSS) (0 to 9) 3. Patient preference
Notes	Psoriasisfonden sponsored the trial.

Sadeghian 2011

Methods	**DESIGN** Between-patient Participant delivery **ALLOCATION**

Sadeghian 2011 *(Continued)*

	Random Method of randomisation: not stated Concealment: unclear **BLINDING** Double-blind (participant/investigator) **WITHDRAWAL/DROPOUT** Described
Participants	N: 60 Treatment duration: 12 wks; FU: 12 wks LF: 0 (0%) BC: yes Age: 32.5 (15.6SD) Gender (per cent men): 51.7% Severity: PASI = 3.9 (1.9SD) **INCLUSION CRITERIA** • Participants aged ≥ 5 with plaque psoriasis • BSA ≤ 10% **EXCLUSION CRITERIA** • Pregnancy • Non-plaque types of psoriasis • Participants with scalp and facial lesions
Interventions	• Zinc pyrithione 0.25% cream twice daily • Placebo cream twice daily
Outcomes	1. PASI (0 to 72)
Notes	The sponsor was not stated.

Vahlquist 2004

Methods	**DESIGN** Within-patient Participant delivery **ALLOCATION** Random Method of randomisation: not stated Concealment: unclear **BLINDING** Double-blind (participant/investigator) **WITHDRAWAL/DROPOUT** Described
Participants	N: 12 Treatment duration: 8 wks; FU: x wks LF: 0 (0%)

Vahlquist 2004 *(Continued)*

	BC: no Age: 43.8 (range = 21 to 58) Gender (per cent men): 83.3% Severity: NS **INCLUSION CRITERIA** • Participants with mild to moderate plaque psoriasis **EXCLUSION CRITERIA** • Systemic or topical therapy within previous 4 wks
Interventions	• Thyroid hormone analogue (TriAc) 0.1% in hydrophilic ointment twice daily • Placebo ointment twice daily
Outcomes	1. Psoriasis Severity Index 2. VAS to assess patient preference
Notes	-

Yang 1999

Methods	This will need to be translated; details to follow at next update.
Participants	N: 60 Treatment duration: 6 wks; FU: 6 wks LF: unclear BC: unclear Age: range = 14 to 65 Gender (per cent men): unclear Severity: unclear **INCLUSION CRITERIA** • Unclear **EXCLUSION CRITERIA** • Unclear
Interventions	• Tacalcitol ointment • 17 alpha hydrocortisone cream
Outcomes	This will need to be translated; details to follow at next update.
Notes	This will need to be translated; details to follow at next update.

Characteristics of ongoing studies *[ordered by study ID]*

NCT00824980

Trial name or title	Combined Inhibition of Dipeptidyl Peptidase IV (DPIV/CD26) and Aminopeptidase N (APN/CD13) in the Treatment of Psoriasis - Phase II Single Center Study
Methods	Allocation: randomised End point classification: safety/efficacy study Intervention model: parallel assignment Masking: double-blind (participant, caregiver, investigator, outcomes assessor) Primary purpose: treatment
Participants	• Age 18 years of age at pre-study • Diagnosis of plaque type psoriasis at least 3 month prior to enrolment • Mild to moderate plaque type psoriasis with at least 2 plaques of approximately 15 cm^2 for which topical treatment is indicated
Interventions	• Drug: IP10.C8 Gel • Placebo Gel
Outcomes	1. Psoriasis Area and Severity Index at 4 weeks
Starting date	January 2009
Contact information	Alexander Narvarini, MD Telephone: +41 44 255 1111 alexander.navarini@usz.ch
Notes	Immune Technologies & Medicine GmbH http://clinicaltrials.gov/show/NCT00824980

NCT01018134

Trial name or title	A Double-Blind, Vehicle-Controlled, Randomized, Dose Ranging, Multiple-Site Clinical Study to Evaluate the Efficacy and Safety of Desoximetasone Topical Sprays (0.05%, 0.25%) in Patients With Moderate to Severe Plaque Psoriasis
Methods	Allocation: randomised End point classification: safety/efficacy study Intervention model: parallel assignment Masking: double-blind (participant, caregiver, investigator, outcomes assessor) Primary purpose: treatment
Participants	• Have a definite clinical diagnosis of stable plaque psoriasis involving ≥ 10% of the body surface area (BSA) • Have a combined Total Lesion Severity Score (TLSS) of ≥ 7 for the target lesion • Have a plaque elevation score ≥ 3 of (moderate) for the target lesion • The target lesion must have an area of at least 5 cm^2

NCT01018134 *(Continued)*

	• Have a Physicians Global Assessment (PGA) score of 3 (moderate) or 4 (severe) at baseline for the overall disease severity
Interventions	• Drug: desoximetasone 0.05% once daily • Drug: desoximetasone 0.05% twice daily • Drug: desoximetasone 0.25% once daily • Drug: desoximetasone 0.25% once daily • Drug: vehicle once daily • Drug: vehicle twice daily
Outcomes	1. Clinical cure: Physician's Global Assessment (PGA) = 0 or 1 (time frame: 28 days) 2. Lesion treatment success, score of 0 or 1, for each of the 3 signs of erythema, scaling, and plaque elevation (time frame: day 28)
Starting date	November 2009
Contact information	Darin B Brimhall, D.O., FACP Study Director Novum Pharmaceutical Research Services
Notes	Taro Pharmaceuticals USA http://clinicaltrials.gov/show/NCT01018134

NCT01206387

Trial name or title	A Double-Blind, Vehicle-Controlled, Randomized, Parallel Design, Multiple-Site Clinical Study to Evaluate the Efficacy and Safety of Desoximetasone 0.25% Topical Spray in Patients With Moderate to Severe Plaque Psoriasis
Methods	Allocation: randomised End point classification: safety/efficacy study Intervention model: parallel assignment Masking: double-blind (participant, investigator, outcomes assessor) Primary purpose: treatment
Participants	Genders eligible for study: both Accepts healthy volunteers: no • Men or non-pregnant, non-lactating women 18 years of age or older • Have a definite clinical diagnosis of stable plaque psoriasis involving ≥10% of the body surface area (BSA) • Have a combined Total Lesion Severity Score (TLSS) of ≥ 7 for the target lesion • Have a plaque elevation score ≥ 3 of (moderate) for the target lesion • The target lesion must have an area of at least 5 cm^2 • Have a Physicians Global Assessment (PGA) score of 3 (moderate) or 4 (severe) at baseline for the overall disease severity
Interventions	• Drug: desoximetasone spray 0.25% • Drug: placebo comparator
Outcomes	1. Clinical success (time frame: 28 days) - a participant is considered a clinical success if the Physician's Global Assessment (PGA) is 0 (clear) or 1 (almost clear)

NCT01206387 *(Continued)*

	2. Treatment success (time frame: 28 days) - a participant is considered a treatment success for the target lesions if the target lesion has a score of 0 or 1 on the Target Lesion Severity Score (TLSS) for each of the 3 signs and symptoms (erythema, scaling, and plaque elevation) **SECONDARY OUTCOMES** 1. Change in PGA (time frame: 28 days) - mean change from baseline to end of treatment in PGA
Starting date	August 2010
Contact information	Gail Gongas Telephone: 412 363 3300 ext: 522 GDGongas@novumprs.com
Notes	Taro Pharmaceuticals USA Study ID number: DSXS-0808 http://clinicaltrials.gov/show/NCT01206387

NCT01206660

Trial name or title	A Double-Blind, Vehicle-Controlled, Randomized, Parallel Design, Multiple-Site Clinical Study to Evaluate the Efficacy and Safety of Desoximetasone 0.25% Topical Spray in Patients With Moderate to Severe Plaque Psoriasis
Methods	Study type: Interventional Study design: Allocation: randomised End point classification: safety/efficacy study Intervention model: parallel assignment Masking: double-blind (participant, investigator, outcomes assessor) Primary purpose: treatment
Participants	Accepts healthy volunteers: no • Men or non-pregnant, non-lactating women 18 years of age or older • Have a definite clinical diagnosis of stable plaque psoriasis involving ≥ 10% of the body surface area (BSA) • Have a combined Total Lesion Severity Score (TLSS) of ≥ 7 for the target lesion • Have a plaque elevation score ≥ 3 of (moderate) for the target lesion • The target lesion must have an area of at least 5 cm^2 • Have a Physicians Global Assessment (PGA) score of 3 (moderate) or 4 (severe) at baseline for the overall disease severity
Interventions	• Drug: desoximetasone spray 0.25% • Drug: placebo
Outcomes	**PRIMARY OUTCOMES** 1. Clinical success (time frame: 28 days) - a participant is considered a clinical success if the Physician's Global Assessment (PGA) is 0 (clear) or 1 (almost clear)

NCT01206660 *(Continued)*

	2. Treatment success (time frame: 28 days) - a participant is considered a treatment success for the target lesions if the target lesion has a score of 0 or 1 on the Target Lesion Severity Score (TLSS) for each of the 3 signs and symptoms (erythema, scaling, and plaque elevation) **SECONDARY OUTCOMES** 1. Change in PGA (time frame: 28 days) 2. Mean change from baseline to end of treatment in PGA
Starting date	August 2010
Contact information	Gail Gongas Telephone: 412 363 3300 ext: 522 GDGongas@novumprs.com
Notes	Taro Pharmaceuticals USA Study ID number: DSXS-0914 http://clinicaltrials.gov/show/NCT01206660

NCT01246583

Trial name or title	A Phase 2a, Multi Site, Randomized, Double Blind, Placebo Controlled, Parallel Group Study Of The Pilot Efficacy, Safety, And Pharmacokinetics Of 2 Ointment Formulations Of CP-690,550 In Subjects With Mild To Moderate Chronic Plaque Psoriasis
Methods	Study type: interventional Study design: allocation: randomised End point classification: safety/efficacy study Intervention model: parallel assignment Masking: double-blind (participant, investigator) Primary purpose: treatment
Participants	Ages eligible for study: 18 years and older Genders eligible for study: both Accepts healthy volunteers: no **INCLUSION CRITERIA** • Mild to moderate chronic plaque psoriasis (psoriasis vulgaris), with the duration of at least 6 months • A target plaque of at least 9 sq. cm **EXCLUSION CRITERIA** • Demonstrates "rebound" or "flare" of chronic plaque psoriasis • Non-plaque form of psoriasis

NCT01246583 *(Continued)*

	• Currently have or history of psoriatic arthritis • Current drug-induced psoriasis • Currently on systemic therapy or was on systemic therapy for psoriasis within the previous 6 months • Currently on phototherapy for psoriasis or was on phototherapy within the previous 3 months
Interventions	• Drug: CP-690,550 ointment 1 • Drug: vehicle 1 • Drug: CP-690,550 ointment 2 • Drug: vehicle 2
Outcomes	**PRIMARY OUTCOMES** • Per cent change from baseline at week 4 in Target Plaque Severity Score (TPSS) **SECONDARY OUTCOMES** • Proportion of participants with Treatment Area Overall Severity of Psoriasis response of "clear" (0) or "almost clear" • Proportion of participants with a difference from baseline of > = 2 steps in Treatment Area Overall Severity of Psoriasis score • Per cent change from baseline at weeks 1, 2, 3, and 4 in target plaque area • Change from baseline at weeks 1, 2, 3, and 4 in TPSS subscores for erythema, induration, and scaling • Per cent change from baseline in TPSS • Actual and change from baseline on the treatment area Itch Severity Item (ISI) • Proportion of participants in each Patient Satisfaction with Study Medication (PSSM) response category • Incidence, nature, and severity of observed and reported administration site adverse events over 4 weeks of treatment • Incidence and severity of burning/stinging of psoriatic or perilesional skin in the treatment area over 4 weeks of treatment • Incidence and severity of reactions of perilesional skin in the treatment area as measured by Draize scoring over 4 weeks of treatment • Incidence and severity of adverse events over 4 weeks of treatment • Incidence of clinical laboratory abnormalities and change from baseline in clinical laboratory values over 4 weeks of treatment • Incidence of clinically significant changes in physical examination from baseline over 4 weeks of treatment • Incidence of vital sign (blood pressure and heart rate) abnormalities and change from baseline in vital sign measures over 4 weeks of treatment • Incidence of electrocardiogram (ECG) abnormalities and change from baseline in ECG measures over 4 weeks of treatment • Plasma CP-690,550 concentrations, from blood sampling
Starting date	November 22 2010
Contact information	Pfizer CT.gov Call Center
Notes	Pfizer

NCT01247818

Trial name or title	A Phase 2 Dose-Randomized, Vehicle-Controlled Study of PH-10-Aqueous Hydrogel for the Treatment of Plaque Psoriasis
Methods	Study type: interventional Study design: allocation: randomised End point classification: safety/efficacy study Intervention model: parallel assignment Masking: single-blind (outcomes assessor) Primary purpose: treatment
Participants	Accepts healthy volunteers: no • Men or women, age 18 or older • Presence of mild to moderate plaque psoriasis on the trunk or extremities (excluding palms, soles, scalp, and facial or intertriginous areas) • Fitzpatrick skin type I to VI • Written informed consent by the participant or legal guardian
Interventions	• Drug: PH-10 (0.002% Rose Bengal) • Drug: PH-10 (0.005% Rose Bengal) • Drug: PH-10 (0.01% Rose Bengal) • Drug: vehicle
Outcomes	**PRIMARY OUTCOMES** • The primary efficacy end point is "Treatment Success," a static end point assessed at day 29 after initial PH-10 treatment and defined as 0 or 1 on all Psoriasis Severity Index (PSI) components and 0 or 1 on the Plaque Response scale (time frame: 28 days) • The primary safety end point is incidence of adverse experiences, including pain and dermatologic/skin toxicity (incidence, severity, frequency, duration, and causality) (time frame: 8 weeks) **SECONDARY OUTCOMES** • Psoriasis Severity Index (PSI) score changes at each visit from day 1 pre-treatment (time frame: 8 weeks) • Plaque Response score changes at each visit from day 1 pre-treatment (time frame: 8 weeks) • Pruritus Self-Assessment score changes at each visit from day 1 pre-treatment (time frame: 8 weeks)
Starting date	December 2010
Contact information	Eric Wachter, PhD Provectus Pharmaceuticals
Notes	Provectus Pharmaceuticals http://clinicaltrials.gov/show/NCT01247818

NCT01422434

Trial name or title	Efficacy and Safety of LEO 90105 Ointment (Calcipotriol Hydrate Plus Betamethasone Dipropionate) in Japanese Subjects With Psoriasis Vulgaris
Methods	Study type: interventional Study design: allocation: randomised End point classification: efficacy study Intervention model: parallel assignment Masking: double-blind (participant, caregiver, investigator, outcomes assessor) Primary purpose: treatment
Participants	Accepts healthy volunteers: No Participants having understood and signed a written informed consent form prior to any study related procedures being carried out. • Japanese participants • 20 years of age or above of either sex • Clinical diagnosis of psoriasis vulgaris amenable to topical treatment, involving arms, trunk, legs, or any of the aforementioned • A minimum mPASI score for extent of 2 in at least 1 body region (i.e. psoriasis affecting at least 10% of arms, 10% of trunk, 10% of legs, or any of the aforementioned) • Psoriasis vulgaris on the trunk/limbs (excluding psoriasis on the genitals/skin folds) of not more than 30% body surface area (BSA) • A target lesion of a minimum of 5 cm at its longest axis and preferably not located on an elbow or knee, scoring at least 3 for each of redness, thickness, and scaliness, and at least 10 in total by the physician's assessment of severity of the target lesion - a physician's global assessment of disease severity of psoriasis on trunk/limbs of mild, moderate, severe, or very severe • Women of childbearing potential must have a negative result for a urine pregnancy test at day 0 (Visit 1) and must agree to use an adequate method of birth control, as judged by the (sub)investigator, during the study. The contraceptive method should have started an adequate amount of time before the pregnancy test, which is dependent on the particular method used and as judged by the (sub)investigator, and must continue for at least 1 week after the last application of study medication. A woman is defined as not of child-bearing potential if she is postmenopausal (12 months with no menses without an alter-native medical cause) or surgically sterile (tubal ligation/section, hysterectomy, or bilateral ovariectomy)
Interventions	• Drug: LEO 90105 = calcipotriol + betamethasone dipropionate • Drug: Dovonex® = calcipotriol • Drug: Rinderon® - DP = betamethasone dipropionate
Outcomes	**PRIMARY OUTCOMES** 1. Change from baseline in Psoriasis Area and Severity Index (PASI) (time frame: week 0, week 4) **SECONDARY OUTCOMES** 1. Change from baseline in target lesion assessment (time frame: week 0, week 4 2. Physician's global assessment of psoriasis (time frame: week 4) 3. Adverse events (time frame: week 4)
Starting date	July 2011
Contact information	Akira Ozawa, MD, Professor, Principal Investigator

NCT01422434 *(Continued)*

	Tokai University School of Medicine
Notes	LEO 90105 ointment contains both calcipotriol and betamethasone dipropionate. It has been approved for the treatment of psoriasis in more than 60 centres, including most European countries, the US, China, Korea, and Taiwan. This trial will investigate its safety and efficacy in the treatment of Japanese participants with psoriasis. LEO Pharma http://clinicaltrials.gov/show/NCT01422434

NCT01465282

Trial name or title	A Randomized, Placebo-controlled, Phase IIb Study to Evaluate the Efficacy, Safety and Tolerability of 0.05%, 0.1% and 0.5% w/w Topical CT327 When Applied Twice Daily in Subjects With Psoriasis Vulgaris
Methods	Study type: interventional Study design: allocation: randomised End point classification: safety/efficacy study Intervention model: single group assignment Masking: double-blind (participant, caregiver, investigator, outcomes assessor) Primary purpose: treatment
Participants	Accepts healthy volunteers: no **INCLUSION CRITERIA** • Men and women aged at least 18 years. • Stable psoriasis vulgaris **EXCLUSION CRITERIA** • Participants with guttate, erythrodermic, exfoliative, or pustular psoriasis.
Interventions	• Drug: CT327 0.05% • Drug: CT327 0.1% • Drug: CT327 0.5% • Drug: placebo
Outcomes	**PRIMARY OUTCOMES** 1. Efficacy of CT327 ointment (0.05%, 0.1%, and 0.5% w/w) compared with placebo ointment **SECONDARY OUTCOMES** 1. Local and systemic toleration
Starting date	November 1, 2011
Contact information	No contacts or locations provided
Notes	Creabilis SA

NCT01536886

Trial name or title	LEO 90100 Compared With Calcipotriol Plus Betamethasone Dipropionate Ointment, LEO 90100 Vehicle and Ointment Vehicle in Subjects With Psoriasis Vulgaris
Methods	Allocation: randomised End point classification: efficacy study Intervention model: parallel assignment Masking: double-blind (caregiver, investigator, outcomes assessor) Primary purpose: treatment
Participants	Accepts healthy volunteers: no

INCLUSION CRITERIA

- Signed and dated informed consent obtained prior to any trial-related activities (including washout period)
- Age 18 years or above
- Either sex
- Any race or ethnicity
- All skin types
- Women of childbearing potential must have a negative pregnancy test at day 0 (Visit 1)
- Women of childbearing potential must agree to use a highly effective method of birth control during the study. A highly effective method of birth control is defined as 1 which results in a low failure rate (less than 1% per year)
- Able to communicate with the investigator and understand and comply with the requirements of the study

EXCLUSION CRITERIA

- Systemic treatment with biological therapies, whether marketed or not, with a possible effect on psoriasis vulgaris within the following time periods prior to randomisation:
  - etanercept - within 4 weeks prior to randomisation
  - adalimumab, alefacept, infliximab - within 8 weeks prior to randomisation
  - ustekinumab - within 16 weeks prior to randomisation
  - other products - 4 weeks/5 half-lives (whichever is longer)
- Systemic treatment with all other therapies with a possible effect on psoriasis vulgaris (e.g. corticosteroids, retinoids, methotrexate, ciclosporin, and other immunosuppressants) within 4 weeks prior to randomisation
- Participants who have received treatment with any non-marketed drug substance (i.e. a drug which has not yet been made available for clinical use following registration) within 4 weeks/5 half-lives (whichever is longer) prior to randomisation
- PUVA therapy within 4 weeks prior to randomisation
- UVB therapy within 2 weeks prior to randomisation
- Planned excessive exposure of area(s) to be treated with study medication to either natural or artificial sunlight (including tanning booths, sun lamps, etc) during the study
- Planned initiation of, or changes to, concomitant medication that could affect psoriasis vulgaris (e.g. beta blockers, antimalarial drugs, lithium, ACE inhibitors) during the study
- Current diagnosis of guttate, erythrodermic, exfoliative, or pustular psoriasis
- Participants with any of the following conditions present on the treatment area: viral (e.g. herpes or varicella) lesions of the skin, fungal and bacterial skin infections, parasitic infections, skin man-

NCT01536886 *(Continued)*

	ifestations in relation to syphilis or tuberculosis, acne vulgaris, atrophic skin, striae atrophicae, fragility of skin veins, icthyosis, ulcers, and wounds • Other inflammatory skin disorders (e.g. seborrhoeic dermatitis or contact dermatitis) on the treatment area that may confound the evaluation of psoriasis vulgaris • Known or suspected disorders of calcium metabolism associated with hypercalcaemia • Known or suspected severe renal insufficiency or severe hepatic disorders. • Known or suspected hypersensitivity to component(s) of the investigational products • Current participation in any other interventional clinical study • Previously randomised in this study • Women who are pregnant, wishing to become pregnant during the study, or are breast-feeding
Interventions	• Drug: LEO 90100 • Drug: betamethasone plus calcipotriol • Drug: ointment vehicle • Drug: LEO 90100 vehicle
Outcomes	1. Investigator's Global Assessment of Disease Severity (time frame: 4 weeks) Designated as safety issue: no
Starting date	May 2012
Contact information	Anders Ninn Hansen, MSc Pharm Telephone: +45 72 26 28 18 ext: 2818 anders.n-hansen@leo-pharma.com
Notes	-

NCT01536938

Trial name or title	LEO 90100 in the Treatment of Psoriasis Vulgaris
Methods	Study type: interventional Study design: allocation: randomised End point classification: efficacy study Intervention model: parallel assignment Masking: double-blind (participant, caregiver, investigator, outcomes assessor) Primary purpose: treatment
Participants	Accepts healthy volunteers: no **INCLUSION CRITERIA** • Signed and dated informed consent obtained prior to any trial related activities (including washout period) • Age 18 years or above of either sex • Any race or ethnicity • All skin types • Women of childbearing potential must have a negative pregnancy test at day 0 (Visit 1) • Women of childbearing potential must agree to use a highly effective method of birth control during the study. A highly effective method of birth control is defined as one which results in a low failure rate (less than 1% per year)

NCT01536938 *(Continued)*

- Able to communicate with the investigator and understand and comply with the requirements of the study

EXCLUSION CRITERIA

- Systemic treatment with biological therapies, whether marketed or not, with a possible effect on psoriasis vulgaris within the following time periods prior to randomisation:
  - etanercept - within 4 weeks prior to randomisation
  - adalimumab, alefacept, infliximab - within 8 weeks prior to randomisation
  - ustekinumab - within 16 weeks prior to randomisation
  - other products - 4 weeks/5 half-lives (whichever is longer)
- Systemic treatment with all other therapies with a possible effect on psoriasis vulgaris (e.g. corticosteroids, retinoids, methotrexate, ciclosporin, and other immunosuppressants) within 4 weeks prior to randomisation
- Participants who have received treatment with any non-marketed drug substance (i.e. a drug which has not yet been made available for clinical use following registration) within 4 weeks/5 half-lives (whichever is longer) prior to randomisation
- PUVA therapy within 4 weeks prior to randomisation
- UVB therapy within 2 weeks prior to randomisation
- Planned excessive exposure of area(s) to be treated with study medication to either natural or artificial sunlight (including tanning booths, sun lamps, etc) during the study
- Planned initiation of, or changes to, concomitant medication that could affect psoriasis vulgaris (e.g. beta blockers, antimalarial drugs, lithium, ACE inhibitors) during the study
- Current diagnosis of guttate, erythrodermic, exfoliative, or pustular psoriasis
- Participants with any of the following conditions present on the treatment area: viral (e.g. herpes or varicella) lesions of the skin, fungal and bacterial skin infections, parasitic infections, skin manifestations in relation to syphilis or tuberculosis, acne vulgaris, atrophic skin, striae atrophicae, fragility of skin veins, icthyosis, ulcers, and wounds
- Other inflammatory skin disorders (e.g. seborrhoeic dermatitis or contact dermatitis) on the treatment area that may confound the evaluation of psoriasis vulgaris
- Known or suspected disorders of calcium metabolism associated with hypercalcaemia
- Known or suspected severe renal insufficiency or severe hepatic disorders
- Known or suspected hypersensitivity to component(s) of the investigational products
- Current participation in any other interventional clinical study
- Previously randomised in this study

Interventions	• Drug: LEO 90100 • Drug: calcipotriol • Drug: betamethasone
Outcomes	1. Investigator's Global Assessment of Disease Severity (time frame: 4 weeks) (Designated as safety issue: no)
Starting date	May 2012
Contact information	Anders Ninn Hansen, MSc Pharm Telephone: +45 72 26 28 18 ext: 2818 anders.n-hansen@leo-pharma.com
Notes	-

DATA AND ANALYSES

Comparison 1. Vitamin D analogues versus placebo

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 IAGI	20		Std. Mean Difference (IV, Random, 95% CI)	Subtotals only
1.1 Calcipotriol	10	2287	Std. Mean Difference (IV, Random, 95% CI)	-0.93 [-1.17, -0.68]
1.2 Calcipotriol plus occlusion	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
1.3 Calcitriol	6	1120	Std. Mean Difference (IV, Random, 95% CI)	-1.03 [-1.71, -0.36]
1.4 Tacalcitol	2	433	Std. Mean Difference (IV, Random, 95% CI)	-0.84 [-1.41, -0.26]
1.5 Maxacalcitol	1	103	Std. Mean Difference (IV, Random, 95% CI)	-1.43 [-1.91, -0.96]
1.6 Paricalcitol OD	1	22	Std. Mean Difference (IV, Random, 95% CI)	-1.66 [-2.66, -0.67]
1.7 Becocalcidiol OD	1	121	Std. Mean Difference (IV, Random, 95% CI)	-0.22 [-0.58, 0.14]
1.8 Becocalcidiol twice daily	1	119	Std. Mean Difference (IV, Random, 95% CI)	-0.67 [-1.04, -0.30]
2 TSS	19		Std. Mean Difference (IV, Random, 95% CI)	Subtotals only
2.1 Calcipotriol	10	1208	Std. Mean Difference (IV, Random, 95% CI)	-1.15 [-1.41, -0.89]
2.2 Calcipotriol plus occlusion	1	187	Std. Mean Difference (IV, Random, 95% CI)	-0.15 [-0.44, 0.14]
2.3 Calcitriol	4	1027	Std. Mean Difference (IV, Random, 95% CI)	-1.22 [-2.38, -0.07]
2.4 Tacalcitol	3	496	Std. Mean Difference (IV, Random, 95% CI)	-0.66 [-0.95, -0.36]
2.5 Maxacalcitol	1	103	Std. Mean Difference (IV, Random, 95% CI)	-1.61 [-2.10, -1.12]
2.6 Paricalcitol OD	1	22	Std. Mean Difference (IV, Random, 95% CI)	-2.15 [-3.24, -1.06]
2.7 Becocalcidiol OD	1	121	Std. Mean Difference (IV, Random, 95% CI)	-0.02 [-0.37, 0.34]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
2.8 Becocalcidiol twice daily	1	119	Std. Mean Difference (IV, Random, 95% CI)	-0.46 [-0.83, -0.10]
3 PASI	9	2422	Std. Mean Difference (IV, Random, 95% CI)	-0.58 [-0.71, -0.45]
3.1 Calcipotriol	8	2195	Std. Mean Difference (IV, Random, 95% CI)	-0.65 [-0.75, -0.55]
3.2 Calcipotriol plus occlusion	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
3.3 Calcitriol	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
3.4 Tacalcitol	1	227	Std. Mean Difference (IV, Random, 95% CI)	-0.27 [-0.56, 0.03]
3.5 Maxacalcitol	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
3.6 Paricalcitol OD	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
3.7 Becocalcidiol OD	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
3.8 Becocalcidiol twice daily	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
4 PAGI	5	1467	Std. Mean Difference (IV, Random, 95% CI)	-0.54 [-0.72, -0.36]
4.1 Calcipotriol	2	439	Std. Mean Difference (IV, Random, 95% CI)	-0.64 [-0.97, -0.30]
4.2 Calcipotriol plus occlusion	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
4.3 Calcitriol	2	801	Std. Mean Difference (IV, Random, 95% CI)	-0.59 [-0.76, -0.41]
4.4 Tacalcitol	1	227	Std. Mean Difference (IV, Random, 95% CI)	-0.24 [-0.53, 0.05]
4.5 Maxacalcitol	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
4.6 Paricalcitol OD	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
4.7 Becocalcidiol OD	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]

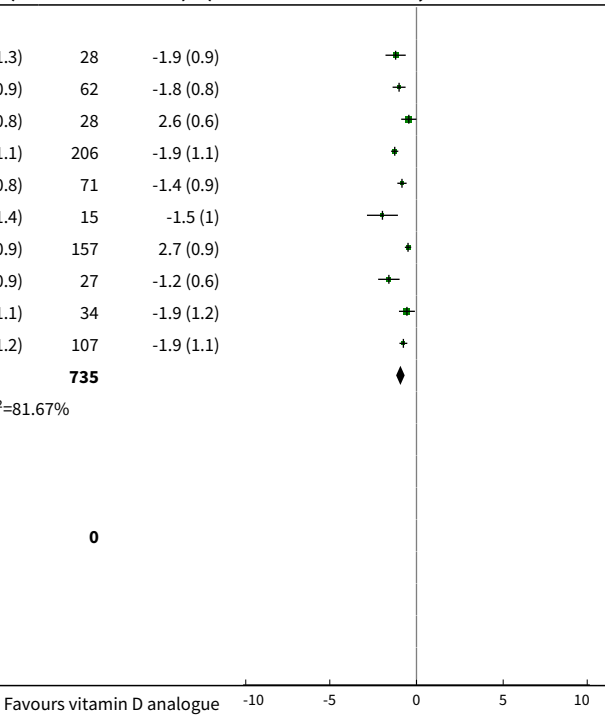
Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
4.8 Becocalcidiol twice daily	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
5 Combined end point (IAGI/TSS/PASI/PAGI)	30		Std. Mean Difference (IV, Random, 95% CI)	Subtotals only
5.1 Calcipotriol	17	3269	Std. Mean Difference (IV, Random, 95% CI)	-0.96 [-1.15, -0.77]
5.2 Calcipotriol plus occlusion	1	187	Std. Mean Difference (IV, Random, 95% CI)	-0.15 [-0.44, 0.14]
5.3 Calcitriol	7	1140	Std. Mean Difference (IV, Random, 95% CI)	-0.92 [-1.54, -0.29]
5.4 Tacalcitol	4	723	Std. Mean Difference (IV, Random, 95% CI)	-0.73 [-1.09, -0.37]
5.5 Maxacalcitol	1	103	Std. Mean Difference (IV, Random, 95% CI)	-1.43 [-1.91, -0.96]
5.6 Paricalcitol OD	1	22	Std. Mean Difference (IV, Random, 95% CI)	-1.66 [-2.66, -0.67]
5.7 Becocalcidiol OD	1	121	Std. Mean Difference (IV, Random, 95% CI)	-0.22 [-0.58, 0.14]
5.8 Becocalcidiol twice daily	1	119	Std. Mean Difference (IV, Random, 95% CI)	-0.67 [-1.04, -0.30]
6 Total withdrawals	25	4715	Risk Difference (M-H, Random, 95% CI)	-0.02 [-0.05, 0.00]
6.1 Calcipotriol	14	3132	Risk Difference (M-H, Random, 95% CI)	-0.03 [-0.06, 0.00]
6.2 Calcipotriol plus occlusion	0	0	Risk Difference (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
6.3 Calcitriol	5	339	Risk Difference (M-H, Random, 95% CI)	-0.00 [-0.02, 0.02]
6.4 Tacalcitol	4	857	Risk Difference (M-H, Random, 95% CI)	-0.05 [-0.14, 0.05]
6.5 Maxacalcitol	1	120	Risk Difference (M-H, Random, 95% CI)	0.11 [-0.01, 0.23]
6.6 Paricalcitol OD	1	22	Risk Difference (M-H, Random, 95% CI)	0.0 [-0.16, 0.16]
6.7 Becocalcidiol OD	1	124	Risk Difference (M-H, Random, 95% CI)	-0.01 [-0.12, 0.11]
6.8 Becocalcidiol twice daily	1	121	Risk Difference (M-H, Random, 95% CI)	-0.01 [-0.13, 0.10]
7 Withdrawals due to adverse events	23	4463	Risk Difference (M-H, Random, 95% CI)	-0.00 [-0.02, 0.01]
7.1 Calcipotriol	12	2880	Risk Difference (M-H, Random, 95% CI)	-0.02 [-0.04, 0.00]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
7.2 Calcipotriol plus occlusion	0	0	Risk Difference (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
7.3 Calcitriol	5	339	Risk Difference (M-H, Random, 95% CI)	-0.00 [-0.02, 0.02]
7.4 Tacalcitol	4	857	Risk Difference (M-H, Random, 95% CI)	0.00 [-0.01, 0.02]
7.5 Maxacalcitol	1	120	Risk Difference (M-H, Random, 95% CI)	-0.01 [-0.08, 0.06]
7.6 Paricalcitol OD	1	22	Risk Difference (M-H, Random, 95% CI)	0.0 [-0.16, 0.16]
7.7 Becocalcidiol OD	1	124	Risk Difference (M-H, Random, 95% CI)	0.03 [-0.02, 0.08]
7.8 Becocalcidiol twice daily	1	121	Risk Difference (M-H, Random, 95% CI)	0.05 [-0.01, 0.11]
8 Withdrawals due to treatment failure	14	2752	Risk Difference (M-H, Random, 95% CI)	-0.03 [-0.05, 0.00]
8.1 Calcipotriol	7	1770	Risk Difference (M-H, Random, 95% CI)	-0.03 [-0.08, 0.01]
8.2 Calcipotriol plus occlusion	0	0	Risk Difference (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
8.3 Calcitriol	4	281	Risk Difference (M-H, Random, 95% CI)	-0.03 [-0.12, 0.05]
8.4 Tacalcitol	1	314	Risk Difference (M-H, Random, 95% CI)	0.0 [-0.01, 0.01]
8.5 Maxacalcitol	1	120	Risk Difference (M-H, Random, 95% CI)	-0.03 [-0.11, 0.04]
8.6 Paricalcitol OD	1	22	Risk Difference (M-H, Random, 95% CI)	0.0 [-0.16, 0.16]
8.7 Becocalcidiol OD	1	124	Risk Difference (M-H, Random, 95% CI)	-0.02 [-0.07, 0.04]
8.8 Becocalcidiol twice daily	1	121	Risk Difference (M-H, Random, 95% CI)	-0.03 [-0.09, 0.02]
9 Adverse events (local)	19	4402	Risk Difference (M-H, Random, 95% CI)	0.00 [-0.01, 0.02]
9.1 Calcipotriol	11	2652	Risk Difference (M-H, Random, 95% CI)	0.01 [-0.03, 0.05]
9.2 Calcipotriol plus occlusion	0	0	Risk Difference (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
9.3 Calcitriol	4	917	Risk Difference (M-H, Random, 95% CI)	-0.01 [-0.03, 0.02]
9.4 Tacalcitol	2	566	Risk Difference (M-H, Random, 95% CI)	-0.00 [-0.03, 0.03]
9.5 Maxacalcitol	0	0	Risk Difference (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
9.6 Paricalcitol OD	1	22	Risk Difference (M-H, Random, 95% CI)	0.0 [-0.16, 0.16]
9.7 Becocalcidiol OD	1	124	Risk Difference (M-H, Random, 95% CI)	0.01 [-0.06, 0.08]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
9.8 Becocalcidiol twice daily	1	121	Risk Difference (M-H, Random, 95% CI)	0.10 [0.00, 0.19]
10 Adverse events (systemic)	14	2463	Risk Difference (M-H, Random, 95% CI)	0.0 [-0.01, 0.01]
10.1 Calcipotriol	8	1182	Risk Difference (M-H, Random, 95% CI)	0.0 [-0.01, 0.01]
10.2 Calcipotriol plus occlusion	0	0	Risk Difference (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
10.3 Calcitriol	3	647	Risk Difference (M-H, Random, 95% CI)	0.0 [-0.01, 0.01]
10.4 Tacalcitol	1	244	Risk Difference (M-H, Random, 95% CI)	0.0 [-0.02, 0.02]
10.5 Maxacalcitol	1	120	Risk Difference (M-H, Random, 95% CI)	0.0 [-0.05, 0.05]
10.6 Paricalcitol OD	1	22	Risk Difference (M-H, Random, 95% CI)	0.0 [-0.16, 0.16]
10.7 Becocalcidiol OD	1	124	Risk Difference (M-H, Random, 95% CI)	0.0 [-0.03, 0.03]
10.8 Becocalcidiol twice daily	1	124	Risk Difference (M-H, Random, 95% CI)	0.0 [-0.03, 0.03]

Analysis 1.1. Comparison 1 Vitamin D analogues versus placebo, Outcome 1 IAGI.

Study or subgroup	Vitamin D analogue N	Vitamin D analogue Mean(SD)	Placebo N	Placebo Mean(SD)	Std. Mean Difference Random, 95% CI	Weight	Std. Mean Difference Random, 95% CI
1.1.1 Calcipotriol							
Barker 1999 (P)	26	-3.2 (1.3)	28	-1.9 (0.9)		7.84%	-1.2[-1.79,-0.62]
Dubertret 1992	62	-2.7 (0.9)	62	-1.8 (0.8)		10.56%	-1[-1.38,-0.63]
Fleming 2010 (P)	74	2.3 (0.8)	28	2.6 (0.6)		9.67%	-0.44[-0.88,-0]
Guenther 2002 (P)	227	-3.3 (1.1)	206	-1.9 (1.1)		12.7%	-1.25[-1.46,-1.05]
Harrington 1996a	290	-2.1 (0.8)	71	-1.4 (0.9)		11.99%	-0.84[-1.1,-0.57]
Kang 1998	15	-3.9 (1.4)	15	-1.5 (1)		4.94%	-1.96[-2.86,-1.07]
Kaufmann 2002 (P)	480	2.2 (0.9)	157	2.7 (0.9)		12.96%	-0.49[-0.67,-0.31]
Kragballe 1988b	27	-2.4 (0.9)	27	-1.2 (0.6)		7.44%	-1.59[-2.21,-0.97]
Oranje 1997	43	-2.5 (1.1)	34	-1.9 (1.2)		9.41%	-0.55[-1.01,-0.09]
Papp 2003 (P)	308	-2.8 (1.2)	107	-1.9 (1.1)		12.48%	-0.76[-0.98,-0.53]
Subtotal ***	**1552**		**735**			**100%**	**-0.93[-1.17,-0.68]**
Heterogeneity: Tau^2=0.11; Chi^2=49.09, df=9(P<0.0001); I^2=81.67%							
Test for overall effect: Z=7.37(P<0.0001)							
1.1.2 Calcipotriol plus occlusion							
Subtotal ***	**0**		**0**				**Not estimable**
Heterogeneity: Not applicable							
Test for overall effect: Not applicable							
1.1.3 Calcitriol							



Study or subgroup	Vitamin D analogue N	Mean(SD)	Placebo N	Mean(SD)	Std. Mean Difference Random, 95% CI	Weight	Std. Mean Difference Random, 95% CI
Langner 1992	29	-4.1 (1.1)	29	-3 (1)		16.17%	-1.04[-1.59,-0.49]
Langner 1993	32	-4 (1.3)	32	-3.3 (1.1)		16.48%	-0.55[-1.05,-0.05]
Langner 2001 (P)	15	-2.4 (1.2)	14	-2.1 (0.7)		14.93%	-0.26[-0.99,0.47]
Lebwohl 2007	202	-3.1 (1.4)	199	-2.4 (1.4)		17.84%	-0.49[-0.69,-0.29]
Perez 1996	84	-3.2 (0.9)	84	-1.1 (0.4)		16.75%	-3.11[-3.57,-2.66]
Powers 2005	199	-2.9 (1.3)	201	-2 (1.3)		17.83%	-0.72[-0.92,-0.51]
Subtotal * **	**561**		**559**			**100%**	**-1.03[-1.71,-0.36]**
Heterogeneity: Tau²=0.65; Chi²=114.17, df=5(P<0.0001); I²=95.62%							
Test for overall effect: Z=3.01(P=0)							
1.1.4 Tacalcitol							
Langley 2011 (P)	163	2.3 (0.9)	64	2.8 (0.8)		50.02%	-0.54[-0.84,-0.25]
Van de Kerkhof 1996a	103	-1.7 (0.9)	103	-0.7 (0.7)		49.98%	-1.13[-1.42,-0.83]
Subtotal * **	**266**		**167**			**100%**	**-0.84[-1.41,-0.26]**
Heterogeneity: Tau²=0.15; Chi²=7.57, df=1(P=0.01); I²=86.78%							
Test for overall effect: Z=2.87(P=0)							
1.1.5 Maxacalcitol							
Barker 1999 (P)	75	-3.5 (1.2)	28	-1.9 (0.9)		100%	-1.43[-1.91,-0.96]
Subtotal * **	**75**		**28**			**100%**	**-1.43[-1.91,-0.96]**
Heterogeneity: Not applicable							
Test for overall effect: Z=5.88(P<0.0001)							
1.1.6 Paricalcitol OD							
Durakovic 2004	11	-2.4 (1.1)	11	-0.7 (0.9)		100%	-1.66[-2.66,-0.67]
Subtotal * **	**11**		**11**			**100%**	**-1.66[-2.66,-0.67]**
Heterogeneity: Not applicable							
Test for overall effect: Z=3.27(P=0)							
1.1.7 Becocalcidiol OD							
Helfrich 2007	63	2.3 (0.8)	58	2.5 (0.7)		100%	-0.22[-0.58,0.14]
Subtotal * **	**63**		**58**			**100%**	**-0.22[-0.58,0.14]**
Heterogeneity: Not applicable							
Test for overall effect: Z=1.21(P=0.23)							
1.1.8 Becocalcidiol twice daily							
Helfrich 2007	61	2 (0.7)	58	2.5 (0.7)		100%	-0.67[-1.04,-0.3]
Subtotal * **	**61**		**58**			**100%**	**-0.67[-1.04,-0.3]**
Heterogeneity: Not applicable							
Test for overall effect: Z=3.55(P=0)							
Test for subgroup differences: Chi²=21.65, df=1 (P=0), I²=72.29%							

Favours vitamin D analogue -10 -5 0 5 10 Favours placebo

Analysis 1.2. Comparison 1 Vitamin D analogues versus placebo, Outcome 2 TSS.

Study or subgroup	Vitamin D analogue N	Mean(SD)	Placebo N	Mean(SD)	Std. Mean Difference Random, 95% CI	Weight	Std. Mean Difference Random, 95% CI
1.2.1 Calcipotriol							
Barker 1999 (P)	26	2.8 (2.3)	28	8.3 (3.2)		7.98%	-1.93[-2.59,-1.28]

Favours vitamin D analogue -5 -2.5 0 2.5 5 Favours placebo

Study or subgroup	Vitamin D analogue N	Vitamin D analogue Mean(SD)	Placebo N	Placebo Mean(SD)	Std. Mean Difference Random, 95% CI	Weight	Std. Mean Difference Random, 95% CI
Dubertret 1992	61	3.2 (1.9)	61	4.7 (1.9)		12.16%	-0.78[-1.15,-0.42]
Highton 1995	124	1.7 (1.2)	123	3.2 (1.2)		13.69%	-1.2[-1.48,-0.93]
Hindsén 2006 (P)	114	5.2 (3.3)	92	10.4 (4.4)		13.18%	-1.35[-1.66,-1.05]
Kang 1998	15	4.5 (3.3)	15	10.8 (3.3)		5.74%	-1.83[-2.7,-0.96]
Kragballe 1988b	27	4.6 (1.9)	27	6.7 (1.4)		8.84%	-1.26[-1.85,-0.67]
Levine 2010 (P)	48	3.5 (2)	48	4.1 (1.9)		11.62%	-0.29[-0.69,0.12]
Pariser 1996	167	2.3 (1.3)	168	3.6 (1.3)		14.32%	-1.02[-1.25,-0.79]
Staberg 1989	9	1.3 (1.6)	9	4.6 (2.2)		4.13%	-1.63[-2.74,-0.53]
Zonneveld 1998 (P)	23	2.6 (1.7)	23	4.6 (1.7)		8.32%	-1.14[-1.76,-0.51]
Subtotal * **	**614**		**594**			**100%**	**-1.15[-1.41,-0.89]**
Heterogeneity: Tau^2=0.11; Chi^2=32.32, df=9(P=0); I^2=72.15%							
Test for overall effect: Z=8.66(P<0.0001)							
1.2.2 Calcipotriol plus occlusion							
Hindsén 2006 (P)	95	9.7 (4.8)	92	10.4 (4.4)		100%	-0.15[-0.44,0.14]
Subtotal * **	**95**		**92**			**100%**	**-0.15[-0.44,0.14]**
Heterogeneity: Not applicable							
Test for overall effect: Z=1.03(P=0.3)							
1.2.3 Calcitriol							
Lebwohl 2007	209	1.9 (0.9)	209	2.2 (0.8)		26.11%	-0.27[-0.46,-0.07]
Perez 1996	84	2.8 (1.5)	84	7.1 (0.1)		24.93%	-4.03[-4.56,-3.5]
Powers 2005	210	1.9 (0.9)	211	2.4 (0.8)		26.11%	-0.52[-0.72,-0.33]
Van de Kerkhof 1989	10	6 (1.5)	10	6.1 (1.5)		22.85%	-0.06[-0.94,0.81]
Subtotal * **	**513**		**514**			**100%**	**-1.22[-2.38,-0.07]**
Heterogeneity: Tau^2=1.33; Chi^2=173.88, df=3(P<0.0001); I^2=98.27%							
Test for overall effect: Z=2.07(P=0.04)							
1.2.4 Tacalcitol							
Scarpa 1997	134	3.4 (1.9)	134	4.3 (1.9)		47.83%	-0.46[-0.71,-0.22]
Seidenari 1997 (P)	11	2.9 (1.9)	11	4.5 (1.4)		9.54%	-0.92[-1.81,-0.03]
Van de Kerkhof 1996a	103	-4 (2.1)	103	-2.3 (2.1)		42.63%	-0.82[-1.11,-0.54]
Subtotal * **	**248**		**248**			**100%**	**-0.66[-0.95,-0.36]**
Heterogeneity: Tau^2=0.03; Chi^2=3.98, df=2(P=0.14); I^2=49.76%							
Test for overall effect: Z=4.38(P<0.0001)							
1.2.5 Maxacalcitol							
Barker 1999 (P)	75	3.1 (3.2)	28	8.4 (3.2)		100%	-1.61[-2.1,-1.12]
Subtotal * **	**75**		**28**			**100%**	**-1.61[-2.1,-1.12]**
Heterogeneity: Not applicable							
Test for overall effect: Z=6.47(P<0.0001)							
1.2.6 Paricalcitol OD							
Durakovic 2004	11	2.7 (1.7)	11	7.6 (2.6)		100%	-2.15[-3.24,-1.06]
Subtotal * **	**11**		**11**			**100%**	**-2.15[-3.24,-1.06]**
Heterogeneity: Not applicable							
Test for overall effect: Z=3.86(P=0)							
1.2.7 Becocalcidiol OD							
Helfrich 2007	63	4.9 (2.2)	58	4.9 (1.6)		100%	-0.02[-0.37,0.34]
Subtotal * **	**63**		**58**			**100%**	**-0.02[-0.37,0.34]**
Heterogeneity: Tau^2=0; Chi^2=0, df=0(P<0.0001); I^2=100%							

Favours vitamin D analogue

Favours placebo

Study or subgroup	Vitamin D analogue N	Vitamin D analogue Mean(SD)	Placebo N	Placebo Mean(SD)	Std. Mean Difference Random, 95% CI	Weight	Std. Mean Difference Random, 95% CI
Test for overall effect: Z=0.08(P=0.93)							
1.2.8 Becocalcidiol twice daily							
Helfrich 2007	61	4 (2)	58	4.9 (1.6)		100%	-0.46[-0.83,-0.1]
Subtotal ***	**61**		**58**			**100%**	**-0.46[-0.83,-0.1]**
Heterogeneity: Tau^2=0; Chi^2=0, df=0(P<0.0001); I^2=100%							
Test for overall effect: Z=2.49(P=0.01)							
Test for subgroup differences: Chi^2=62.06, df=1 (P<0.0001), I^2=88.72%							

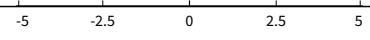
Favours vitamin D analogue -5 -2.5 0 2.5 5 Favours placebo

Analysis 1.3. Comparison 1 Vitamin D analogues versus placebo, Outcome 3 PASI.

Study or subgroup	Vitamin D analogue N	Vitamin D analogue Mean(SD)	Placebo N	Placebo Mean(SD)	Std. Mean Difference Random, 95% CI	Weight	Std. Mean Difference Random, 95% CI
1.3.1 Calcipotriol							
Dubertret 1992	65	6.3 (6.5)	65	9.2 (8.3)		9.24%	-0.38[-0.73,-0.03]
Fleming 2010 (P)	74	4.3 (2.8)	28	5.5 (3.5)		6.58%	-0.4[-0.83,0.04]
Guenther 2002 (P)	227	4.2 (3.3)	207	7.7 (5.5)		17.18%	-0.78[-0.97,-0.58]
Harrington 1996a	296	-4.3 (5.1)	70	-0.8 (5.4)		12.87%	-0.67[-0.94,-0.41]
Kaufmann 2002 (P)	480	-0.5 (0.3)	157	-0.2 (0.3)		17.96%	-0.72[-0.91,-0.54]
Mortensen 1993b	17	6.5 (2.5)	17	9 (4.7)		3.06%	-0.65[-1.34,0.04]
Oranje 1997	43	-0.5 (0.5)	34	-0.4 (0.4)		6.25%	-0.35[-0.8,0.11]
Papp 2003 (P)	308	-0.5 (0.3)	107	-0.3 (0.3)		15.26%	-0.63[-0.85,-0.4]
Subtotal ***	**1510**		**685**			**88.4%**	**-0.65[-0.75,-0.55]**
Heterogeneity: Tau^2=0; Chi^2=7.65, df=7(P=0.36); I^2=8.47%							
Test for overall effect: Z=12.44(P<0.0001)							
1.3.2 Calcipotriol plus occlusion							
Subtotal ***	**0**		**0**				**Not estimable**
Heterogeneity: Not applicable							
Test for overall effect: Not applicable							
1.3.3 Calcitriol							
Subtotal ***	**0**		**0**				**Not estimable**
Heterogeneity: Not applicable							
Test for overall effect: Not applicable							
1.3.4 Tacalcitol							
Langley 2011 (P)	163	5.4 (4.4)	64	6.5 (3.6)		11.6%	-0.27[-0.56,0.03]
Subtotal ***	**163**		**64**			**11.6%**	**-0.27[-0.56,0.03]**
Heterogeneity: Not applicable							
Test for overall effect: Z=1.79(P=0.07)							
1.3.5 Maxacalcitol							
Subtotal ***	**0**		**0**				**Not estimable**
Heterogeneity: Not applicable							
Test for overall effect: Not applicable							
1.3.6 Paricalcitol OD							

Favours vitamin D analogue -5 -2.5 0 2.5 5 Favours placebo

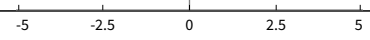
Study or subgroup	Vitamin D analogue N	Vitamin D analogue Mean(SD)	Placebo N	Placebo Mean(SD)	Std. Mean Difference Random, 95% CI	Weight	Std. Mean Difference Random, 95% CI
Subtotal ***	**0**		**0**				**Not estimable**
Heterogeneity: Not applicable							
Test for overall effect: Not applicable							
1.3.7 Becocalcidiol OD							
Subtotal ***	**0**		**0**				**Not estimable**
Heterogeneity: Not applicable							
Test for overall effect: Not applicable							
1.3.8 Becocalcidiol twice daily							
Subtotal ***	**0**		**0**				**Not estimable**
Heterogeneity: Not applicable							
Test for overall effect: Not applicable							
Total ***	**1673**		**749**			**100%**	**-0.58[-0.71,-0.45]**
Heterogeneity: Tau^2=0.01; Chi^2=13.87, df=8(P=0.09); I^2=42.34%							
Test for overall effect: Z=8.87(P<0.0001)							
Test for subgroup differences: Chi^2=5.94, df=1 (P=0.01), I^2=83.16%							



Favours vitamin D analogue — Favours placebo

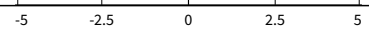
Analysis 1.4. Comparison 1 Vitamin D analogues versus placebo, Outcome 4 PAGI.

Study or subgroup	Vitamin D analogue N	Vitamin D analogue Mean(SD)	Placebo N	Placebo Mean(SD)	Std. Mean Difference Random, 95% CI	Weight	Std. Mean Difference Random, 95% CI
1.4.1 Calcipotriol							
Harrington 1996a	291	-2.3 (1)	71	-1.5 (1.1)		20.23%	-0.77[-1.03,-0.5]
Oranje 1997	43	-2.4 (1)	34	-1.9 (1.2)		10.68%	-0.41[-0.86,0.05]
Subtotal ***	**334**		**105**			**30.91%**	**-0.64[-0.97,-0.3]**
Heterogeneity: Tau^2=0.03; Chi^2=1.8, df=1(P=0.18); I^2=44.36%							
Test for overall effect: Z=3.67(P=0)							
1.4.2 Calcipotriol plus occlusion							
Subtotal ***	**0**		**0**				**Not estimable**
Heterogeneity: Not applicable							
Test for overall effect: Not applicable							
1.4.3 Calcitriol							
Lebwohl 2007	202	-3 (1.4)	199	-2.3 (1.4)		25.38%	-0.5[-0.7,-0.3]
Powers 2005	199	-2.8 (1.3)	201	-1.9 (1.3)		25.15%	-0.68[-0.88,-0.47]
Subtotal ***	**401**		**400**			**50.52%**	**-0.59[-0.76,-0.41]**
Heterogeneity: Tau^2=0.01; Chi^2=1.49, df=1(P=0.22); I^2=33.02%							
Test for overall effect: Z=6.65(P<0.0001)							
1.4.4 Tacalcitol							
Langley 2011 (P)	163	2.3 (0.9)	64	2.5 (1)		18.57%	-0.24[-0.53,0.05]
Subtotal ***	**163**		**64**			**18.57%**	**-0.24[-0.53,0.05]**
Heterogeneity: Tau^2=0; Chi^2=0, df=0(P<0.0001); I^2=100%							
Test for overall effect: Z=1.64(P=0.1)							



Favours vitamin D analogue — Favours placebo

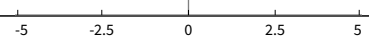
Study or subgroup	Vitamin D analogue N	Vitamin D analogue Mean(SD)	Placebo N	Placebo Mean(SD)	Std. Mean Difference Random, 95% CI	Weight	Std. Mean Difference Random, 95% CI
1.4.5 Maxacalcitol							
Subtotal ***	**0**		**0**				**Not estimable**
Heterogeneity: Not applicable							
Test for overall effect: Not applicable							
1.4.6 Paricalcitol OD							
Subtotal ***	**0**		**0**				**Not estimable**
Heterogeneity: Not applicable							
Test for overall effect: Not applicable							
1.4.7 Becocalcidiol OD							
Subtotal ***	**0**		**0**				**Not estimable**
Heterogeneity: Not applicable							
Test for overall effect: Not applicable							
1.4.8 Becocalcidiol twice daily							
Subtotal ***	**0**		**0**				**Not estimable**
Heterogeneity: Not applicable							
Test for overall effect: Not applicable							
Total ***	**898**		**569**			**100%**	**-0.54[-0.72,-0.36]**
Heterogeneity: Tau^2=0.02; Chi^2=8.99, df=4(P=0.06); I^2=55.51%							
Test for overall effect: Z=6.02(P<0.0001)							
Test for subgroup differences: Chi^2=4.54, df=1 (P=0.1), I^2=55.93%							



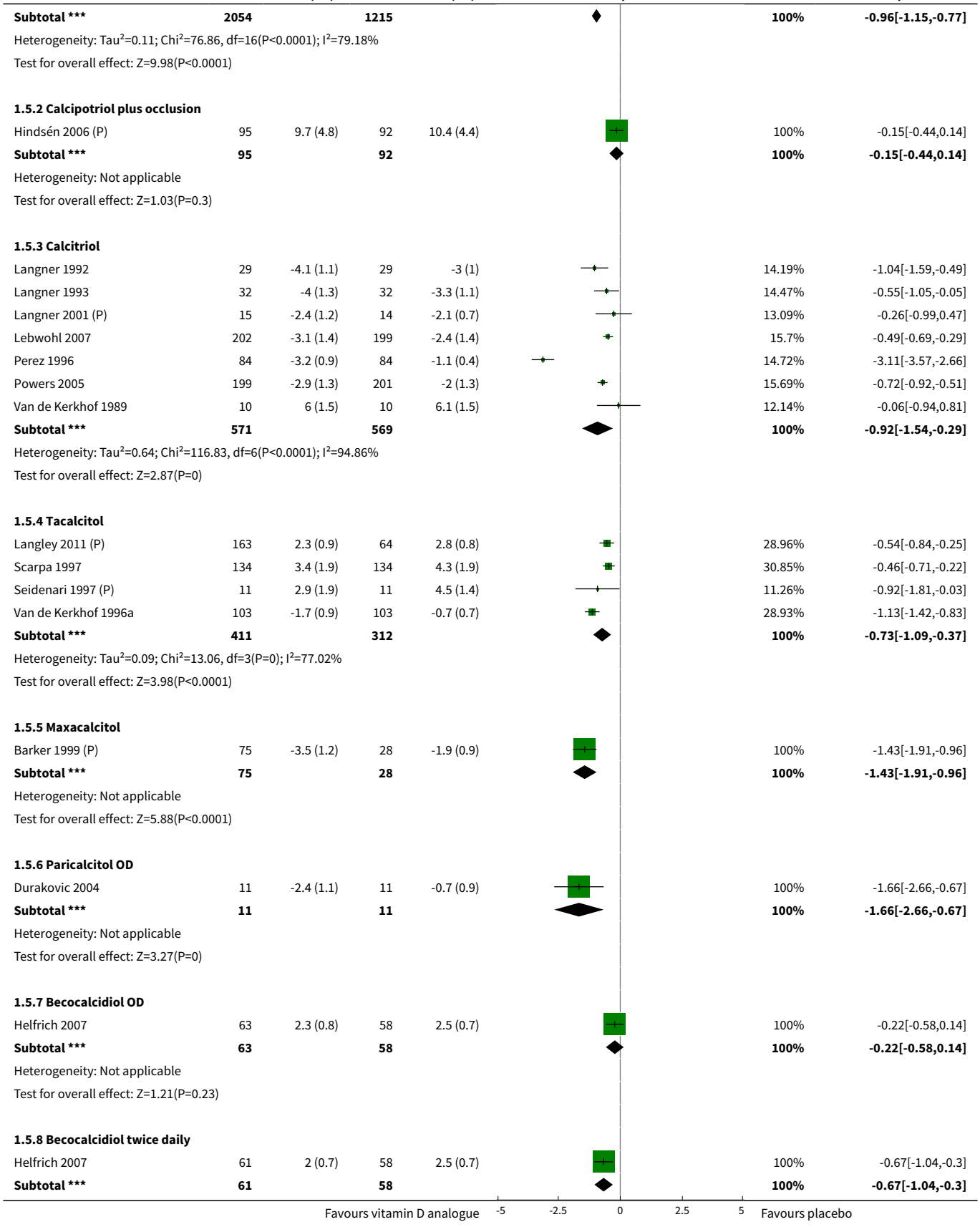
Favours vitamin D analogue — Favours placebo

Analysis 1.5. Comparison 1 Vitamin D analogues versus placebo, Outcome 5 Combined end point (IAGI/TSS/PASI/PAGI).

Study or subgroup	Vitamin D analogue N	Vitamin D analogue Mean(SD)	Placebo N	Placebo Mean(SD)	Std. Mean Difference Random, 95% CI	Weight	Std. Mean Difference Random, 95% CI
1.5.1 Calcipotriol							
Barker 1999 (P)	26	-3.2 (1.3)	28	-1.9 (0.9)		4.72%	-1.2[-1.79,-0.62]
Dubertret 1992	62	-2.7 (0.9)	62	-1.8 (0.8)		6.45%	-1[-1.38,-0.63]
Fleming 2010 (P)	74	2.3 (0.8)	28	2.6 (0.6)		5.88%	-0.44[-0.88,-0]
Guenther 2002 (P)	227	-3.3 (1.1)	206	-1.9 (1.1)		7.85%	-1.25[-1.46,-1.05]
Harrington 1996a	290	-2.1 (0.8)	71	-1.4 (0.9)		7.38%	-0.84[-1.1,-0.57]
Highton 1995	124	1.7 (1.2)	123	3.2 (1.2)		7.34%	-1.2[-1.48,-0.93]
Hindsén 2006 (P)	114	5.2 (3.3)	92	10.4 (4.4)		7.06%	-1.35[-1.66,-1.05]
Kang 1998	15	-3.9 (1.4)	15	-1.5 (1)		2.94%	-1.96[-2.86,-1.07]
Kaufmann 2002 (P)	480	2.2 (0.9)	157	2.7 (0.9)		8.01%	-0.49[-0.67,-0.31]
Kragballe 1988b	27	-2.4 (0.9)	27	-1.2 (0.6)		4.48%	-1.59[-2.21,-0.97]
Levine 2010 (P)	48	3.5 (2)	48	4.1 (1.9)		6.21%	-0.29[-0.69,0.12]
Mortensen 1993b	17	6.5 (2.5)	17	9 (4.7)		3.99%	-0.65[-1.34,0.04]
Oranje 1997	43	-2.5 (1.1)	34	-1.9 (1.2)		5.72%	-0.55[-1.01,-0.09]
Papp 2003 (P)	308	-2.8 (1.2)	107	-1.9 (1.1)		7.7%	-0.76[-0.98,-0.53]
Pariser 1996	167	2.3 (1.3)	168	3.6 (1.3)		7.69%	-1.02[-1.25,-0.79]
Staberg 1989	9	1.3 (1.6)	9	4.6 (2.2)		2.17%	-1.63[-2.74,-0.53]
Zonneveld 1998 (P)	23	2.6 (1.7)	23	4.6 (1.7)		4.41%	-1.14[-1.76,-0.51]



Favours vitamin D analogue — Favours placebo



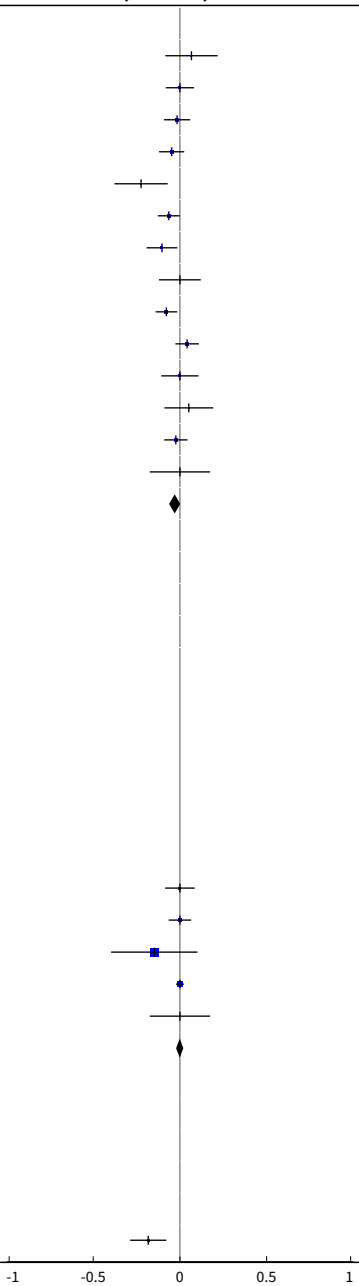
Study or subgroup	Vitamin D analogue N	Vitamin D analogue Mean(SD)	Placebo N	Placebo Mean(SD)	Std. Mean Difference Random, 95% CI	Weight	Std. Mean Difference Random, 95% CI
Subtotal ***	**2054**		**1215**			**100%**	**-0.96[-1.15,-0.77]**
Heterogeneity: Tau²=0.11; Chi²=76.86, df=16(P<0.0001); I²=79.18%							
Test for overall effect: Z=9.98(P<0.0001)							
1.5.2 Calcipotriol plus occlusion							
Hindsén 2006 (P)	95	9.7 (4.8)	92	10.4 (4.4)		100%	-0.15[-0.44,0.14]
Subtotal ***	**95**		**92**			**100%**	**-0.15[-0.44,0.14]**
Heterogeneity: Not applicable							
Test for overall effect: Z=1.03(P=0.3)							
1.5.3 Calcitriol							
Langner 1992	29	-4.1 (1.1)	29	-3 (1)		14.19%	-1.04[-1.59,-0.49]
Langner 1993	32	-4 (1.3)	32	-3.3 (1.1)		14.47%	-0.55[-1.05,-0.05]
Langner 2001 (P)	15	-2.4 (1.2)	14	-2.1 (0.7)		13.09%	-0.26[-0.99,0.47]
Lebwohl 2007	202	-3.1 (1.4)	199	-2.4 (1.4)		15.7%	-0.49[-0.69,-0.29]
Perez 1996	84	-3.2 (0.9)	84	-1.1 (0.4)		14.72%	-3.11[-3.57,-2.66]
Powers 2005	199	-2.9 (1.3)	201	-2 (1.3)		15.69%	-0.72[-0.92,-0.51]
Van de Kerkhof 1989	10	6 (1.5)	10	6.1 (1.5)		12.14%	-0.06[-0.94,0.81]
Subtotal ***	**571**		**569**			**100%**	**-0.92[-1.54,-0.29]**
Heterogeneity: Tau²=0.64; Chi²=116.83, df=6(P<0.0001); I²=94.86%							
Test for overall effect: Z=2.87(P=0)							
1.5.4 Tacalcitol							
Langley 2011 (P)	163	2.3 (0.9)	64	2.8 (0.8)		28.96%	-0.54[-0.84,-0.25]
Scarpa 1997	134	3.4 (1.9)	134	4.3 (1.9)		30.85%	-0.46[-0.71,-0.22]
Seidenari 1997 (P)	11	2.9 (1.9)	11	4.5 (1.4)		11.26%	-0.92[-1.81,-0.03]
Van de Kerkhof 1996a	103	-1.7 (0.9)	103	-0.7 (0.7)		28.93%	-1.13[-1.42,-0.83]
Subtotal ***	**411**		**312**			**100%**	**-0.73[-1.09,-0.37]**
Heterogeneity: Tau²=0.09; Chi²=13.06, df=3(P=0); I²=77.02%							
Test for overall effect: Z=3.98(P<0.0001)							
1.5.5 Maxacalcitol							
Barker 1999 (P)	75	-3.5 (1.2)	28	-1.9 (0.9)		100%	-1.43[-1.91,-0.96]
Subtotal ***	**75**		**28**			**100%**	**-1.43[-1.91,-0.96]**
Heterogeneity: Not applicable							
Test for overall effect: Z=5.88(P<0.0001)							
1.5.6 Paricalcitol OD							
Durakovic 2004	11	-2.4 (1.1)	11	-0.7 (0.9)		100%	-1.66[-2.66,-0.67]
Subtotal ***	**11**		**11**			**100%**	**-1.66[-2.66,-0.67]**
Heterogeneity: Not applicable							
Test for overall effect: Z=3.27(P=0)							
1.5.7 Becocalcidiol OD							
Helfrich 2007	63	2.3 (0.8)	58	2.5 (0.7)		100%	-0.22[-0.58,0.14]
Subtotal ***	**63**		**58**			**100%**	**-0.22[-0.58,0.14]**
Heterogeneity: Not applicable							
Test for overall effect: Z=1.21(P=0.23)							
1.5.8 Becocalcidiol twice daily							
Helfrich 2007	61	2 (0.7)	58	2.5 (0.7)		100%	-0.67[-1.04,-0.3]
Subtotal ***	**61**		**58**			**100%**	**-0.67[-1.04,-0.3]**

Study or subgroup	Vitamin D analogue N	Vitamin D analogue Mean(SD)	Placebo N	Placebo Mean(SD)	Std. Mean Difference Random, 95% CI	Weight	Std. Mean Difference Random, 95% CI
Heterogeneity: Not applicable							
Test for overall effect: Z=3.55(P=0)							
Test for subgroup differences: Chi²=41.16, df=1 (P<0.0001), I²=82.99%							

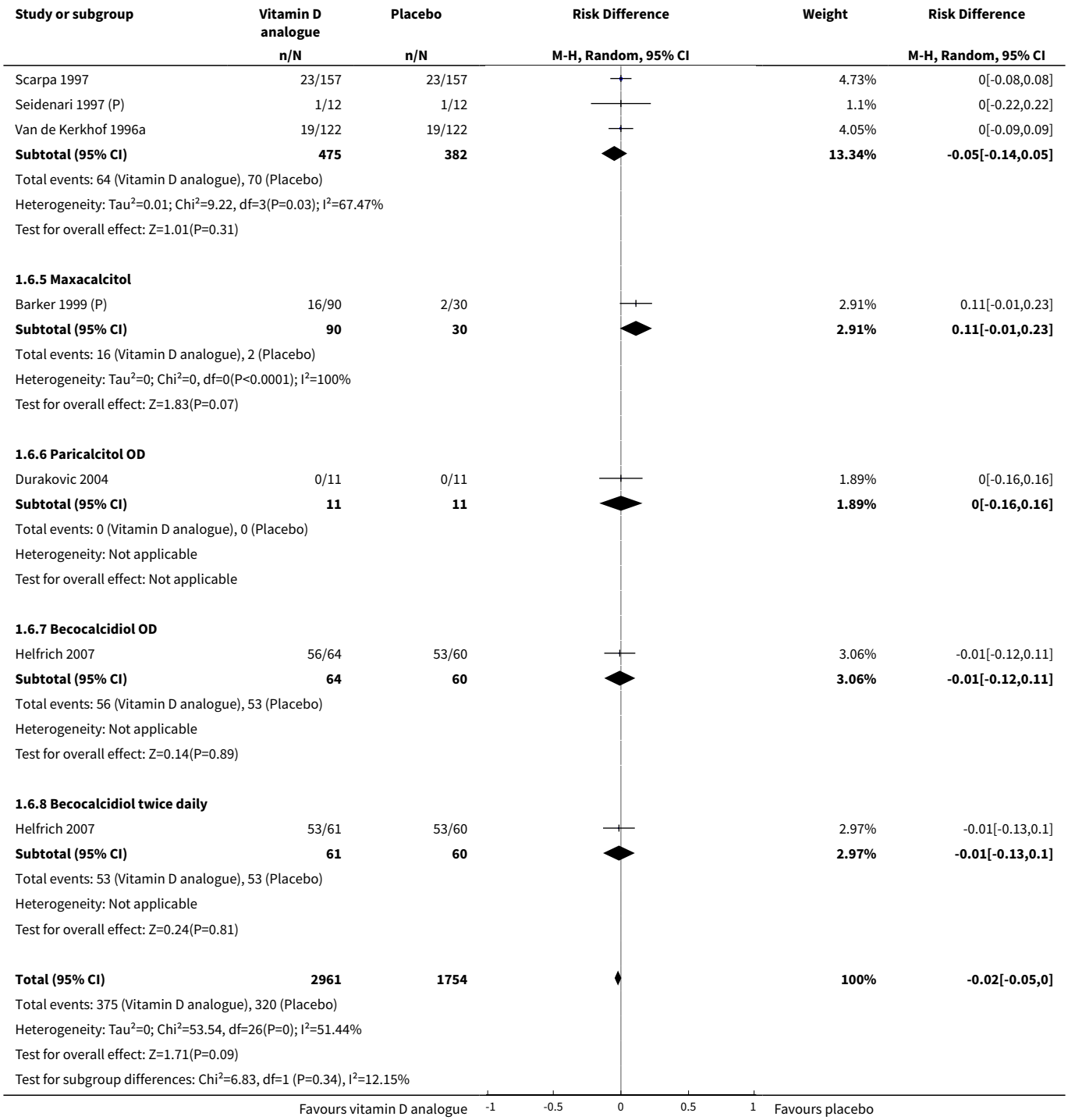
Favours vitamin D analogue — Favours placebo

Analysis 1.6. Comparison 1 Vitamin D analogues versus placebo, Outcome 6 Total withdrawals.

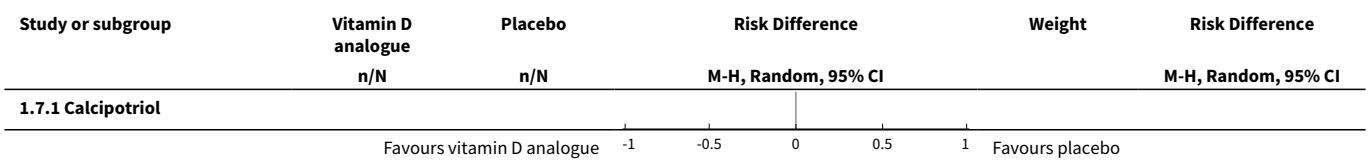
Study or subgroup	Vitamin D analogue n/N	Placebo n/N	Risk Difference M-H, Random, 95% CI	Weight	Risk Difference M-H, Random, 95% CI
1.6.1 Calcipotriol					
Barker 1999 (P)	4/30	2/30		2.07%	0.07[-0.08,0.22]
Dubertret 1992	4/66	4/66		4.55%	0[-0.08,0.08]
Feldman 2010 (1)	24/214	14/109		4.88%	-0.02[-0.09,0.06]
Feldman 2010 (2)	19/223	15/113		5.07%	-0.05[-0.12,0.02]
Fleming 2010 (P)	6/79	12/40		2.01%	-0.22[-0.38,-0.07]
Guenther 2002 (P)	23/231	34/208		5.65%	-0.06[-0.13,-0]
Harrington 1996a	30/326	17/87		4.15%	-0.1[-0.19,-0.01]
Kang 1998	0/15	0/15		2.87%	0[-0.12,0.12]
Kaufmann 2002 (P)	39/480	25/157		5.73%	-0.08[-0.14,-0.02]
Levine 2010 (P)	2/48	0/48		5.37%	0.04[-0.03,0.11]
Mortensen 1993b	0/17	0/17		3.34%	0[-0.11,0.11]
Oranje 1997	6/43	3/34		2.3%	0.05[-0.09,0.19]
Papp 2003 (P)	27/308	12/108		5.41%	-0.02[-0.09,0.04]
Staberg 1989	0/10	0/10		1.65%	0[-0.17,0.17]
Subtotal (95% CI)	**2090**	**1042**		**55.04%**	**-0.03[-0.06,0]**
Total events: 184 (Vitamin D analogue), 138 (Placebo)					
Heterogeneity: Tau²=0; Chi²=23.15, df=13(P=0.04); I²=43.84%					
Test for overall effect: Z=1.84(P=0.07)					
1.6.2 Calcipotriol plus occlusion					
Subtotal (95% CI)	**0**	**0**			**Not estimable**
Total events: 0 (Vitamin D analogue), 0 (Placebo)					
Heterogeneity: Not applicable					
Test for overall effect: Not applicable					
1.6.3 Calcitriol					
Langner 1992	1/32	1/32		4.35%	0[-0.09,0.09]
Langner 1993	0/29	0/29		5.56%	0[-0.06,0.06]
Langner 2001 (P)	1/15	3/14		0.89%	-0.15[-0.4,0.1]
Perez 1996	0/84	0/84		8.34%	0[-0.02,0.02]
Van de Kerkhof 1989	0/10	0/10		1.65%	0[-0.17,0.17]
Subtotal (95% CI)	**170**	**169**		**20.79%**	**-0[-0.02,0.02]**
Total events: 2 (Vitamin D analogue), 4 (Placebo)					
Heterogeneity: Tau²=0; Chi²=2.53, df=4(P=0.64); I²=0%					
Test for overall effect: Z=0.1(P=0.92)					
1.6.4 Tacalcitol					
Langley 2011 (P)	21/184	27/91		3.45%	-0.18[-0.29,-0.08]



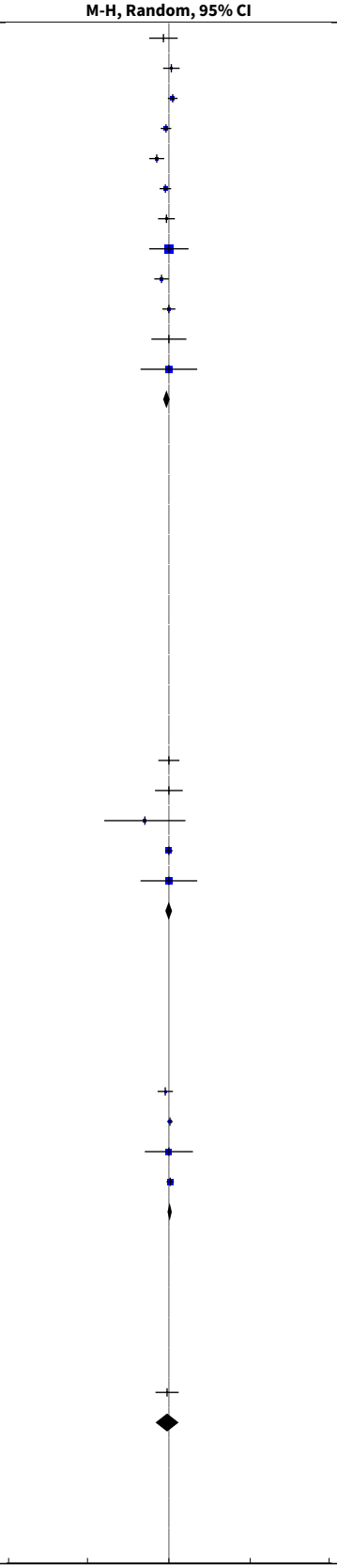
Favours vitamin D analogue — Favours placebo



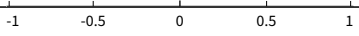
Analysis 1.7. Comparison 1 Vitamin D analogues versus placebo, Outcome 7 Withdrawals due to adverse events.



Study or subgroup	Vitamin D analogue n/N	Placebo n/N	Risk Difference M-H, Random, 95% CI	Weight	Risk Difference M-H, Random, 95% CI
Barker 1999 (P)	0/30	1/30		1.72%	-0.03[-0.12,0.05]
Dubertret 1992	2/66	1/66		4.12%	0.02[-0.04,0.07]
Feldman 2010 (1)	7/214	1/109		7.7%	0.02[-0.01,0.05]
Feldman 2010 (2)	2/223	3/113		7.18%	-0.02[-0.05,0.01]
Guenther 2002 (P)	6/227	21/208		4.73%	-0.07[-0.12,-0.03]
Harrington 1996a	8/326	8/174		6.5%	-0.02[-0.06,0.01]
Highton 1995	6/139	8/138		4.03%	-0.01[-0.07,0.04]
Kang 1998	0/15	0/15		0.96%	0[-0.12,0.12]
Kaufmann 2002 (P)	15/480	12/157		4.95%	-0.05[-0.09,-0]
Levine 2010 (P)	0/48	0/48		5.68%	0[-0.04,0.04]
Mortensen 1993b	0/17	0/17		1.19%	0[-0.11,0.11]
Staberg 1989	0/10	0/10		0.48%	0[-0.17,0.17]
Subtotal (95% CI)	**1795**	**1085**		**49.25%**	**-0.02[-0.04,0]**
Total events: 46 (Vitamin D analogue), 55 (Placebo)					
Heterogeneity: Tau²=0; Chi²=20.47, df=11(P=0.04); I²=46.26%					
Test for overall effect: Z=1.47(P=0.14)					
1.7.2 Calcipotriol plus occlusion					
Subtotal (95% CI)	**0**	**0**			**Not estimable**
Total events: 0 (Vitamin D analogue), 0 (Placebo)					
Heterogeneity: Not applicable					
Test for overall effect: Not applicable					
1.7.3 Calcitriol					
Langner 1992	0/29	0/29		2.85%	0[-0.06,0.06]
Langner 1993	1/32	1/32		1.8%	0[-0.09,0.09]
Langner 2001 (P)	1/15	3/14		0.24%	-0.15[-0.4,0.1]
Perez 1996	0/84	0/84		9.45%	0[-0.02,0.02]
Van de Kerkhof 1989	0/10	0/10		0.48%	0[-0.17,0.17]
Subtotal (95% CI)	**170**	**169**		**14.82%**	**-0[-0.02,0.02]**
Total events: 2 (Vitamin D analogue), 4 (Placebo)					
Heterogeneity: Tau²=0; Chi²=2.53, df=4(P=0.64); I²=0%					
Test for overall effect: Z=0.1(P=0.92)					
1.7.4 Tacalcitol					
Langley 2011 (P)	4/184	4/91		4.58%	-0.02[-0.07,0.02]
Scarpa 1997	1/157	0/157		10.99%	0.01[-0.01,0.02]
Seidenari 1997 (P)	0/12	0/12		0.65%	0[-0.15,0.15]
Van de Kerkhof 1996a	1/122	0/122		9.61%	0.01[-0.01,0.03]
Subtotal (95% CI)	**475**	**382**		**25.83%**	**0[-0.01,0.02]**
Total events: 6 (Vitamin D analogue), 4 (Placebo)					
Heterogeneity: Tau²=0; Chi²=2.3, df=3(P=0.51); I²=0%					
Test for overall effect: Z=0.7(P=0.48)					
1.7.5 Maxacalcitol					
Barker 1999 (P)	2/90	1/30		2.45%	-0.01[-0.08,0.06]
Subtotal (95% CI)	**90**	**30**		**2.45%**	**-0.01[-0.08,0.06]**
Total events: 2 (Vitamin D analogue), 1 (Placebo)					
Heterogeneity: Not applicable					
Test for overall effect: Z=0.31(P=0.76)					



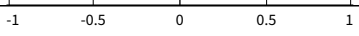
Study or subgroup	Vitamin D analogue n/N	Placebo n/N	Risk Difference M-H, Random, 95% CI	Weight	Risk Difference M-H, Random, 95% CI
1.7.6 Paricalcitol OD					
Durakovic 2004	0/11	0/11		0.56%	0[-0.16,0.16]
Subtotal (95% CI)	**11**	**11**		**0.56%**	**0[-0.16,0.16]**
Total events: 0 (Vitamin D analogue), 0 (Placebo)					
Heterogeneity: Not applicable					
Test for overall effect: Not applicable					
1.7.7 Becocalcidiol OD					
Helfrich 2007	2/64	0/60		3.99%	0.03[-0.02,0.08]
Subtotal (95% CI)	**64**	**60**		**3.99%**	**0.03[-0.02,0.08]**
Total events: 2 (Vitamin D analogue), 0 (Placebo)					
Heterogeneity: Not applicable					
Test for overall effect: Z=1.18(P=0.24)					
1.7.8 Becocalcidiol twice daily					
Helfrich 2007	3/61	0/60		3.08%	0.05[-0.01,0.11]
Subtotal (95% CI)	**61**	**60**		**3.08%**	**0.05[-0.01,0.11]**
Total events: 3 (Vitamin D analogue), 0 (Placebo)					
Heterogeneity: Not applicable					
Test for overall effect: Z=1.56(P=0.12)					
Total (95% CI)	**2666**	**1797**		**100%**	**-0[-0.02,0.01]**
Total events: 61 (Vitamin D analogue), 64 (Placebo)					
Heterogeneity: Tau^2=0; Chi^2=37.74, df=24(P=0.04); I^2=36.41%					
Test for overall effect: Z=0.73(P=0.47)					
Test for subgroup differences: Chi^2=6.56, df=1 (P=0.36), I^2=8.58%					



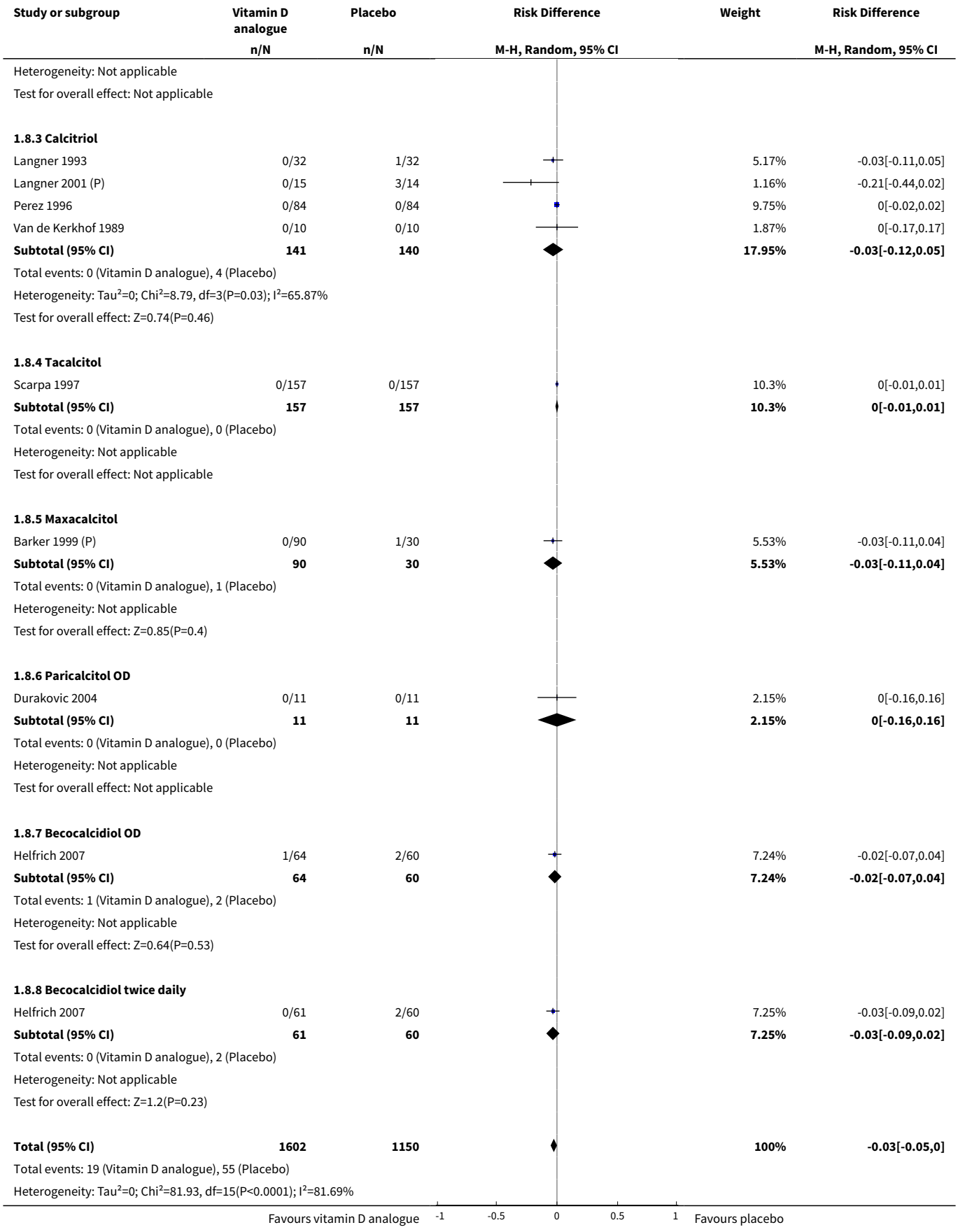
Favours vitamin D analogue — Favours placebo

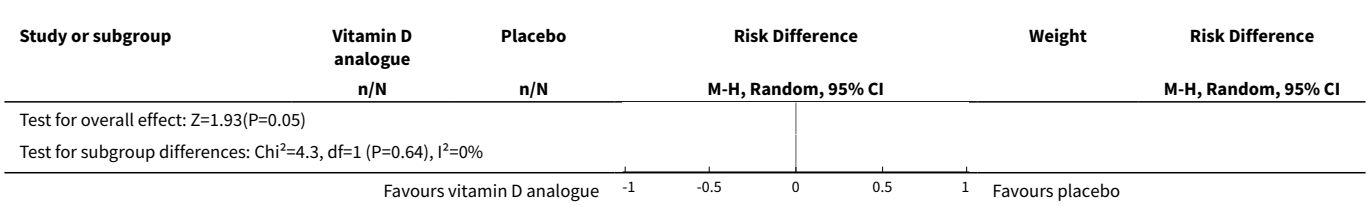
Analysis 1.8. Comparison 1 Vitamin D analogues versus placebo, Outcome 8 Withdrawals due to treatment failure.

Study or subgroup	Vitamin D analogue n/N	Placebo n/N	Risk Difference M-H, Random, 95% CI	Weight	Risk Difference M-H, Random, 95% CI
1.8.1 Calcipotriol					
Barker 1999 (P)	0/30	1/30		4.85%	-0.03[-0.12,0.05]
Feldman 2010 (1)	4/214	3/109		8.82%	-0.01[-0.04,0.03]
Feldman 2010 (2)	3/223	1/113		9.75%	0[-0.02,0.03]
Guenther 2002 (P)	2/227	19/208		8.39%	-0.08[-0.12,-0.04]
Harrington 1996a	9/326	22/174		7.42%	-0.1[-0.15,-0.05]
Levine 2010 (P)	0/48	0/48		8.49%	0[-0.04,0.04]
Staberg 1989	0/10	0/10		1.87%	0[-0.17,0.17]
Subtotal (95% CI)	**1078**	**692**		**49.59%**	**-0.03[-0.08,0.01]**
Total events: 18 (Vitamin D analogue), 46 (Placebo)					
Heterogeneity: Tau^2=0; Chi^2=39.89, df=6(P<0.0001); I^2=84.96%					
Test for overall effect: Z=1.45(P=0.15)					
1.8.2 Calcipotriol plus occlusion					
Subtotal (95% CI)	**0**	**0**			**Not estimable**
Total events: 0 (Vitamin D analogue), 0 (Placebo)					

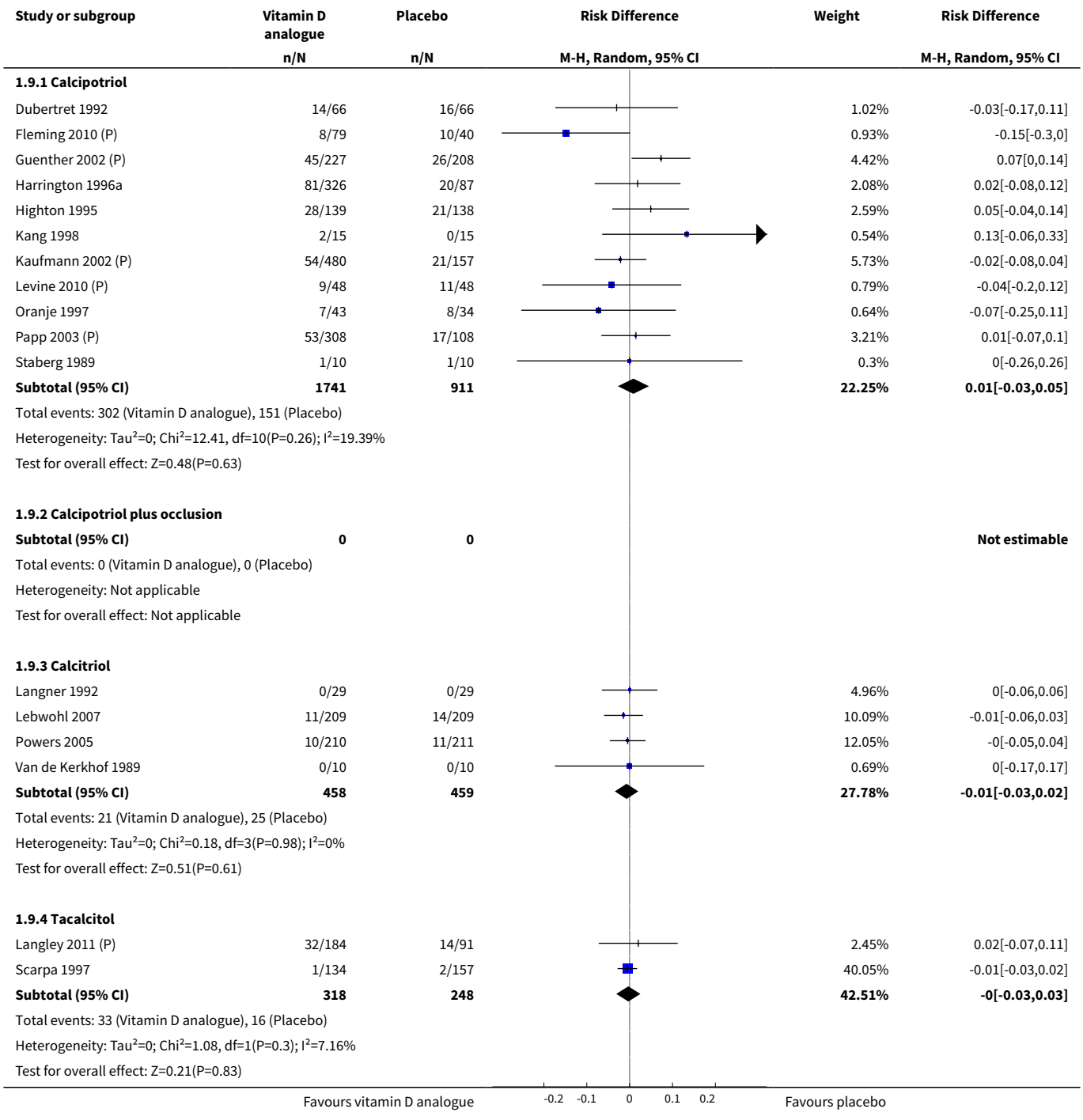


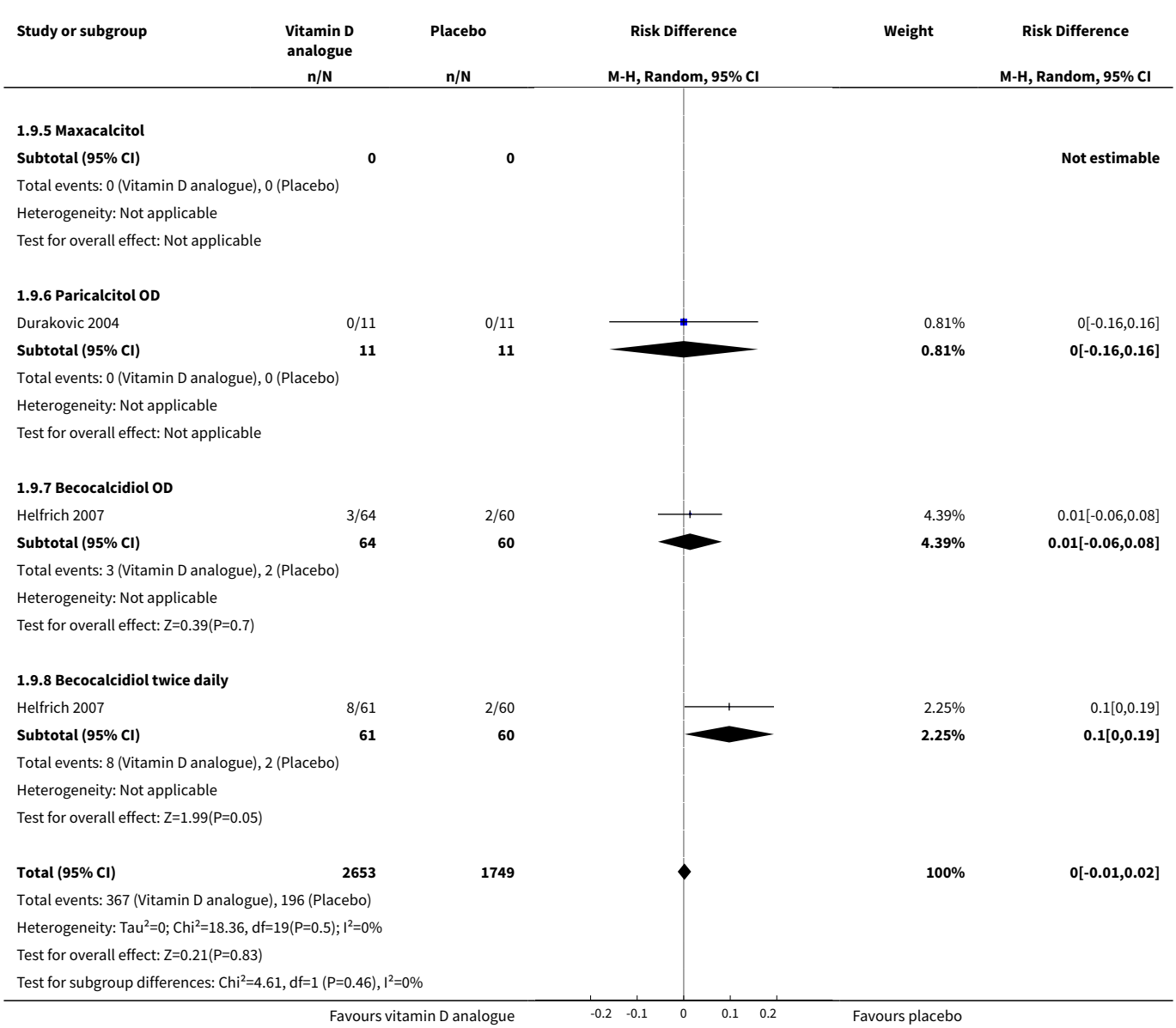
Favours vitamin D analogue — Favours placebo



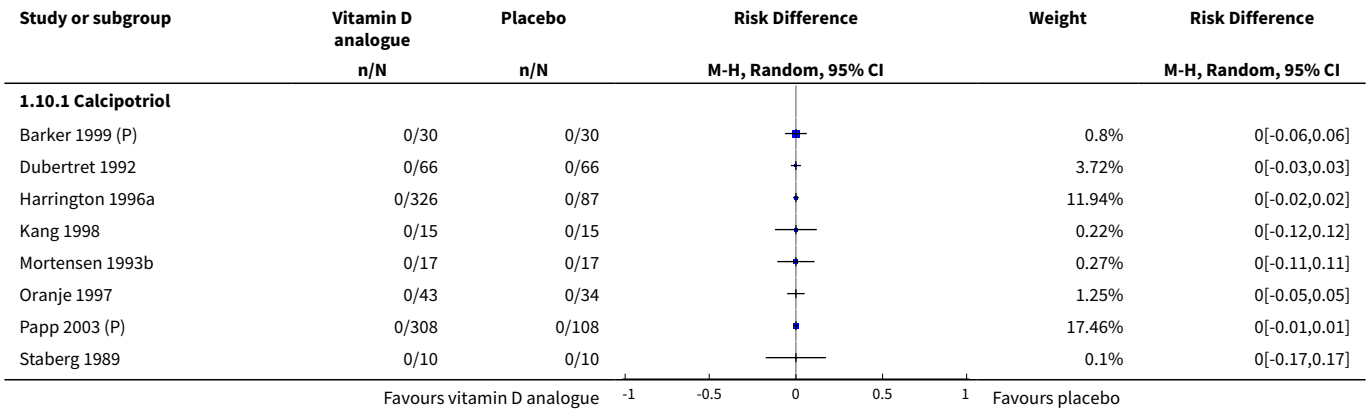


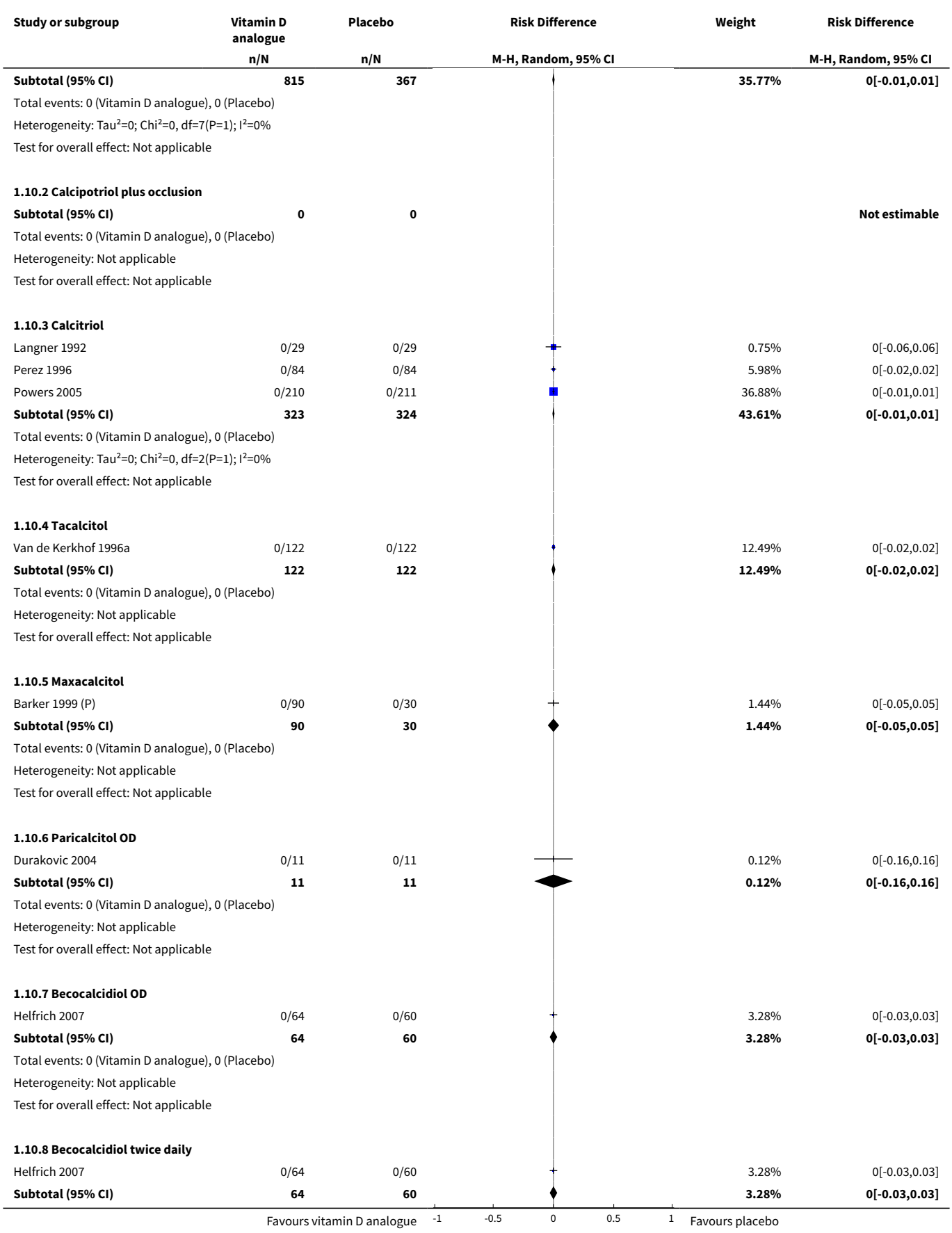
Analysis 1.9. Comparison 1 Vitamin D analogues versus placebo, Outcome 9 Adverse events (local).



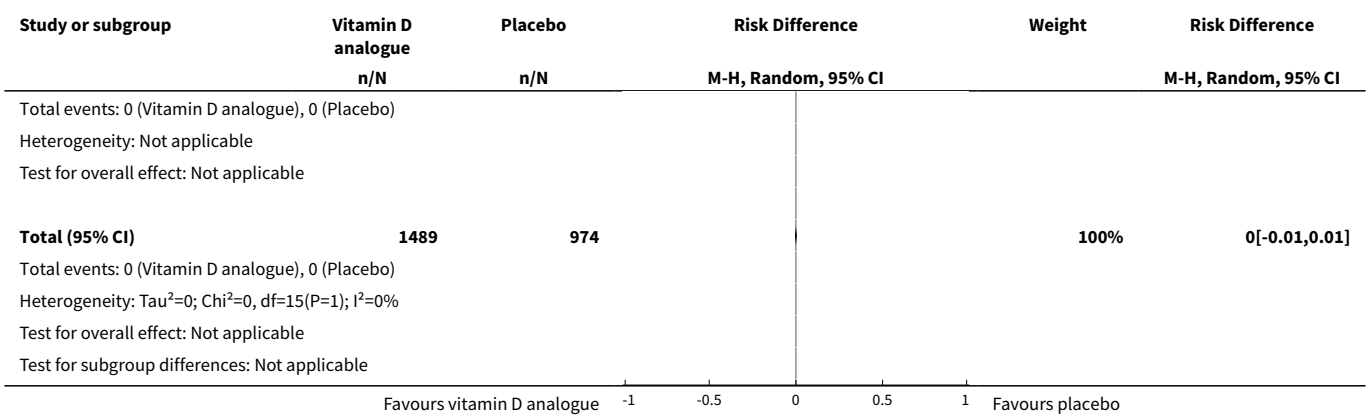


Analysis 1.10. Comparison 1 Vitamin D analogues versus placebo, Outcome 10 Adverse events (systemic).





Study or subgroup	Vitamin D analogue n/N	Placebo n/N	Risk Difference M-H, Random, 95% CI	Weight	Risk Difference M-H, Random, 95% CI
Subtotal (95% CI)	**815**	**367**		**35.77%**	**0[-0.01,0.01]**
Total events: 0 (Vitamin D analogue), 0 (Placebo)					
Heterogeneity: Tau²=0; Chi²=0, df=7(P=1); I²=0%					
Test for overall effect: Not applicable					
1.10.2 Calcipotriol plus occlusion					
Subtotal (95% CI)	**0**	**0**			**Not estimable**
Total events: 0 (Vitamin D analogue), 0 (Placebo)					
Heterogeneity: Not applicable					
Test for overall effect: Not applicable					
1.10.3 Calcitriol					
Langner 1992	0/29	0/29		0.75%	0[-0.06,0.06]
Perez 1996	0/84	0/84		5.98%	0[-0.02,0.02]
Powers 2005	0/210	0/211		36.88%	0[-0.01,0.01]
Subtotal (95% CI)	**323**	**324**		**43.61%**	**0[-0.01,0.01]**
Total events: 0 (Vitamin D analogue), 0 (Placebo)					
Heterogeneity: Tau²=0; Chi²=0, df=2(P=1); I²=0%					
Test for overall effect: Not applicable					
1.10.4 Tacalcitol					
Van de Kerkhof 1996a	0/122	0/122		12.49%	0[-0.02,0.02]
Subtotal (95% CI)	**122**	**122**		**12.49%**	**0[-0.02,0.02]**
Total events: 0 (Vitamin D analogue), 0 (Placebo)					
Heterogeneity: Not applicable					
Test for overall effect: Not applicable					
1.10.5 Maxacalcitol					
Barker 1999 (P)	0/90	0/30		1.44%	0[-0.05,0.05]
Subtotal (95% CI)	**90**	**30**		**1.44%**	**0[-0.05,0.05]**
Total events: 0 (Vitamin D analogue), 0 (Placebo)					
Heterogeneity: Not applicable					
Test for overall effect: Not applicable					
1.10.6 Paricalcitol OD					
Durakovic 2004	0/11	0/11		0.12%	0[-0.16,0.16]
Subtotal (95% CI)	**11**	**11**		**0.12%**	**0[-0.16,0.16]**
Total events: 0 (Vitamin D analogue), 0 (Placebo)					
Heterogeneity: Not applicable					
Test for overall effect: Not applicable					
1.10.7 Becocalcidiol OD					
Helfrich 2007	0/64	0/60		3.28%	0[-0.03,0.03]
Subtotal (95% CI)	**64**	**60**		**3.28%**	**0[-0.03,0.03]**
Total events: 0 (Vitamin D analogue), 0 (Placebo)					
Heterogeneity: Not applicable					
Test for overall effect: Not applicable					
1.10.8 Becocalcidiol twice daily					
Helfrich 2007	0/64	0/60		3.28%	0[-0.03,0.03]
Subtotal (95% CI)	**64**	**60**		**3.28%**	**0[-0.03,0.03]**



Comparison 2. Corticosteroid (potent) versus placebo

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 IAGI	11	1904	Std. Mean Difference (IV, Random, 95% CI)	1.00 [-1.18, -0.82]
1.1 Betamethasone dipropionate OD	2	739	Std. Mean Difference (IV, Random, 95% CI)	-0.81 [-0.98, -0.64]
1.2 Betamethasone dipropionate twice daily	4	537	Std. Mean Difference (IV, Random, 95% CI)	-1.35 [-1.56, -1.15]
1.3 Betamethasone dipropionate, maintenance	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
1.4 Betamethasone valerate	1	74	Std. Mean Difference (IV, Random, 95% CI)	-1.41 [-1.92, -0.90]
1.5 Budesonide	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
1.6 Desonide	1	76	Std. Mean Difference (IV, Random, 95% CI)	-0.81 [-1.34, -0.28]
1.7 Diflorasone diacetate	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
1.8 Fluticasone propionate	2	383	Std. Mean Difference (IV, Random, 95% CI)	-0.93 [-1.14, -0.72]
1.9 Hydrocortisone buteprate	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
1.10 Mometasone furoate	1	95	Std. Mean Difference (IV, Random, 95% CI)	-0.75 [-1.17, -0.34]
2 TSS	7	611	Std. Mean Difference (IV, Random, 95% CI)	-0.77 [-1.01, -0.52]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
2.1 Betamethasone dipropionate OD	1	93	Std. Mean Difference (IV, Random, 95% CI)	-0.74 [-1.16, -0.32]
2.2 Betamethasone dipropionate twice daily	1	33	Std. Mean Difference (IV, Random, 95% CI)	-0.77 [-1.48, -0.06]
2.3 Betamethasone dipropionate, maintenance	1	38	Std. Mean Difference (IV, Random, 95% CI)	-0.95 [-1.62, -0.27]
2.4 Betamethasone valerate	1	22	Std. Mean Difference (IV, Random, 95% CI)	-1.09 [-2.00, -0.18]
2.5 Budesonide	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
2.6 Desonide	1	76	Std. Mean Difference (IV, Random, 95% CI)	-1.16 [-1.70, -0.61]
2.7 Diflorasone diacetate	1	93	Std. Mean Difference (IV, Random, 95% CI)	-0.32 [-0.73, 0.09]
2.8 Fluticasone propionate	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
2.9 Hydrocortisone buteprate	1	161	Std. Mean Difference (IV, Random, 95% CI)	-0.46 [-0.77, -0.15]
2.10 Mometasone furoate	1	95	Std. Mean Difference (IV, Random, 95% CI)	-1.12 [-1.55, -0.68]
3 PASI	3	1158	Std. Mean Difference (IV, Random, 95% CI)	-0.97 [-1.31, -0.62]
3.1 Betamethasone dipropionate OD	2	739	Std. Mean Difference (IV, Random, 95% CI)	-0.79 [-1.44, -0.14]
3.2 Betamethasone dipropionate twice daily	1	419	Std. Mean Difference (IV, Random, 95% CI)	-1.21 [-1.44, -0.97]
3.3 Betamethasone dipropionate, maintenance	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
3.4 Betamethasone valerate	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
3.5 Budesonide	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
3.6 Desonide	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
3.7 Diflorasone diacetate	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
3.8 Fluticasone propionate	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
3.9 Hydrocortisone buteprate	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
3.10 Mometasone furoate	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
4 PAGI	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
4.1 Betamethasone dipropionate OD	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
4.2 Betamethasone dipropionate twice daily	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
4.3 Betamethasone dipropionate, maintenance	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
4.4 Betamethasone valerate	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
4.5 Budesonide	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
4.6 Desonide	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
4.7 Diflorasone diacetate	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
4.8 Fluticasone propionate	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
4.9 Hydrocortisone buteprate	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
4.10 Mometasone furoate	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
5 Combined end point (IAGI/TSS/PASI/PAGI)	15	2311	Std. Mean Difference (IV, Random, 95% CI)	-0.89 [-1.06, -0.72]
5.1 Betamethasone dipropionate OD	3	832	Std. Mean Difference (IV, Random, 95% CI)	-0.80 [-0.96, -0.64]
5.2 Betamethasone dipropionate twice daily	4	537	Std. Mean Difference (IV, Random, 95% CI)	-1.35 [-1.56, -1.15]
5.3 Betamethasone dipropionate, maintenance	1	38	Std. Mean Difference (IV, Random, 95% CI)	-0.95 [-1.62, -0.27]

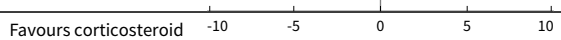
Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
5.4 Betamethasone valerate	2	96	Std. Mean Difference (IV, Random, 95% CI)	-1.33 [-1.78, -0.89]
5.5 Budesonide	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
5.6 Desonide	1	76	Std. Mean Difference (IV, Random, 95% CI)	-0.81 [-1.34, -0.28]
5.7 Diflorasone diacetate	1	93	Std. Mean Difference (IV, Random, 95% CI)	-0.32 [-0.73, 0.09]
5.8 Fluticasone propionate	2	383	Std. Mean Difference (IV, Random, 95% CI)	-0.93 [-1.14, -0.72]
5.9 Hydrocortisone buteprate	1	161	Std. Mean Difference (IV, Random, 95% CI)	-0.46 [-0.77, -0.15]
5.10 Mometasone furoate	1	95	Std. Mean Difference (IV, Random, 95% CI)	-0.75 [-1.17, -0.34]
6 Total withdrawals	9	1673	Risk Difference (M-H, Random, 95% CI)	-0.14 [-0.22, -0.05]
6.1 Betamethasone dipropionate OD	2	756	Risk Difference (M-H, Random, 95% CI)	-0.16 [-0.28, -0.04]
6.2 Betamethasone dipropionate twice daily	1	421	Risk Difference (M-H, Random, 95% CI)	-0.06 [-0.12, 0.01]
6.3 Betamethasone dipropionate, maintenance	2	134	Risk Difference (M-H, Random, 95% CI)	-0.45 [-0.60, -0.30]
6.4 Betamethasone valerate	1	80	Risk Difference (M-H, Random, 95% CI)	0.0 [-0.12, 0.12]
6.5 Budesonide	1	22	Risk Difference (M-H, Random, 95% CI)	0.0 [-0.16, 0.16]
6.6 Desonide	1	80	Risk Difference (M-H, Random, 95% CI)	-0.18 [-0.38, 0.02]
6.7 Diflorasone diacetate	0	0	Risk Difference (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
6.8 Fluticasone propionate	0	0	Risk Difference (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
6.9 Hydrocortisone buteprate	1	180	Risk Difference (M-H, Random, 95% CI)	0.00 [-0.09, 0.10]
6.10 Mometasone furoate	0	0	Risk Difference (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
7 Withdrawals due to adverse events	9	1292	Risk Difference (M-H, Random, 95% CI)	-0.01 [-0.05, 0.02]
7.1 Betamethasone dipropionate OD	1	633	Risk Difference (M-H, Random, 95% CI)	-0.07 [-0.11, -0.02]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
7.2 Betamethasone dipropionate twice daily	1	33	Risk Difference (M-H, Random, 95% CI)	0.0 [-0.11, 0.11]
7.3 Betamethasone dipropionate, maintenance	2	134	Risk Difference (M-H, Random, 95% CI)	0.0 [-0.04, 0.04]
7.4 Betamethasone valerate	1	80	Risk Difference (M-H, Random, 95% CI)	0.08 [-0.02, 0.17]
7.5 Budesonide	1	22	Risk Difference (M-H, Random, 95% CI)	0.0 [-0.16, 0.16]
7.6 Desonide	1	80	Risk Difference (M-H, Random, 95% CI)	-0.1 [-0.24, 0.04]
7.7 Diflorasone diacetate	0	0	Risk Difference (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
7.8 Fluticasone propionate	0	0	Risk Difference (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
7.9 Hydrocortisone buteprate	1	190	Risk Difference (M-H, Random, 95% CI)	0.01 [-0.02, 0.04]
7.10 Mometasone furoate	1	120	Risk Difference (M-H, Random, 95% CI)	-0.05 [-0.11, 0.01]
8 Withdrawals due to treatment failure	6		Risk Difference (M-H, Random, 95% CI)	Subtotals only
8.1 Betamethasone dipropionate OD	0	0	Risk Difference (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
8.2 Betamethasone dipropionate twice daily	0	0	Risk Difference (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
8.3 Betamethasone dipropionate, maintenance	2	130	Risk Difference (M-H, Random, 95% CI)	-0.46 [-0.61, -0.31]
8.4 Betamethasone valerate	1	80	Risk Difference (M-H, Random, 95% CI)	0.0 [-0.05, 0.05]
8.5 Budesonide	1	22	Risk Difference (M-H, Random, 95% CI)	0.0 [-0.16, 0.16]
8.6 Desonide	1	80	Risk Difference (M-H, Random, 95% CI)	0.0 [-0.07, 0.07]
8.7 Diflorasone diacetate	0	0	Risk Difference (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
8.8 Fluticasone propionate	0	0	Risk Difference (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
8.9 Hydrocortisone buteprate	1	190	Risk Difference (M-H, Random, 95% CI)	0.0 [-0.02, 0.02]
8.10 Mometasone furoate	0	0	Risk Difference (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
9 Adverse events (local)	10	2117	Risk Difference (M-H, Random, 95% CI)	-0.04 [-0.08, -0.00]
9.1 Betamethasone dipropionate OD	2	756	Risk Difference (M-H, Random, 95% CI)	-0.10 [-0.15, -0.04]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
9.2 Betamethasone dipropionate twice daily	2	454	Risk Difference (M-H, Random, 95% CI)	-0.05 [-0.12, 0.03]
9.3 Betamethasone dipropionate, maintenance	2	134	Risk Difference (M-H, Random, 95% CI)	0.0 [-0.04, 0.04]
9.4 Betamethasone valerate	0	0	Risk Difference (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
9.5 Budesonide	0	0	Risk Difference (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
9.6 Desonide	1	80	Risk Difference (M-H, Random, 95% CI)	0.0 [-0.11, 0.11]
9.7 Diflorasone diacetate	0	0	Risk Difference (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
9.8 Fluticasone propionate	1	383	Risk Difference (M-H, Random, 95% CI)	0.00 [-0.05, 0.05]
9.9 Hydrocortisone buteprate	1	190	Risk Difference (M-H, Random, 95% CI)	-0.06 [-0.18, 0.07]
9.10 Mometasone furoate	1	120	Risk Difference (M-H, Random, 95% CI)	-0.10 [-0.23, 0.02]
10 Adverse events (systemic)	4	675	Risk Difference (M-H, Random, 95% CI)	0.00 [-0.01, 0.01]
10.1 Betamethasone dipropionate OD	0	0	Risk Difference (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
10.2 Betamethasone dipropionate twice daily	1	421	Risk Difference (M-H, Random, 95% CI)	0.0 [-0.01, 0.01]
10.3 Betamethasone dipropionate, maintenance	2	134	Risk Difference (M-H, Random, 95% CI)	0.01 [-0.07, 0.10]
10.4 Budesonide	0	0	Risk Difference (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
10.5 Desonide	0	0	Risk Difference (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
10.6 Diflorasone diacetate	0	0	Risk Difference (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
10.7 Fluticasone propionate	0	0	Risk Difference (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
10.8 Hydrocortisone buteprate	0	0	Risk Difference (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
10.9 Betamethasone valerate	0	0	Risk Difference (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
10.10 Mometasone furoate	1	120	Risk Difference (M-H, Random, 95% CI)	0.0 [-0.03, 0.03]

Analysis 2.1. Comparison 2 Corticosteroid (potent) versus placebo, Outcome 1 IAGI.

Study or subgroup	Corticosteroid (potent) N	Mean(SD)	Placebo N	Mean(SD)	Std. Mean Difference Random, 95% CI	Weight	Std. Mean Difference Random, 95% CI
2.1.1 Betamethasone dipropionate OD							
Fleming 2010 (P)	78	2 (1.1)	28	2.6 (0.6)		8.77%	-0.63[-1.07,-0.19]
Kaufmann 2002 (P)	476	1.9 (0.9)	157	2.7 (0.9)		15.4%	-0.84[-1.03,-0.65]
Subtotal ***	**554**		**185**			**24.17%**	**-0.81[-0.98,-0.64]**
Heterogeneity: Tau^2=0; Chi^2=0.76, df=1(P=0.38); I^2=0%							
Test for overall effect: Z=9.23(P<0.0001)							
2.1.2 Betamethasone dipropionate twice daily							
Papp 2003 (P)	312	-3.4 (1.1)	107	-1.9 (1.1)		13.88%	-1.44[-1.68,-1.2]
Vanderploeg 1976	17	-3.2 (1)	16	-2.1 (0.9)		4.39%	-1.21[-1.96,-0.46]
Wortzel 1975 (1)	39	-3 (1.1)	37	-1.7 (1.2)		7.87%	-1.12[-1.61,-0.64]
Wortzel 1975 (2)	5	-2.2 (1.1)	4	-1.2 (0.5)		1.44%	-0.94[-2.38,0.49]
Subtotal ***	**373**		**164**			**27.58%**	**-1.35[-1.56,-1.15]**
Heterogeneity: Tau^2=0; Chi^2=1.79, df=3(P=0.62); I^2=0%							
Test for overall effect: Z=12.96(P<0.0001)							
2.1.3 Betamethasone dipropionate, maintenance							
Subtotal ***	**0**		**0**				**Not estimable**
Heterogeneity: Not applicable							
Test for overall effect: Not applicable							
2.1.4 Betamethasone valerate							
Stein 2001	37	-3.1 (1.2)	37	-1.4 (1.2)		7.4%	-1.41[-1.92,-0.9]
Subtotal ***	**37**		**37**			**7.4%**	**-1.41[-1.92,-0.9]**
Heterogeneity: Not applicable							
Test for overall effect: Z=5.39(P<0.0001)							
2.1.5 Budesonide							
Subtotal ***	**0**		**0**				**Not estimable**
Heterogeneity: Not applicable							
Test for overall effect: Not applicable							
2.1.6 Desonide							
Greenspan 1993	56	-2.8 (1)	20	-2 (1)		7.14%	-0.81[-1.34,-0.28]
Subtotal ***	**56**		**20**			**7.14%**	**-0.81[-1.34,-0.28]**
Heterogeneity: Not applicable							
Test for overall effect: Z=3(P=0)							
2.1.7 Diflorasone diacetate							
Subtotal ***	**0**		**0**				**Not estimable**
Heterogeneity: Not applicable							
Test for overall effect: Not applicable							
2.1.8 Fluticasone propionate							
Olsen 1996 (1)	88	-2.9 (1.4)	90	-1.7 (1.2)		11.93%	-0.94[-1.25,-0.63]
Olsen 1996 (2)	105	-2.8 (1.2)	100	-1.7 (1.2)		12.52%	-0.92[-1.21,-0.64]
Subtotal ***	**193**		**190**			**24.44%**	**-0.93[-1.14,-0.72]**
Heterogeneity: Tau^2=0; Chi^2=0, df=1(P=0.96); I^2=0%							
Test for overall effect: Z=8.63(P<0.0001)							



Study or subgroup	Corticosteroid (potent) N	Mean(SD)	Placebo N	Mean(SD)	Std. Mean Difference Random, 95% CI	Weight	Std. Mean Difference Random, 95% CI
2.1.9 Hydrocortisone buteprate							
Subtotal ***	**0**		**0**				**Not estimable**
Heterogeneity: Not applicable							
Test for overall effect: Not applicable							
2.1.10 Mometasone furoate							
Medansky 1987	50	-2 (0.9)	45	-1.2 (1)		9.26%	-0.75[-1.17,-0.34]
Subtotal ***	**50**		**45**			**9.26%**	**-0.75[-1.17,-0.34]**
Heterogeneity: Not applicable							
Test for overall effect: Z=3.54(P=0)							
Total ***	**1263**		**641**			**100%**	**-1[-1.18,-0.82]**
Heterogeneity: Tau^2=0.05; Chi^2=23.6, df=10(P=0.01); I^2=57.64%							
Test for overall effect: Z=10.87(P<0.0001)							
Test for subgroup differences: Chi^2=21.05, df=1 (P=0), I^2=76.25%							

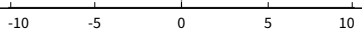
Favours corticosteroid -10 -5 0 5 10 Favours placebo

Analysis 2.2. Comparison 2 Corticosteroid (potent) versus placebo, Outcome 2 TSS.

Study or subgroup	Corticosteroid (potent) N	Mean(SD)	Placebo N	Mean(SD)	Std. Mean Difference Random, 95% CI	Weight	Std. Mean Difference Random, 95% CI
2.2.1 Betamethasone dipropionate OD							
Lane 1983	46	4.5 (2.8)	47	6.6 (2.8)		15.36%	-0.74[-1.16,-0.32]
Subtotal ***	**46**		**47**			**15.36%**	**-0.74[-1.16,-0.32]**
Heterogeneity: Not applicable							
Test for overall effect: Z=3.46(P=0)							
2.2.2 Betamethasone dipropionate twice daily							
Vanderploeg 1976	17	3.2 (2.8)	16	5.4 (2.8)		8.28%	-0.77[-1.48,-0.06]
Subtotal ***	**17**		**16**			**8.28%**	**-0.77[-1.48,-0.06]**
Heterogeneity: Not applicable							
Test for overall effect: Z=2.11(P=0.03)							
2.2.3 Betamethasone dipropionate, maintenance							
Katz 1987a	19	0.8 (1.3)	19	2.1 (1.3)		8.9%	-0.95[-1.62,-0.27]
Subtotal ***	**19**		**19**			**8.9%**	**-0.95[-1.62,-0.27]**
Heterogeneity: Tau^2=0; Chi^2=0, df=0(P<0.0001); I^2=100%							
Test for overall effect: Z=2.76(P=0.01)							
2.2.4 Betamethasone valerate							
Ormerod 1997	11	4.9 (2.5)	11	7.8 (2.5)		5.71%	-1.09[-2,-0.18]
Subtotal ***	**11**		**11**			**5.71%**	**-1.09[-2,-0.18]**
Heterogeneity: Not applicable							
Test for overall effect: Z=2.36(P=0.02)							
2.2.5 Budesonide							
Subtotal ***	**0**		**0**				**Not estimable**

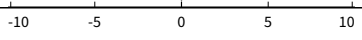
Favours corticosteroid -10 -5 0 5 10 Favours placebo

Study or subgroup	Corticosteroid (potent) N	Mean(SD)	Placebo N	Mean(SD)	Std. Mean Difference Random, 95% CI	Weight	Std. Mean Difference Random, 95% CI
Heterogeneity: Not applicable							
Test for overall effect: Not applicable							
2.2.6 Desonide							
Greenspan 1993	56	3.1 (1)	20	4.1 (0.7)		11.72%	-1.16[-1.7,-0.61]
Subtotal ***	**56**		**20**			**11.72%**	**-1.16[-1.7,-0.61]**
Heterogeneity: Not applicable							
Test for overall effect: Z=4.16(P<0.0001)							
2.2.7 Diflorasone diacetate							
Lane 1983	46	5.7 (2.8)	47	6.6 (2.8)		15.76%	-0.32[-0.73,0.09]
Subtotal ***	**46**		**47**			**15.76%**	**-0.32[-0.73,0.09]**
Heterogeneity: Not applicable							
Test for overall effect: Z=1.53(P=0.13)							
2.2.8 Fluticasone propionate							
Subtotal ***	**0**		**0**				**Not estimable**
Heterogeneity: Not applicable							
Test for overall effect: Not applicable							
2.2.9 Hydrocortisone buteprate							
Sears 1997	78	-2 (1.7)	83	-1.3 (1.3)		19.35%	-0.46[-0.77,-0.15]
Subtotal ***	**78**		**83**			**19.35%**	**-0.46[-0.77,-0.15]**
Heterogeneity: Not applicable							
Test for overall effect: Z=2.89(P=0)							
2.2.10 Mometasone furoate							
Medansky 1987	50	2.7 (1.3)	45	4.2 (1.3)		14.92%	-1.12[-1.55,-0.68]
Subtotal ***	**50**		**45**			**14.92%**	**-1.12[-1.55,-0.68]**
Heterogeneity: Not applicable							
Test for overall effect: Z=5.05(P<0.0001)							
Total ***	**323**		**288**			**100%**	**-0.77[-1.01,-0.52]**
Heterogeneity: Tau^2=0.05; Chi^2=13.13, df=7(P=0.07); I^2=46.68%							
Test for overall effect: Z=6.19(P<0.0001)							
Test for subgroup differences: Chi^2=13.13, df=1 (P=0.07), I^2=46.68%							

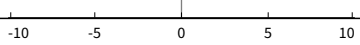


Analysis 2.3. Comparison 2 Corticosteroid (potent) versus placebo, Outcome 3 PASI.

Study or subgroup	Corticosteroid (potent) N	Mean(SD)	Placebo N	Mean(SD)	Std. Mean Difference Random, 95% CI	Weight	Std. Mean Difference Random, 95% CI
2.3.1 Betamethasone dipropionate OD							
Fleming 2010 (P)	78	3.9 (3.8)	28	5.5 (3.5)		25.48%	-0.43[-0.86,0.01]
Kaufmann 2002 (P)	476	-0.6 (0.3)	157	-0.2 (0.3)		38.38%	-1.09[-1.28,-0.9]
Subtotal ***	**554**		**185**			**63.86%**	**-0.79[-1.44,-0.14]**
Heterogeneity: Tau^2=0.19; Chi^2=7.58, df=1(P=0.01); I^2=86.8%							
Test for overall effect: Z=2.38(P=0.02)							



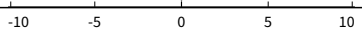
Study or subgroup	Corticosteroid (potent) N	Mean(SD)	Placebo N	Mean(SD)	Std. Mean Difference Random, 95% CI	Weight	Std. Mean Difference Random, 95% CI
2.3.2 Betamethasone dipropionate twice daily							
Papp 2003 (P)	312	-0.6 (0.3)	107	-0.3 (0.3)		36.14%	-1.21[-1.44,-0.97]
Subtotal ***	**312**		**107**			**36.14%**	**-1.21[-1.44,-0.97]**
Heterogeneity: Not applicable							
Test for overall effect: Z=10.11(P<0.0001)							
2.3.3 Betamethasone dipropionate, maintenance							
Subtotal ***	**0**		**0**				**Not estimable**
Heterogeneity: Not applicable							
Test for overall effect: Not applicable							
2.3.4 Betamethasone valerate							
Subtotal ***	**0**		**0**				**Not estimable**
Heterogeneity: Not applicable							
Test for overall effect: Not applicable							
2.3.5 Budesonide							
Subtotal ***	**0**		**0**				**Not estimable**
Heterogeneity: Not applicable							
Test for overall effect: Not applicable							
2.3.6 Desonide							
Subtotal ***	**0**		**0**				**Not estimable**
Heterogeneity: Not applicable							
Test for overall effect: Not applicable							
2.3.7 Diflorasone diacetate							
Subtotal ***	**0**		**0**				**Not estimable**
Heterogeneity: Not applicable							
Test for overall effect: Not applicable							
2.3.8 Fluticasone propionate							
Subtotal ***	**0**		**0**				**Not estimable**
Heterogeneity: Not applicable							
Test for overall effect: Not applicable							
2.3.9 Hydrocortisone buteprate							
Subtotal ***	**0**		**0**				**Not estimable**
Heterogeneity: Not applicable							
Test for overall effect: Not applicable							
2.3.10 Mometasone furoate							
Subtotal ***	**0**		**0**				**Not estimable**
Heterogeneity: Not applicable							
Test for overall effect: Not applicable							
Total ***	**866**		**292**			**100%**	**-0.97[-1.31,-0.62]**
Heterogeneity: Tau^2=0.07; Chi^2=9.79, df=2(P=0.01); I^2=79.57%							
Test for overall effect: Z=5.54(P<0.0001)							
Test for subgroup differences: Chi^2=1.4, df=1 (P=0.24), I^2=28.79%							

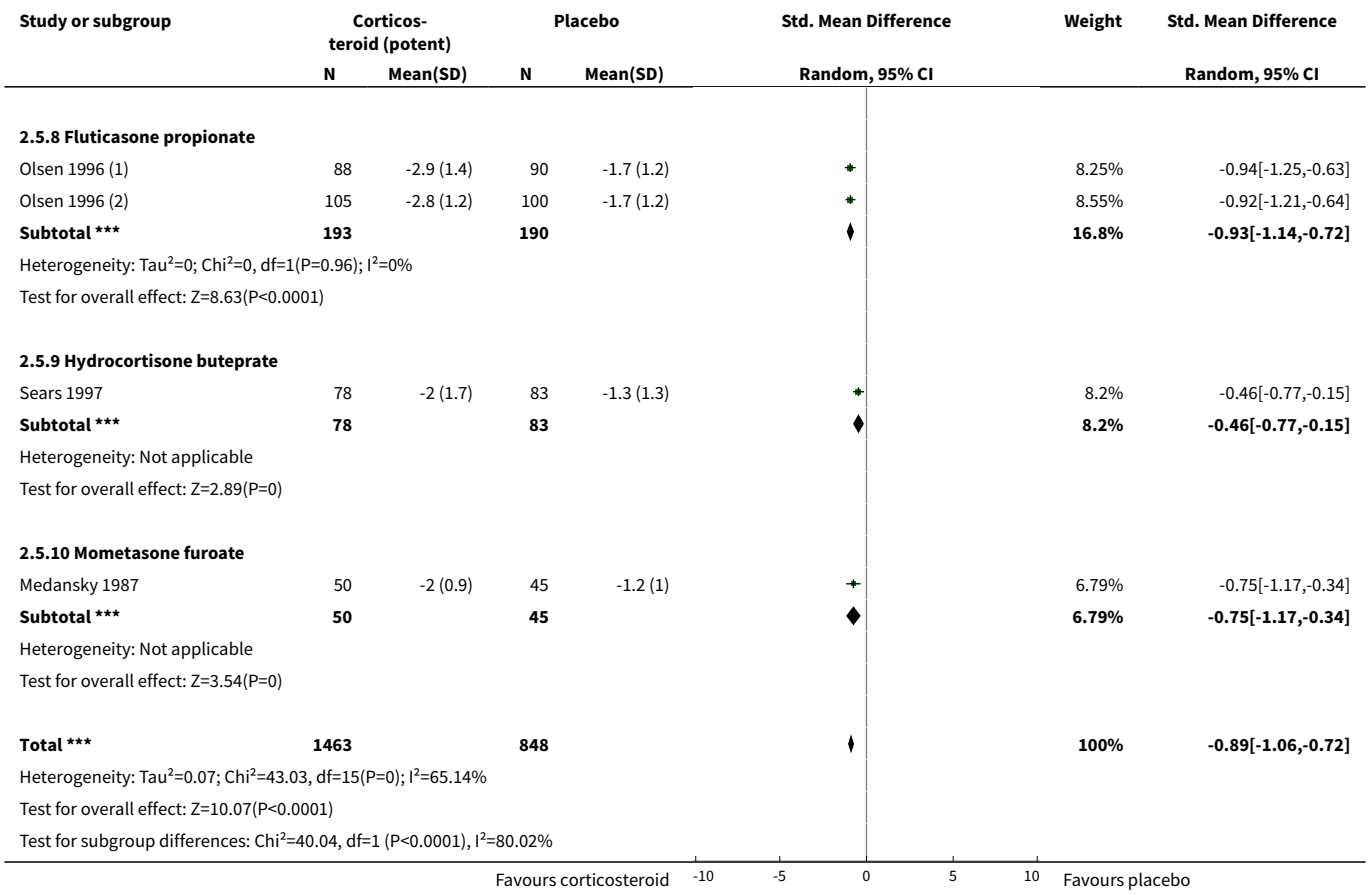


Favours corticosteroid Favours placebo

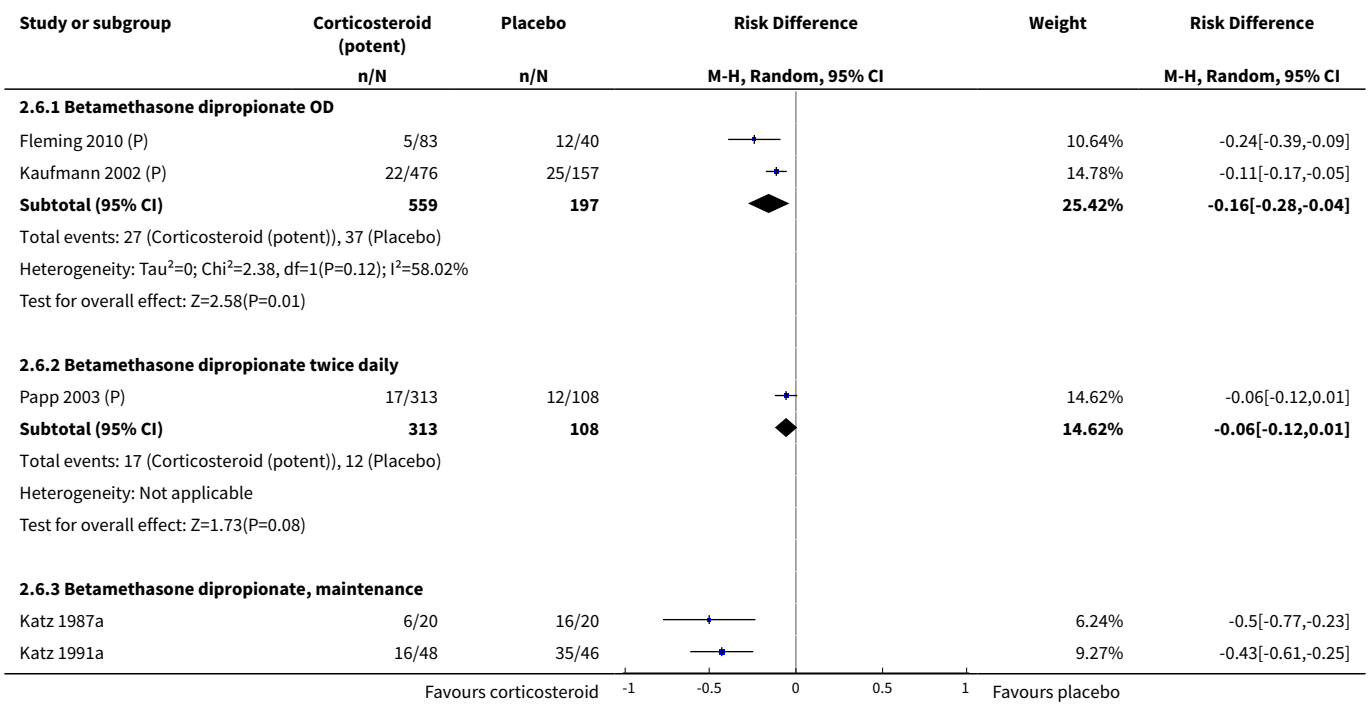
Analysis 2.5. Comparison 2 Corticosteroid (potent) versus placebo, Outcome 5 Combined end point (IAGI/TSS/PASI/PAGI).

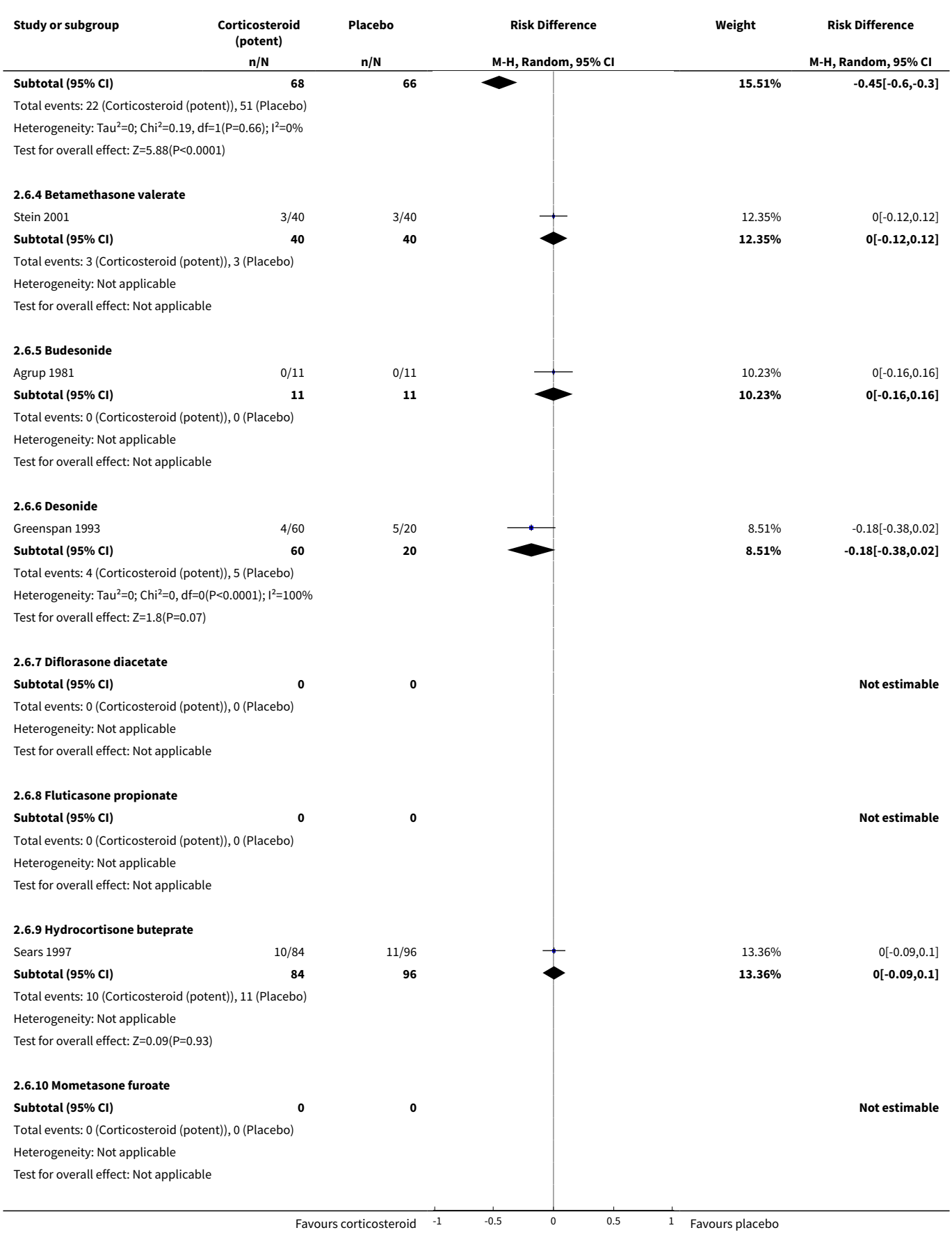
Study or subgroup	Corticosteroid (potent) N	Mean(SD)	Placebo N	Mean(SD)	Std. Mean Difference Random, 95% CI	Weight	Std. Mean Difference Random, 95% CI
2.5.1 Betamethasone dipropionate OD							
Fleming 2010 (P)	78	2 (1.1)	28	2.6 (0.6)		6.5%	-0.63[-1.07,-0.19]
Kaufmann 2002 (P)	476	1.9 (0.9)	157	2.7 (0.9)		9.92%	-0.84[-1.03,-0.65]
Lane 1983	46	4.5 (2.8)	47	6.6 (2.8)		6.75%	-0.74[-1.16,-0.32]
Subtotal ***	**600**		**232**			**23.17%**	**-0.8[-0.96,-0.64]**
Heterogeneity: Tau^2=0; Chi^2=0.84, df=2(P=0.66); I^2=0%							
Test for overall effect: Z=9.86(P<0.0001)							
2.5.2 Betamethasone dipropionate twice daily							
Papp 2003 (P)	312	-3.4 (1.1)	107	-1.9 (1.1)		9.22%	-1.44[-1.68,-1.2]
Vanderploeg 1976	17	-3.2 (1)	16	-2.1 (0.9)		3.61%	-1.21[-1.96,-0.46]
Wortzel 1975 (1)	39	-3 (1.1)	37	-1.7 (1.2)		5.96%	-1.12[-1.61,-0.64]
Wortzel 1975 (2)	5	-2.2 (1.1)	4	-1.2 (0.5)		1.29%	-0.94[-2.38,0.49]
Subtotal ***	**373**		**164**			**20.08%**	**-1.35[-1.56,-1.15]**
Heterogeneity: Tau^2=0; Chi^2=1.79, df=3(P=0.62); I^2=0%							
Test for overall effect: Z=12.96(P<0.0001)							
2.5.3 Betamethasone dipropionate, maintenance							
Katz 1987a	19	0.8 (1.3)	19	2.1 (1.3)		4.15%	-0.95[-1.62,-0.27]
Subtotal ***	**19**		**19**			**4.15%**	**-0.95[-1.62,-0.27]**
Heterogeneity: Tau^2=0; Chi^2=0, df=0(P<0.0001); I^2=100%							
Test for overall effect: Z=2.76(P=0.01)							
2.5.4 Betamethasone valerate							
Ormerod 1997	11	4.9 (2.5)	11	7.8 (2.5)		2.75%	-1.09[-2,-0.18]
Stein 2001	37	-3.1 (1.2)	37	-1.4 (1.2)		5.67%	-1.41[-1.92,-0.9]
Subtotal ***	**48**		**48**			**8.41%**	**-1.33[-1.78,-0.89]**
Heterogeneity: Tau^2=0; Chi^2=0.35, df=1(P=0.55); I^2=0%							
Test for overall effect: Z=5.85(P<0.0001)							
2.5.5 Budesonide							
Subtotal ***	**0**		**0**				**Not estimable**
Heterogeneity: Not applicable							
Test for overall effect: Not applicable							
2.5.6 Desonide							
Greenspan 1993	56	-2.8 (1)	20	-2 (1)		5.5%	-0.81[-1.34,-0.28]
Subtotal ***	**56**		**20**			**5.5%**	**-0.81[-1.34,-0.28]**
Heterogeneity: Not applicable							
Test for overall effect: Z=3(P=0)							
2.5.7 Diflorasone diacetate							
Lane 1983	46	5.7 (2.8)	47	6.6 (2.8)		6.9%	-0.32[-0.73,0.09]
Subtotal ***	**46**		**47**			**6.9%**	**-0.32[-0.73,0.09]**
Heterogeneity: Not applicable							
Test for overall effect: Z=1.53(P=0.13)							

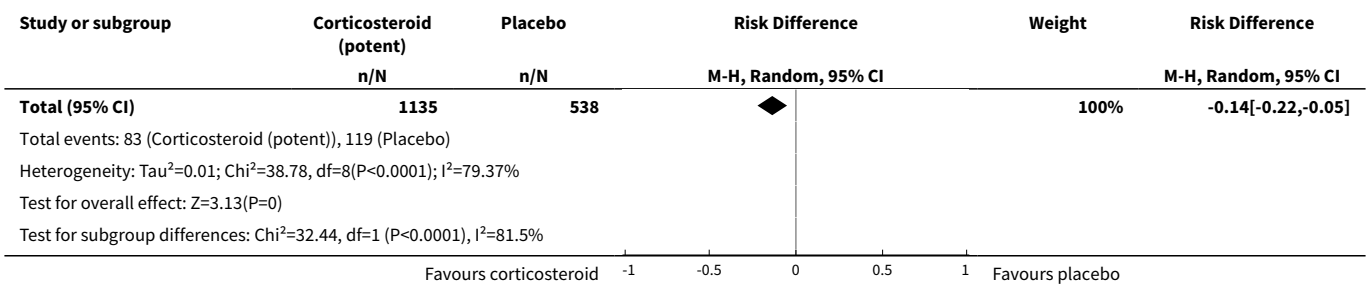




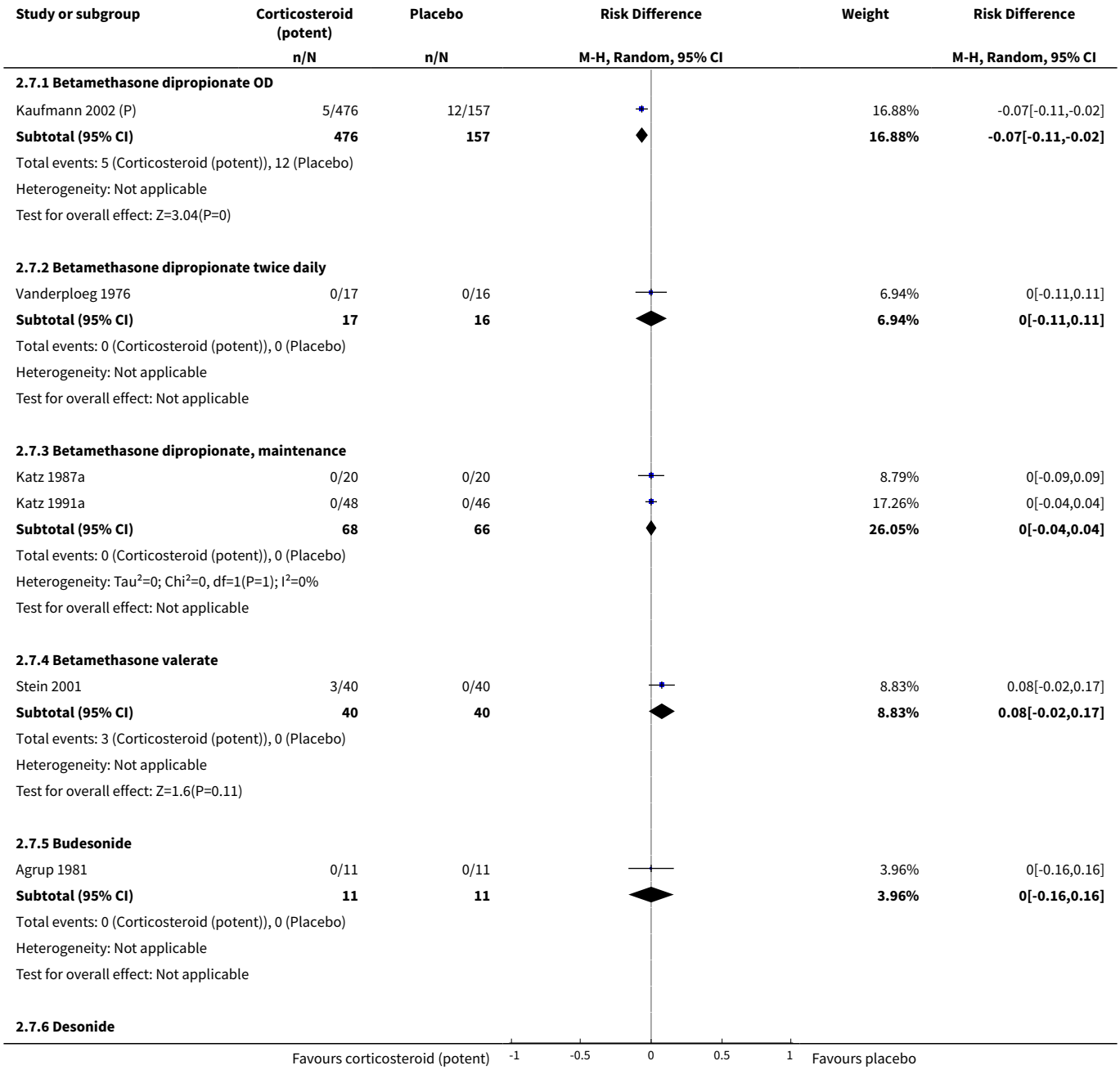
Analysis 2.6. Comparison 2 Corticosteroid (potent) versus placebo, Outcome 6 Total withdrawals.



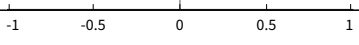




Analysis 2.7. Comparison 2 Corticosteroid (potent) versus placebo, Outcome 7 Withdrawals due to adverse events.



Study or subgroup	Corticosteroid (potent) n/N	Placebo n/N	Risk Difference M-H, Random, 95% CI	Weight	Risk Difference M-H, Random, 95% CI
Greenspan 1993	0/60	2/20		4.88%	-0.1[-0.24,0.04]
Subtotal (95% CI)	**60**	**20**		**4.88%**	**-0.1[-0.24,0.04]**
Total events: 0 (Corticosteroid (potent)), 2 (Placebo)					
Heterogeneity: Not applicable					
Test for overall effect: Z=1.4(P=0.16)					
2.7.7 Diflorasone diacetate					
Subtotal (95% CI)	**0**	**0**			**Not estimable**
Total events: 0 (Corticosteroid (potent)), 0 (Placebo)					
Heterogeneity: Not applicable					
Test for overall effect: Not applicable					
2.7.8 Fluticasone propionate					
Subtotal (95% CI)	**0**	**0**			**Not estimable**
Total events: 0 (Corticosteroid (potent)), 0 (Placebo)					
Heterogeneity: Not applicable					
Test for overall effect: Not applicable					
2.7.9 Hydrocortisone buteprate					
Sears 1997	1/94	0/96		19.51%	0.01[-0.02,0.04]
Subtotal (95% CI)	**94**	**96**		**19.51%**	**0.01[-0.02,0.04]**
Total events: 1 (Corticosteroid (potent)), 0 (Placebo)					
Heterogeneity: Tau^2=0; Chi^2=0, df=0(P<0.0001); I^2=100%					
Test for overall effect: Z=0.72(P=0.47)					
2.7.10 Mometasone furoate					
Medansky 1987	0/61	3/59		12.96%	-0.05[-0.11,0.01]
Subtotal (95% CI)	**61**	**59**		**12.96%**	**-0.05[-0.11,0.01]**
Total events: 0 (Corticosteroid (potent)), 3 (Placebo)					
Heterogeneity: Not applicable					
Test for overall effect: Z=1.57(P=0.12)					
Total (95% CI)	**827**	**465**		**100%**	**-0.01[-0.05,0.02]**
Total events: 9 (Corticosteroid (potent)), 17 (Placebo)					
Heterogeneity: Tau^2=0; Chi^2=20.46, df=8(P=0.01); I^2=60.9%					
Test for overall effect: Z=0.78(P=0.44)					
Test for subgroup differences: Chi^2=15.38, df=1 (P=0.03), I^2=54.5%					

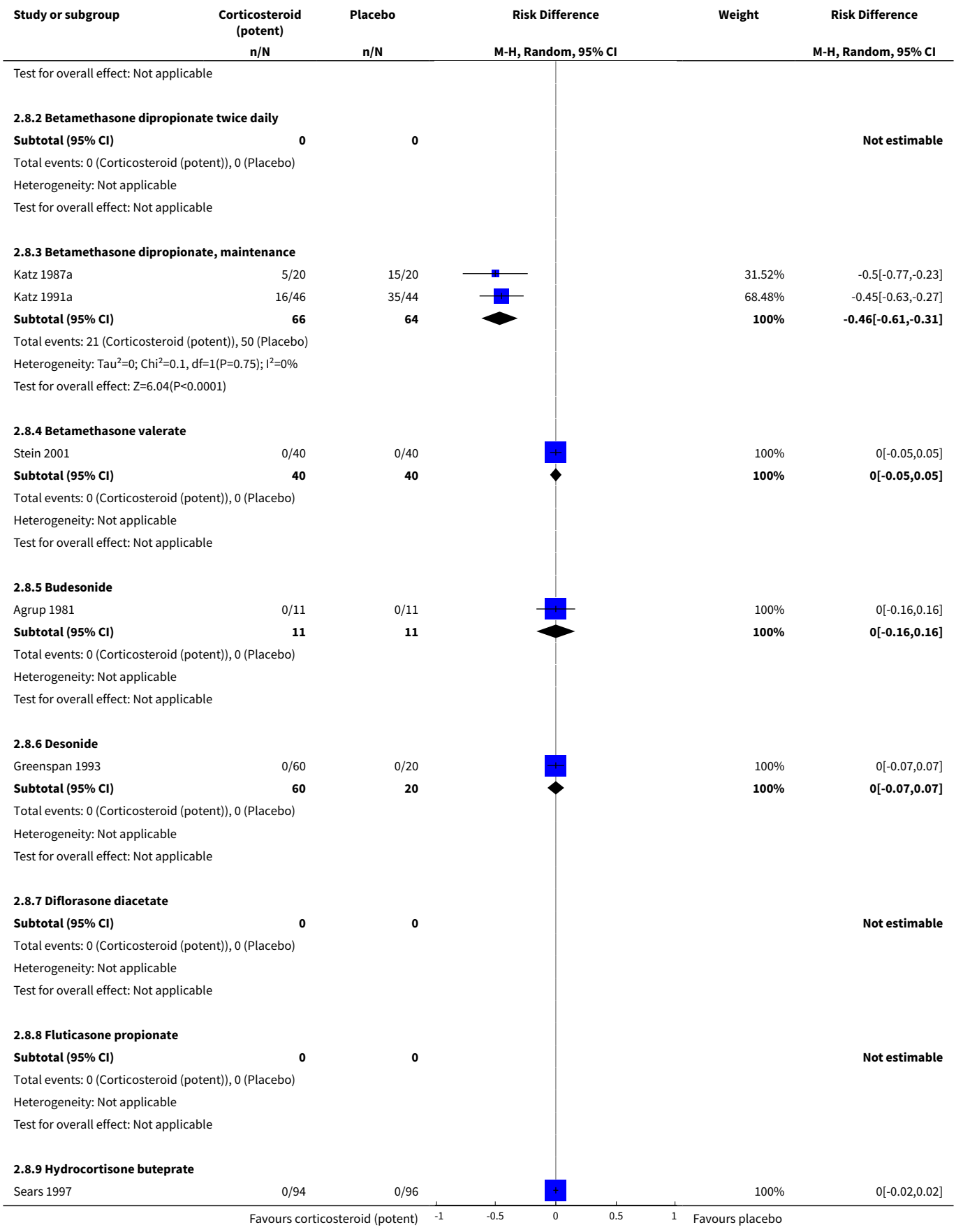


Favours corticosteroid (potent) Favours placebo

Analysis 2.8. Comparison 2 Corticosteroid (potent) versus placebo, Outcome 8 Withdrawals due to treatment failure.

Study or subgroup	Corticosteroid (potent) n/N	Placebo n/N	Risk Difference M-H, Random, 95% CI	Weight	Risk Difference M-H, Random, 95% CI
2.8.1 Betamethasone dipropionate OD					
Subtotal (95% CI)	**0**	**0**			**Not estimable**
Total events: 0 (Corticosteroid (potent)), 0 (Placebo)					
Heterogeneity: Not applicable					

Favours corticosteroid (potent) Favours placebo



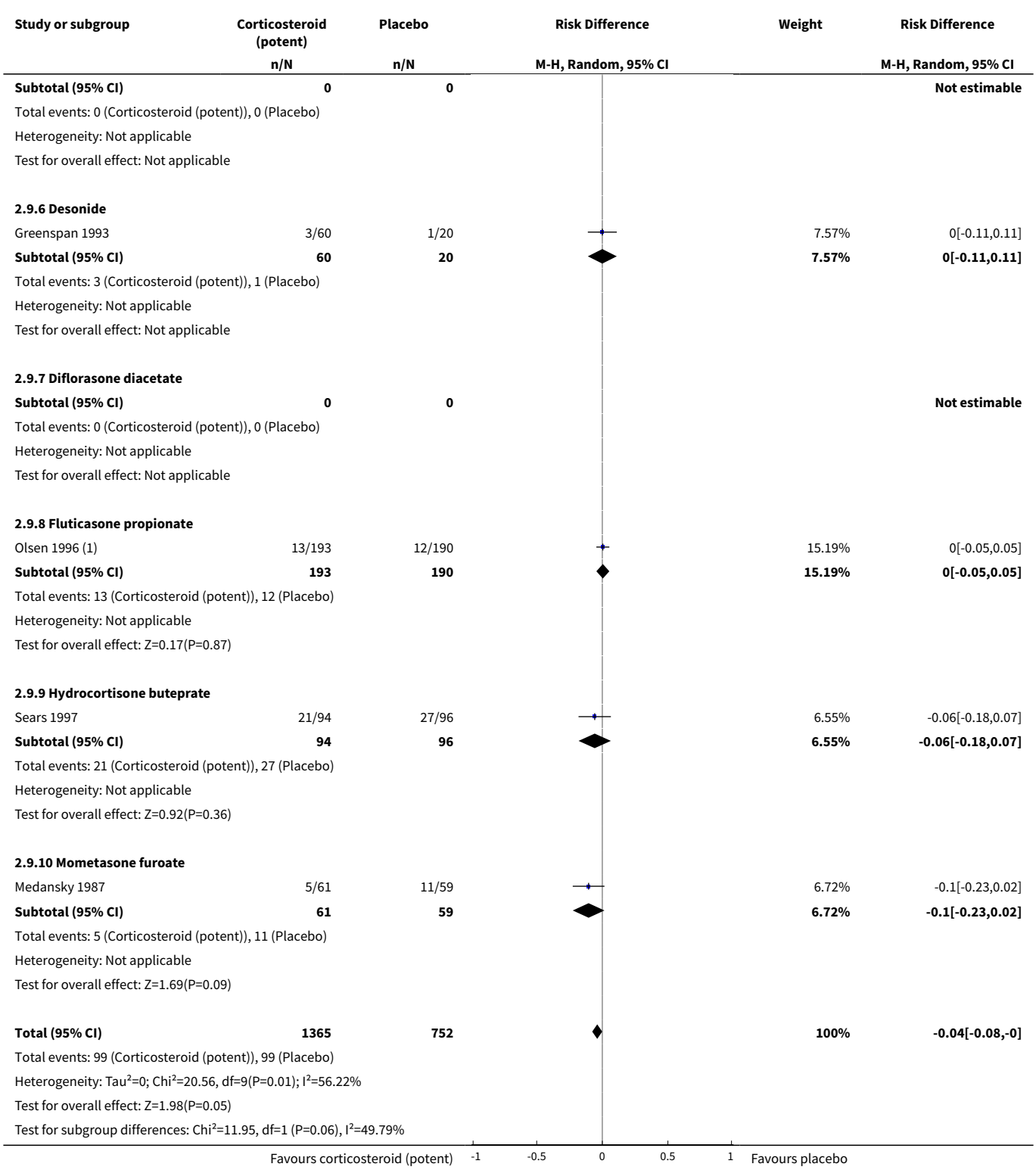
Study or subgroup	Corticosteroid (potent) n/N	Placebo n/N	Risk Difference M-H, Random, 95% CI	Weight	Risk Difference M-H, Random, 95% CI
Subtotal (95% CI)	**94**	**96**		**100%**	**0[-0.02,0.02]**
Total events: 0 (Corticosteroid (potent)), 0 (Placebo)					
Heterogeneity: Not applicable					
Test for overall effect: Not applicable					
2.8.10 Mometasone furoate					
Subtotal (95% CI)	**0**	**0**			**Not estimable**
Total events: 0 (Corticosteroid (potent)), 0 (Placebo)					
Heterogeneity: Not applicable					
Test for overall effect: Not applicable					
Test for subgroup differences: Chi^2=35.94, df=1 (P<0.0001), I^2=88.87%					

Favours corticosteroid (potent) -1 -0.5 0 0.5 1 Favours placebo

Analysis 2.9. Comparison 2 Corticosteroid (potent) versus placebo, Outcome 9 Adverse events (local).

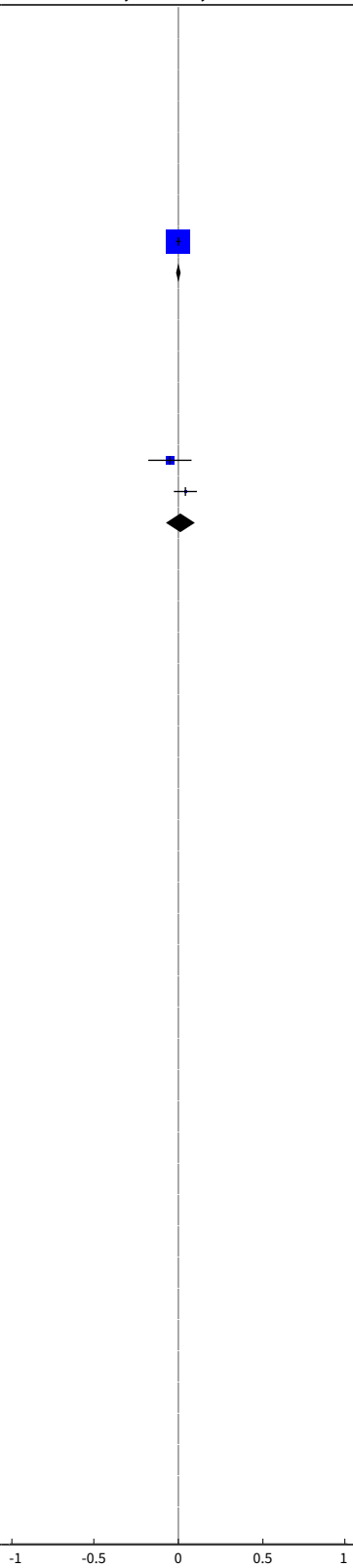
Study or subgroup	Corticosteroid (potent) n/N	Placebo n/N	Risk Difference M-H, Random, 95% CI	Weight	Risk Difference M-H, Random, 95% CI
2.9.1 Betamethasone dipropionate OD					
Fleming 2010 (P)	7/83	10/40		5.09%	-0.17[-0.31,-0.02]
Kaufmann 2002 (P)	23/476	21/157		14.08%	-0.09[-0.14,-0.03]
Subtotal (95% CI)	**559**	**197**		**19.17%**	**-0.1[-0.15,-0.04]**
Total events: 30 (Corticosteroid (potent)), 31 (Placebo)					
Heterogeneity: Tau^2=0; Chi^2=1.03, df=1(P=0.31); I^2=2.53%					
Test for overall effect: Z=3.43(P=0)					
2.9.2 Betamethasone dipropionate twice daily					
Papp 2003 (P)	27/313	17/108		11.37%	-0.07[-0.15,0]
Vanderploeg 1976	0/17	0/16		7.55%	0[-0.11,0.11]
Subtotal (95% CI)	**330**	**124**		**18.92%**	**-0.05[-0.12,0.03]**
Total events: 27 (Corticosteroid (potent)), 17 (Placebo)					
Heterogeneity: Tau^2=0; Chi^2=1.34, df=1(P=0.25); I^2=25.32%					
Test for overall effect: Z=1.19(P=0.23)					
2.9.3 Betamethasone dipropionate, maintenance					
Katz 1987a	0/20	0/20		9.33%	0[-0.09,0.09]
Katz 1991a	0/48	0/46		16.56%	0[-0.04,0.04]
Subtotal (95% CI)	**68**	**66**		**25.89%**	**0[-0.04,0.04]**
Total events: 0 (Corticosteroid (potent)), 0 (Placebo)					
Heterogeneity: Tau^2=0; Chi^2=0, df=1(P=1); I^2=0%					
Test for overall effect: Not applicable					
2.9.4 Betamethasone valerate					
Subtotal (95% CI)	**0**	**0**			**Not estimable**
Total events: 0 (Corticosteroid (potent)), 0 (Placebo)					
Heterogeneity: Not applicable					
Test for overall effect: Not applicable					
2.9.5 Budesonide					

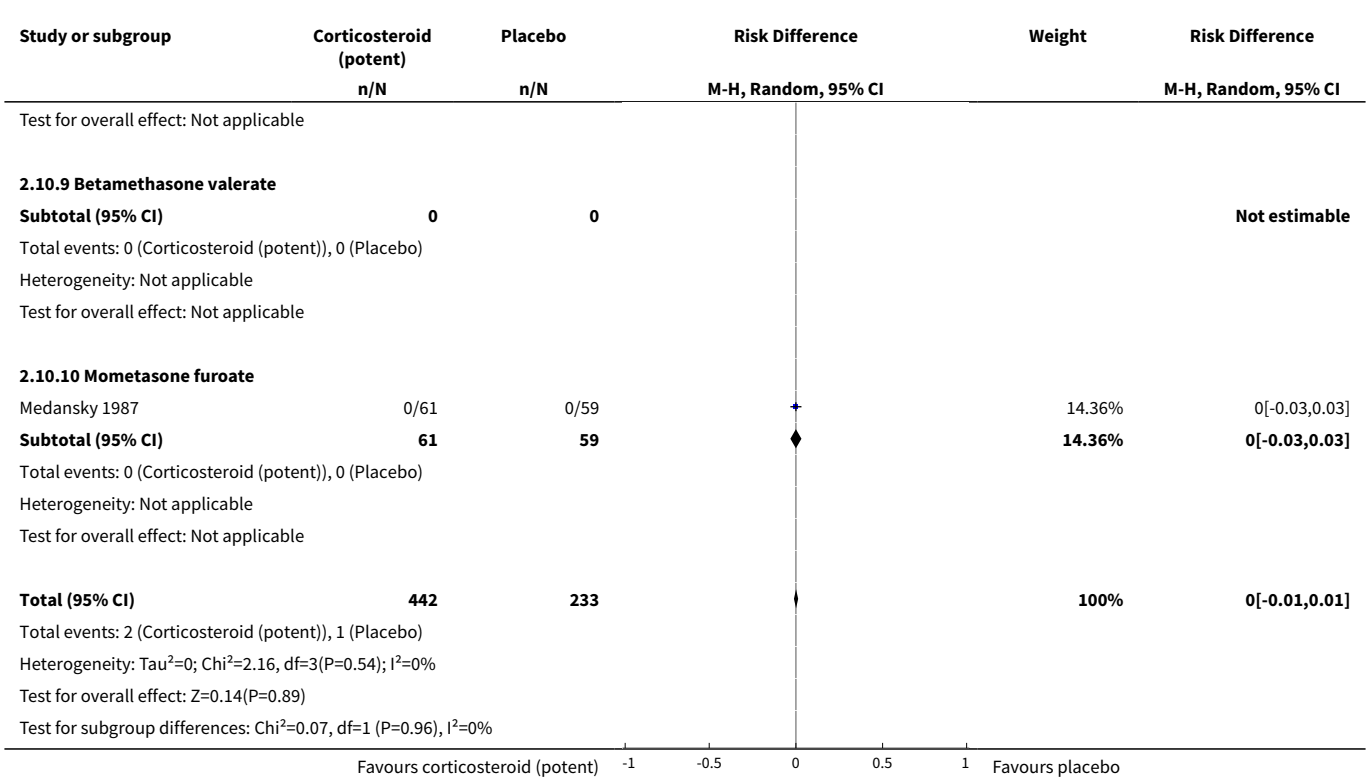
Favours corticosteroid (potent) -1 -0.5 0 0.5 1 Favours placebo



Analysis 2.10. Comparison 2 Corticosteroid (potent) versus placebo, Outcome 10 Adverse events (systemic).

Study or subgroup	Corticosteroid (potent) n/N	Placebo n/N	Risk Difference M-H, Random, 95% CI	Weight	Risk Difference M-H, Random, 95% CI
2.10.1 Betamethasone dipropionate OD					
Subtotal (95% CI)	**0**	**0**			**Not estimable**
Total events: 0 (Corticosteroid (potent)), 0 (Placebo)					
Heterogeneity: Not applicable					
Test for overall effect: Not applicable					
2.10.2 Betamethasone dipropionate twice daily					
Papp 2003 (P)	0/313	0/108		81.58%	0[-0.01,0.01]
Subtotal (95% CI)	**313**	**108**		**81.58%**	**0[-0.01,0.01]**
Total events: 0 (Corticosteroid (potent)), 0 (Placebo)					
Heterogeneity: Not applicable					
Test for overall effect: Not applicable					
2.10.3 Betamethasone dipropionate, maintenance					
Katz 1987a	0/20	1/20		0.9%	-0.05[-0.18,0.08]
Katz 1991a	2/48	0/46		3.16%	0.04[-0.03,0.11]
Subtotal (95% CI)	**68**	**66**		**4.06%**	**0.01[-0.07,0.1]**
Total events: 2 (Corticosteroid (potent)), 1 (Placebo)					
Heterogeneity: Tau^2=0; Chi^2=1.59, df=1(P=0.21); I^2=37%					
Test for overall effect: Z=0.27(P=0.78)					
2.10.4 Budesonide					
Subtotal (95% CI)	**0**	**0**			**Not estimable**
Total events: 0 (Corticosteroid (potent)), 0 (Placebo)					
Heterogeneity: Not applicable					
Test for overall effect: Not applicable					
2.10.5 Desonide					
Subtotal (95% CI)	**0**	**0**			**Not estimable**
Total events: 0 (Corticosteroid (potent)), 0 (Placebo)					
Heterogeneity: Not applicable					
Test for overall effect: Not applicable					
2.10.6 Diflorasone diacetate					
Subtotal (95% CI)	**0**	**0**			**Not estimable**
Total events: 0 (Corticosteroid (potent)), 0 (Placebo)					
Heterogeneity: Not applicable					
Test for overall effect: Not applicable					
2.10.7 Fluticasone propionate					
Subtotal (95% CI)	**0**	**0**			**Not estimable**
Total events: 0 (Corticosteroid (potent)), 0 (Placebo)					
Heterogeneity: Not applicable					
Test for overall effect: Not applicable					
2.10.8 Hydrocortisone buteprate					
Subtotal (95% CI)	**0**	**0**			**Not estimable**
Total events: 0 (Corticosteroid (potent)), 0 (Placebo)					
Heterogeneity: Not applicable					





Comparison 3. Corticosteroid (very potent) versus placebo

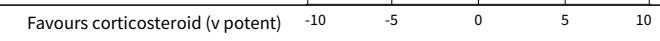
Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 IAGI	5	540	Std. Mean Difference (IV, Random, 95% CI)	-1.87 [-2.38, -1.36]
1.1 Clobetasol propionate	4	471	Std. Mean Difference (IV, Random, 95% CI)	-1.89 [-2.53, -1.24]
1.2 Halcinonide	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
1.3 Halobetasol	1	69	Std. Mean Difference (IV, Random, 95% CI)	-1.81 [-2.37, -1.24]
2 TSS	3	545	Std. Mean Difference (IV, Random, 95% CI)	-1.35 [-1.80, -0.89]
2.1 Clobetasol propionate	3	545	Std. Mean Difference (IV, Random, 95% CI)	-1.35 [-1.80, -0.89]
2.2 Halcinonide	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
2.3 Halobetasol	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
3 PASI	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
3.1 Clobetasol propionate	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
3.2 Halcinonide	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]

Outcome or sub-group title	No. of studies	No. of partici-pants	Statistical method	Effect size
3.3 Halobetasol	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
4 PAGI	3	487	Std. Mean Difference (IV, Random, 95% CI)	-1.22 [-1.42, -1.02]
4.1 Clobetasol propi-onate	1	79	Std. Mean Difference (IV, Random, 95% CI)	-1.01 [-1.55, -0.47]
4.2 Halcinonide	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
4.3 Halobetasol	2	408	Std. Mean Difference (IV, Random, 95% CI)	-1.25 [-1.46, -1.04]
5 Combined end point (IAGI/TSS/PASI/PAGI)	10	1493	Std. Mean Difference (IV, Random, 95% CI)	-1.56 [-1.87, -1.26]
5.1 Clobetasol propi-onate	7	1016	Std. Mean Difference (IV, Random, 95% CI)	-1.65 [-2.10, -1.20]
5.2 Halcinonide	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
5.3 Halobetasol	3	477	Std. Mean Difference (IV, Random, 95% CI)	-1.36 [-1.65, -1.07]
6 Total withdrawals	8	1181	Risk Difference (M-H, Random, 95% CI)	-0.05 [-0.10, 0.01]
6.1 Clobetasol propi-onate	7	1037	Risk Difference (M-H, Random, 95% CI)	-0.06 [-0.13, 0.01]
6.2 Halcinonide	0	0	Risk Difference (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
6.3 Halobetasol	1	144	Risk Difference (M-H, Random, 95% CI)	0.0 [-0.03, 0.03]
7 Withdrawals due to adverse events	10	1601	Risk Difference (M-H, Random, 95% CI)	-0.00 [-0.01, 0.01]
7.1 Clobetasol propi-onate	7	1037	Risk Difference (M-H, Random, 95% CI)	-0.00 [-0.02, 0.01]
7.2 Halcinonide	0	0	Risk Difference (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
7.3 Halobetasol	3	564	Risk Difference (M-H, Random, 95% CI)	0.0 [-0.01, 0.01]
8 Withdrawals due to treatment failure	8	1189	Risk Difference (M-H, Random, 95% CI)	-0.00 [-0.02, 0.01]
8.1 Clobetasol propi-onate	6	845	Risk Difference (M-H, Random, 95% CI)	-0.01 [-0.03, 0.01]
8.2 Halcinonide	0	0	Risk Difference (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
8.3 Halobetasol	2	344	Risk Difference (M-H, Random, 95% CI)	0.0 [-0.02, 0.02]
9 Adverse events (lo-cal)	8	1265	Risk Difference (M-H, Random, 95% CI)	0.00 [-0.02, 0.02]
9.1 Clobetasol propi-onate	6	845	Risk Difference (M-H, Random, 95% CI)	0.00 [-0.03, 0.03]

Outcome or sub-group title	No. of studies	No. of partici-pants	Statistical method	Effect size
9.2 Halcinonide	0	0	Risk Difference (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
9.3 Halobetasol	2	420	Risk Difference (M-H, Random, 95% CI)	0.0 [-0.02, 0.02]
10 Adverse events (systemic)	6	1056	Risk Difference (M-H, Random, 95% CI)	-0.00 [-0.01, 0.01]
10.1 Clobetasol propi-onate	3	480	Risk Difference (M-H, Random, 95% CI)	-0.01 [-0.02, 0.01]
10.2 Halcinonide	1	156	Risk Difference (M-H, Random, 95% CI)	0.0 [-0.02, 0.02]
10.3 Halobetasol	2	420	Risk Difference (M-H, Random, 95% CI)	0.0 [-0.01, 0.01]

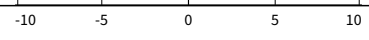
Analysis 3.1. Comparison 3 Corticosteroid (very potent) versus placebo, Outcome 1 IAGI.

Study or subgroup	Corticosteroid (very potent) N	Mean(SD)	Placebo N	Mean(SD)	Std. Mean Difference Random, 95% CI	Weight	Std. Mean Difference Random, 95% CI
3.1.1 Clobetasol propionate							
Beutner 2006	25	0.2 (0.4)	25	2.2 (1.1)		16.63%	-2.45[-3.19,-1.7]
Decroix 2004	189	-4.9 (1.1)	33	-2.2 (1.7)		21.91%	-2.27[-2.7,-1.85]
Jarratt 2006	60	1.1 (1)	60	2.7 (0.6)		21.7%	-1.99[-2.43,-1.55]
Lebwohl 2002	60	-2.8 (1.5)	19	-1.6 (1.2)		20.13%	-0.89[-1.43,-0.36]
Subtotal ***	**334**		**137**			**80.37%**	**-1.89[-2.53,-1.24]**
Heterogeneity: Tau^2=0.36; Chi^2=18.67, df=3(P=0); I^2=83.93%							
Test for overall effect: Z=5.74(P<0.0001)							
3.1.2 Halcinonide							
Subtotal ***	**0**		**0**				**Not estimable**
Heterogeneity: Not applicable							
Test for overall effect: Not applicable							
3.1.3 Halobetasol							
Bernhard 1991(2)	36	-3 (1)	33	-1.3 (0.9)		19.63%	-1.81[-2.37,-1.24]
Subtotal ***	**36**		**33**			**19.63%**	**-1.81[-2.37,-1.24]**
Heterogeneity: Tau^2=0; Chi^2=0, df=0(P<0.0001); I^2=100%							
Test for overall effect: Z=6.26(P<0.0001)							
Total ***	**370**		**170**			**100%**	**-1.87[-2.38,-1.36]**
Heterogeneity: Tau^2=0.26; Chi^2=18.76, df=4(P=0); I^2=78.68%							
Test for overall effect: Z=7.21(P<0.0001)							
Test for subgroup differences: Chi^2=0.04, df=1 (P=0.85), I^2=0%							



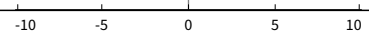
Analysis 3.2. Comparison 3 Corticosteroid (very potent) versus placebo, Outcome 2 TSS.

Study or subgroup	Corticosteroid (very potent) N	Mean(SD)	Placebo N	Mean(SD)	Std. Mean Difference Random, 95% CI	Weight	Std. Mean Difference Random, 95% CI
3.2.1 Clobetasol propionate							
Gottlieb 2003	139	-4 (2.4)	140	-1.5 (2.4)		39.48%	-1.03[-1.28,-0.78]
Jorizzo 1997	35	-4.3 (2)	39	-1.6 (2)		28.67%	-1.35[-1.86,-0.84]
Lowe 2005	163	2.4 (2)	29	5.9 (1.9)		31.85%	-1.74[-2.17,-1.31]
Subtotal ***	**337**		**208**			**100%**	**-1.35[-1.8,-0.89]**
Heterogeneity: Tau^2=0.12; Chi^2=8.1, df=2(P=0.02); I^2=75.31%							
Test for overall effect: Z=5.83(P<0.0001)							
3.2.2 Halcinonide							
Subtotal ***	**0**		**0**				**Not estimable**
Heterogeneity: Not applicable							
Test for overall effect: Not applicable							
3.2.3 Halobetasol							
Subtotal ***	**0**		**0**				**Not estimable**
Heterogeneity: Not applicable							
Test for overall effect: Not applicable							
Total ***	**337**		**208**			**100%**	**-1.35[-1.8,-0.89]**
Heterogeneity: Tau^2=0.12; Chi^2=8.1, df=2(P=0.02); I^2=75.31%							
Test for overall effect: Z=5.83(P<0.0001)							
Test for subgroup differences: Not applicable							



Analysis 3.4. Comparison 3 Corticosteroid (very potent) versus placebo, Outcome 4 PAGI.

Study or subgroup	Corticosteroid (very potent) N	Mean(SD)	Placebo N	Mean(SD)	Std. Mean Difference Random, 95% CI	Weight	Std. Mean Difference Random, 95% CI
3.4.1 Clobetasol propionate							
Lebwohl 2002	60	-3.1 (1.4)	19	-1.7 (1.3)		13.4%	-1.01[-1.55,-0.47]
Subtotal ***	**60**		**19**			**13.4%**	**-1.01[-1.55,-0.47]**
Heterogeneity: Not applicable							
Test for overall effect: Z=3.65(P=0)							
3.4.2 Halcinonide							
Subtotal ***	**0**		**0**				**Not estimable**
Heterogeneity: Not applicable							
Test for overall effect: Not applicable							
3.4.3 Halobetasol							
Bernhard 1991 (1)	96	-2.9 (1.2)	96	-1.5 (1.3)		41.67%	-1.17[-1.47,-0.86]
Katz 1991b	108	-2.5 (1.5)	108	-0.7 (1.1)		44.93%	-1.33[-1.62,-1.03]
Subtotal ***	**204**		**204**			**86.6%**	**-1.25[-1.46,-1.04]**
Heterogeneity: Tau^2=0; Chi^2=0.55, df=1(P=0.46); I^2=0%							
Test for overall effect: Z=11.54(P<0.0001)							



Study or subgroup	Corticosteroid (very potent) N	Mean(SD)	Placebo N	Mean(SD)	Std. Mean Difference Random, 95% CI	Weight	Std. Mean Difference Random, 95% CI
Total ***	**264**		**223**			**100%**	**-1.22[-1.42,-1.02]**
Heterogeneity: Tau^2=0; Chi^2=1.23, df=2(P=0.54); I^2=0%							
Test for overall effect: Z=12.08(P<0.0001)							
Test for subgroup differences: Chi^2=0.68, df=1 (P=0.41), I^2=0%							

Favours corticosteroid (v potent) -10 -5 0 5 10 Favours placebo

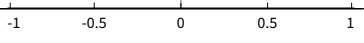
Analysis 3.5. Comparison 3 Corticosteroid (very potent) versus placebo, Outcome 5 Combined end point (IAGI/TSS/PASI/PAGI).

Study or subgroup	Corticosteroid (very potent) N	Mean(SD)	Placebo N	Mean(SD)	Std. Mean Difference Random, 95% CI	Weight	Std. Mean Difference Random, 95% CI
3.5.1 Clobetasol propionate							
Beutner 2006	25	0.2 (0.4)	25	2.2 (1.1)		7.21%	-2.45[-3.19,-1.7]
Decroix 2004	189	-4.9 (1.1)	33	-2.2 (1.7)		10.25%	-2.27[-2.7,-1.85]
Gottlieb 2003	139	-4 (2.4)	140	-1.5 (2.4)		11.85%	-1.03[-1.28,-0.78]
Jarratt 2006	60	1.1 (1)	60	2.7 (0.6)		10.12%	-1.99[-2.43,-1.55]
Jorizzo 1997	35	-4.3 (2)	39	-1.6 (2)		9.44%	-1.35[-1.86,-0.84]
Lebwohl 2002	60	-2.8 (1.5)	19	-1.6 (1.2)		9.17%	-0.89[-1.43,-0.36]
Lowe 2005	163	2.4 (2)	29	5.9 (1.9)		10.2%	-1.74[-2.17,-1.31]
Subtotal ***	**671**		**345**			**68.25%**	**-1.65[-2.1,-1.2]**
Heterogeneity: Tau^2=0.31; Chi^2=43.69, df=6(P<0.0001); I^2=86.27%							
Test for overall effect: Z=7.21(P<0.0001)							
3.5.2 Halcinonide							
Subtotal ***	**0**		**0**				**Not estimable**
Heterogeneity: Not applicable							
Test for overall effect: Not applicable							
3.5.3 Halobetasol							
Bernhard 1991 (1)	96	-2.9 (1.2)	96	-1.5 (1.3)		11.39%	-1.17[-1.47,-0.86]
Bernhard 1991(2)	36	-3 (1)	33	-1.3 (0.9)		8.88%	-1.81[-2.37,-1.24]
Katz 1991b	108	-2.5 (1.5)	108	-0.7 (1.1)		11.48%	-1.33[-1.62,-1.03]
Subtotal ***	**240**		**237**			**31.75%**	**-1.36[-1.65,-1.07]**
Heterogeneity: Tau^2=0.03; Chi^2=3.78, df=2(P=0.15); I^2=47.06%							
Test for overall effect: Z=9.18(P<0.0001)							
Total ***	**911**		**582**			**100%**	**-1.56[-1.87,-1.26]**
Heterogeneity: Tau^2=0.18; Chi^2=49.13, df=9(P<0.0001); I^2=81.68%							
Test for overall effect: Z=10.17(P<0.0001)							
Test for subgroup differences: Chi^2=1.16, df=1 (P=0.28), I^2=13.6%							

Favours corticosteroid (v potent) -5 -2.5 0 2.5 5 Favours placebo

Analysis 3.6. Comparison 3 Corticosteroid (very potent) versus placebo, Outcome 6 Total withdrawals.

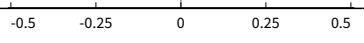
Study or subgroup	Corticosteroid (very potent) n/N	Placebo n/N	Risk Difference M-H, Random, 95% CI	Weight	Risk Difference M-H, Random, 95% CI
3.6.1 Clobetasol propionate					
Beutner 2006	2/27	2/27		9.06%	0[-0.14,0.14]
Decroix 2004	5/189	4/33		11.12%	-0.09[-0.21,0.02]
Gottlieb 2003	4/139	4/140		18.34%	0[-0.04,0.04]
Jarratt 2006	0/60	0/60		18.89%	0[-0.03,0.03]
Jorizzo 1997	6/44	15/45		7.11%	-0.2[-0.37,-0.03]
Lebwohl 2002	3/61	2/20		8.88%	-0.05[-0.19,0.09]
Lowe 2005	9/163	8/29		7.36%	-0.22[-0.39,-0.05]
Subtotal (95% CI)	**683**	**354**		**80.76%**	**-0.06[-0.13,0.01]**
Total events: 29 (Corticosteroid (very potent)), 35 (Placebo)					
Heterogeneity: Tau²=0.01; Chi²=33.33, df=6(P<0.0001); I²=82%					
Test for overall effect: Z=1.66(P=0.1)					
3.6.2 Halcinonide					
Subtotal (95% CI)	**0**	**0**			**Not estimable**
Total events: 0 (Corticosteroid (very potent)), 0 (Placebo)					
Heterogeneity: Not applicable					
Test for overall effect: Not applicable					
3.6.3 Halobetasol					
Bernhard 1991(2)	0/72	0/72		19.24%	0[-0.03,0.03]
Subtotal (95% CI)	**72**	**72**		**19.24%**	**0[-0.03,0.03]**
Total events: 0 (Corticosteroid (very potent)), 0 (Placebo)					
Heterogeneity: Not applicable					
Test for overall effect: Not applicable					
Total (95% CI)	**755**	**426**		**100%**	**-0.05[-0.1,0.01]**
Total events: 29 (Corticosteroid (very potent)), 35 (Placebo)					
Heterogeneity: Tau²=0; Chi²=43.07, df=7(P<0.0001); I²=83.75%					
Test for overall effect: Z=1.56(P=0.12)					
Test for subgroup differences: Chi²=2.43, df=1 (P=0.12), I²=58.76%					



Favours corticosteroid (v potent) — Favours placebo

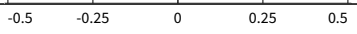
Analysis 3.7. Comparison 3 Corticosteroid (very potent) versus placebo, Outcome 7 Withdrawals due to adverse events.

Study or subgroup	Corticosteroid (very potent) n/N	Placebo n/N	Risk Difference M-H, Random, 95% CI	Weight	Risk Difference M-H, Random, 95% CI
3.7.1 Clobetasol propionate					
Beutner 2006	0/27	0/27		1.66%	0[-0.07,0.07]
Decroix 2004	1/189	0/33		4.44%	0.01[-0.04,0.05]
Gottlieb 2003	0/139	1/140		20.75%	-0.01[-0.03,0.01]
Jarratt 2006	0/60	0/60		7.79%	0[-0.03,0.03]
Jorizzo 1997	1/44	1/45		2.1%	0[-0.06,0.06]
Lebwohl 2002	0/61	0/20		1.68%	0[-0.07,0.07]
Lowe 2005	1/163	0/29		3.45%	0.01[-0.04,0.05]



Favours corticosteroid (v potent) — Favours placebo

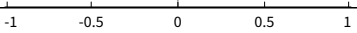
Study or subgroup	Corticosteroid (very potent) n/N	Placebo n/N	Risk Difference M-H, Random, 95% CI	Weight	Risk Difference M-H, Random, 95% CI
Subtotal (95% CI)	**683**	**354**		**41.87%**	**-0[-0.02,0.01]**
Total events: 3 (Corticosteroid (very potent)), 2 (Placebo)					
Heterogeneity: Tau^2=0; Chi^2=0.56, df=6(P=1); I^2=0%					
Test for overall effect: Z=0.35(P=0.73)					
3.7.2 Halcinonide					
Subtotal (95% CI)	**0**	**0**			**Not estimable**
Total events: 0 (Corticosteroid (very potent)), 0 (Placebo)					
Heterogeneity: Not applicable					
Test for overall effect: Not applicable					
3.7.3 Halobetasol					
Bernhard 1991 (1)	0/100	0/100		21.29%	0[-0.02,0.02]
Bernhard 1991(2)	0/72	0/72		11.14%	0[-0.03,0.03]
Katz 1991b	0/110	0/110		25.7%	0[-0.02,0.02]
Subtotal (95% CI)	**282**	**282**		**58.13%**	**0[-0.01,0.01]**
Total events: 0 (Corticosteroid (very potent)), 0 (Placebo)					
Heterogeneity: Tau^2=0; Chi^2=0, df=2(P=1); I^2=0%					
Test for overall effect: Not applicable					
Total (95% CI)	**965**	**636**		**100%**	**-0[-0.01,0.01]**
Total events: 3 (Corticosteroid (very potent)), 2 (Placebo)					
Heterogeneity: Tau^2=0; Chi^2=0.59, df=9(P=1); I^2=0%					
Test for overall effect: Z=0.22(P=0.82)					
Test for subgroup differences: Chi^2=0.07, df=1 (P=0.79), I^2=0%					



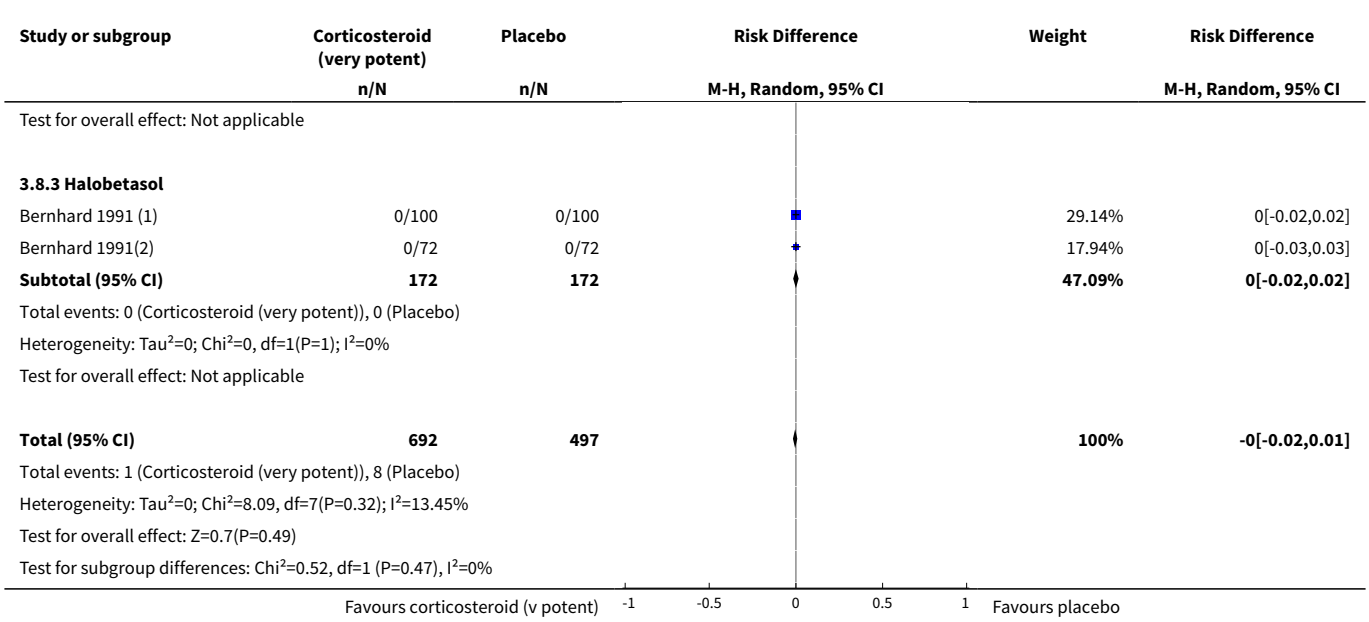
Favours corticosteroid (v potent) — Favours placebo

Analysis 3.8. Comparison 3 Corticosteroid (very potent) versus placebo, Outcome 8 Withdrawals due to treatment failure.

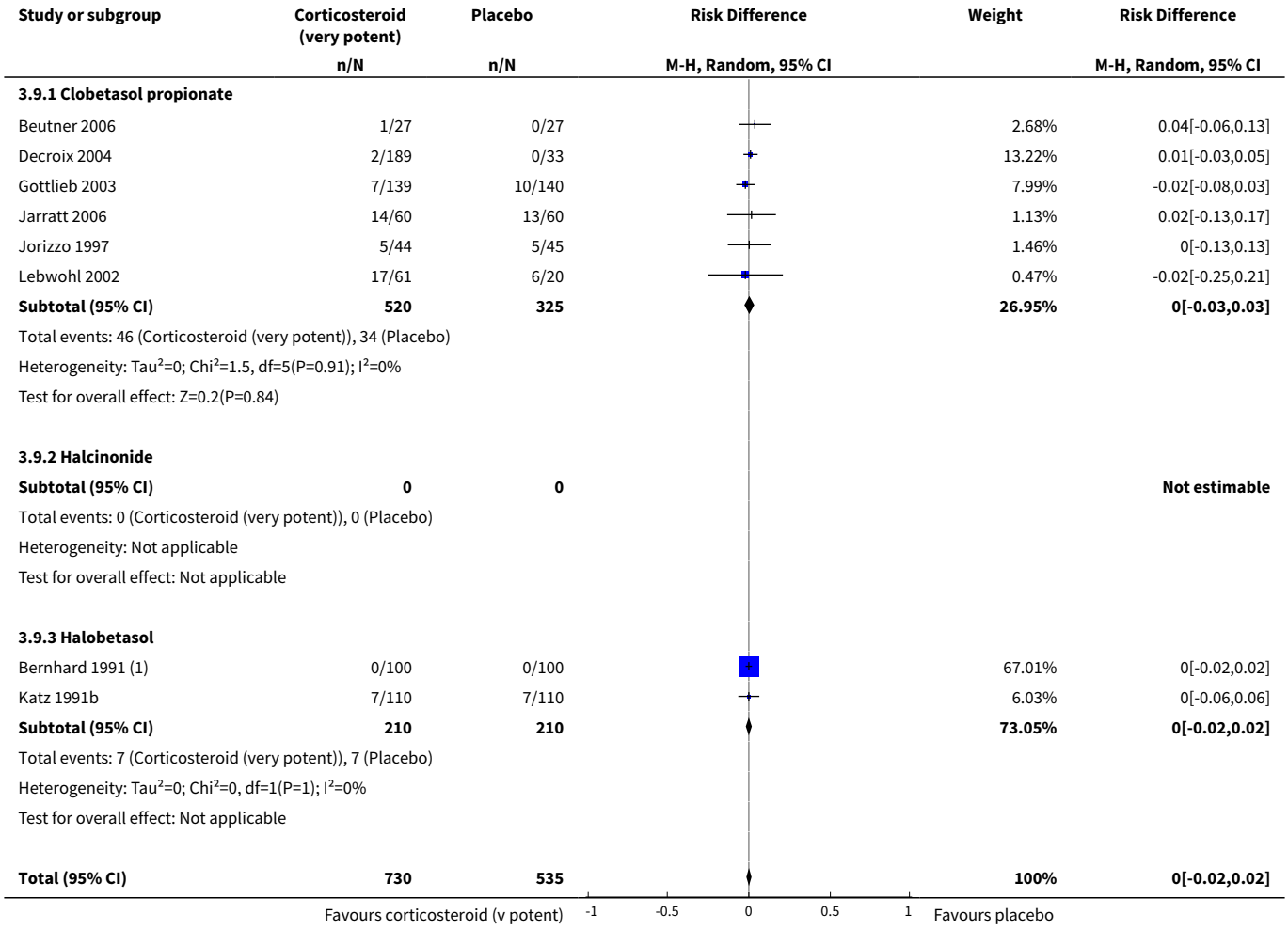
Study or subgroup	Corticosteroid (very potent) n/N	Placebo n/N	Risk Difference M-H, Random, 95% CI	Weight	Risk Difference M-H, Random, 95% CI
3.8.1 Clobetasol propionate					
Beutner 2006	0/27	0/27		3.2%	0[-0.07,0.07]
Decroix 2004	0/189	1/33		3.19%	-0.03[-0.1,0.04]
Gottlieb 2003	0/139	1/140		28.64%	-0.01[-0.03,0.01]
Jarratt 2006	0/60	0/60		13.32%	0[-0.03,0.03]
Jorizzo 1997	1/44	6/45		1.33%	-0.11[-0.22,-0]
Lebwohl 2002	0/61	0/20		3.24%	0[-0.07,0.07]
Subtotal (95% CI)	**520**	**325**		**52.91%**	**-0.01[-0.03,0.01]**
Total events: 1 (Corticosteroid (very potent)), 8 (Placebo)					
Heterogeneity: Tau^2=0; Chi^2=7.11, df=5(P=0.21); I^2=29.64%					
Test for overall effect: Z=0.88(P=0.38)					
3.8.2 Halcinonide					
Subtotal (95% CI)	**0**	**0**			**Not estimable**
Total events: 0 (Corticosteroid (very potent)), 0 (Placebo)					
Heterogeneity: Not applicable					

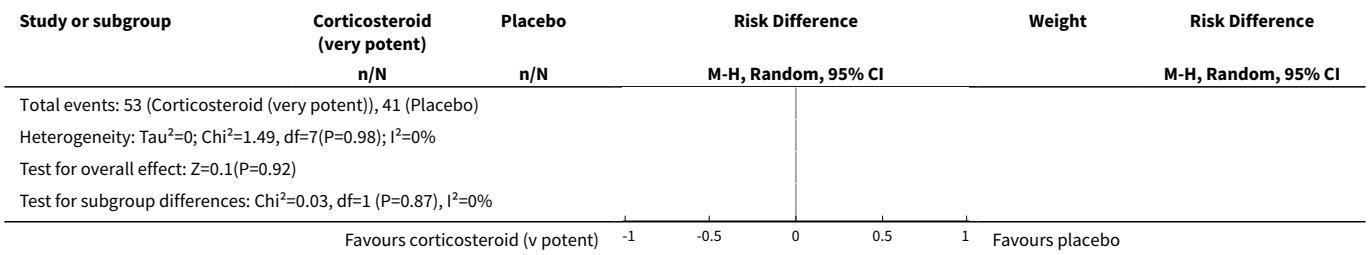


Favours corticosteroid (v potent) — Favours placebo

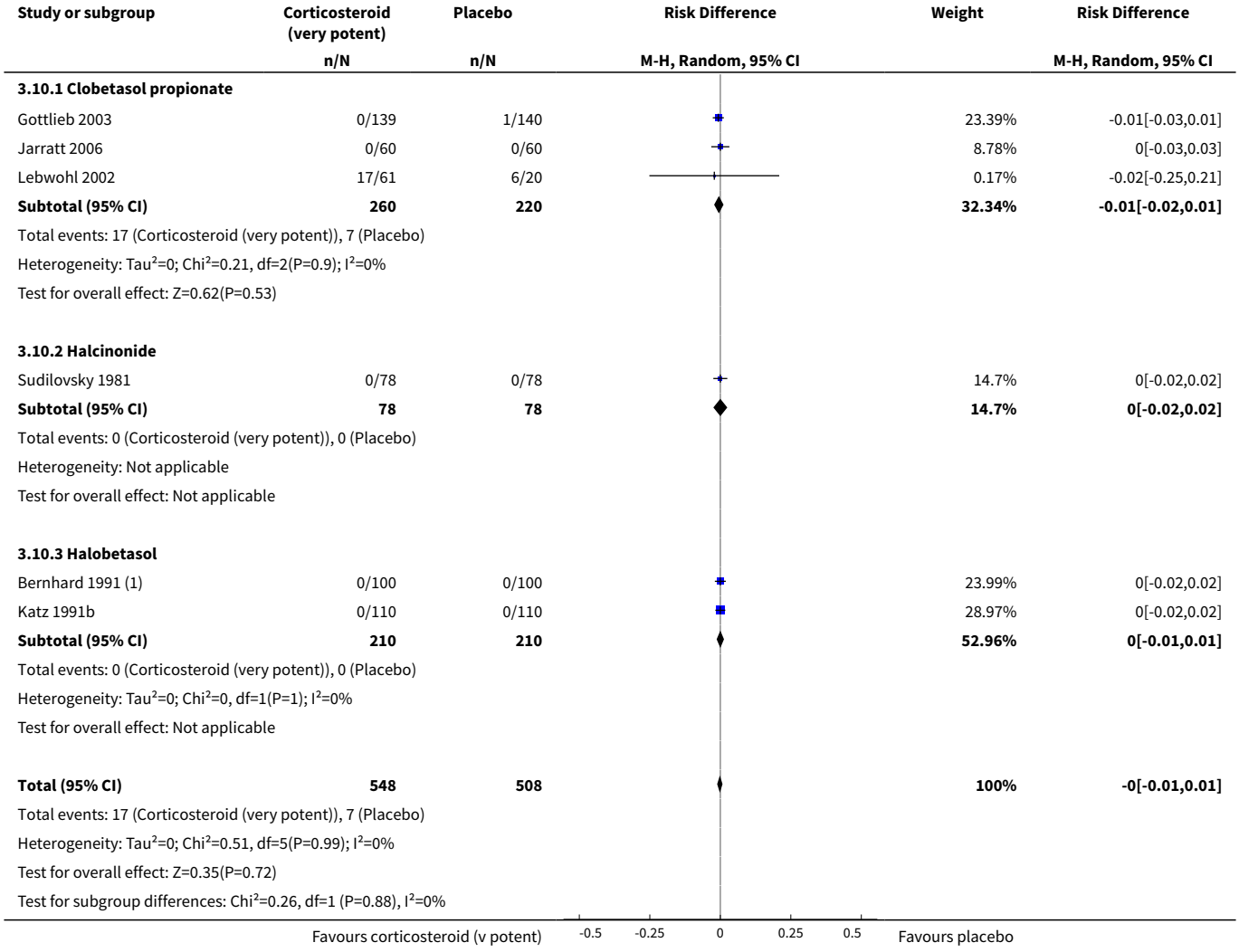


Analysis 3.9. Comparison 3 Corticosteroid (very potent) versus placebo, Outcome 9 Adverse events (local).





Analysis 3.10. Comparison 3 Corticosteroid (very potent) versus placebo, Outcome 10 Adverse events (systemic).

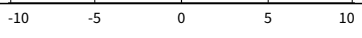


Comparison 4. Dithranol versus placebo

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 IAGI	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
2 TSS	3	94	Std. Mean Difference (IV, Random, 95% CI)	-1.06 [-1.66, -0.46]
3 PASI	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
4 PAGI	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
5 Combined end point (IAGI/TSS/PASI/PAGI)	3	94	Std. Mean Difference (IV, Random, 95% CI)	-1.06 [-1.66, -0.46]
6 Total withdrawals	4	124	Risk Difference (M-H, Random, 95% CI)	0.0 [-0.09, 0.09]
7 Withdrawals due to adverse events	3	104	Risk Difference (M-H, Random, 95% CI)	0.0 [-0.05, 0.05]
8 Withdrawals due to treatment failure	2	44	Risk Difference (M-H, Random, 95% CI)	0.0 [-0.11, 0.11]
9 Adverse events (local)	3	94	Risk Difference (M-H, Random, 95% CI)	0.26 [-0.30, 0.82]
10 Adverse events (systemic)	1	20	Risk Difference (M-H, Random, 95% CI)	0.0 [-0.35, 0.35]

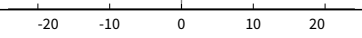
Analysis 4.2. Comparison 4 Dithranol versus placebo, Outcome 2 TSS.

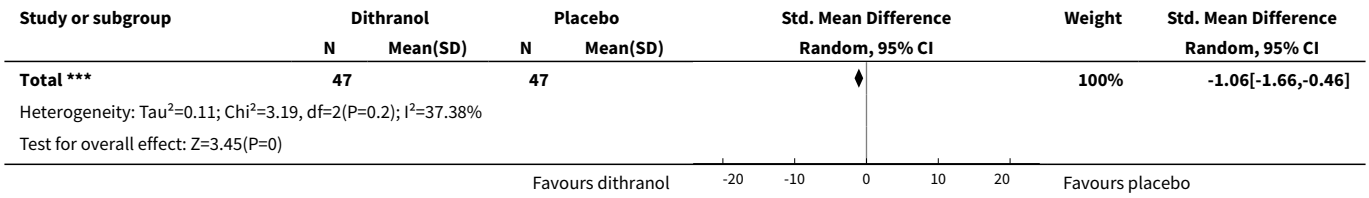
Study or subgroup	Dithranol N	Dithranol Mean(SD)	Placebo N	Placebo Mean(SD)	Std. Mean Difference Random, 95% CI	Weight	Std. Mean Difference Random, 95% CI
Buckley 1978	8	-0.5 (0.3)	8	-0.3 (0.1)		22.71%	-1.16[-2.25,-0.08]
Grattan 1997 (P)	12	1.2 (1.8)	12	4.1 (1.6)		27.32%	-1.66[-2.62,-0.71]
Jekler 1992	27	1 (0.5)	27	1.3 (0.4)		49.98%	-0.69[-1.24,-0.14]
Total * **	**47**		**47**			**100%**	**-1.06[-1.66,-0.46]**
Heterogeneity: Tau^2=0.11; Chi^2=3.19, df=2(P=0.2); I^2=37.38%							
Test for overall effect: Z=3.45(P=0)							



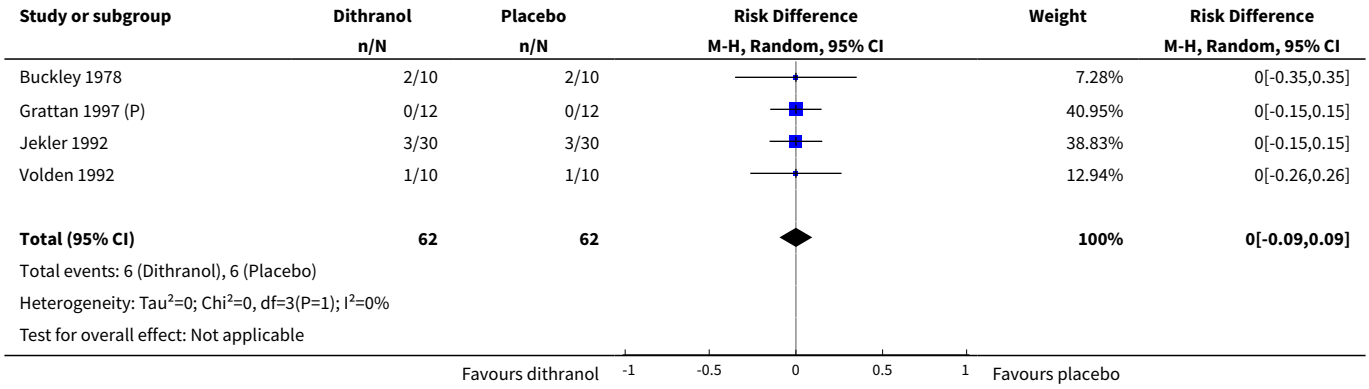
Analysis 4.5. Comparison 4 Dithranol versus placebo, Outcome 5 Combined end point (IAGI/TSS/PASI/PAGI).

Study or subgroup	Dithranol N	Dithranol Mean(SD)	Placebo N	Placebo Mean(SD)	Std. Mean Difference Random, 95% CI	Weight	Std. Mean Difference Random, 95% CI
Buckley 1978	8	-0.5 (0.3)	8	-0.3 (0.1)		22.71%	-1.16[-2.25,-0.08]
Grattan 1997 (P)	12	1.2 (1.8)	12	4.1 (1.6)		27.32%	-1.66[-2.62,-0.71]
Jekler 1992	27	1 (0.5)	27	1.3 (0.4)		49.98%	-0.69[-1.24,-0.14]

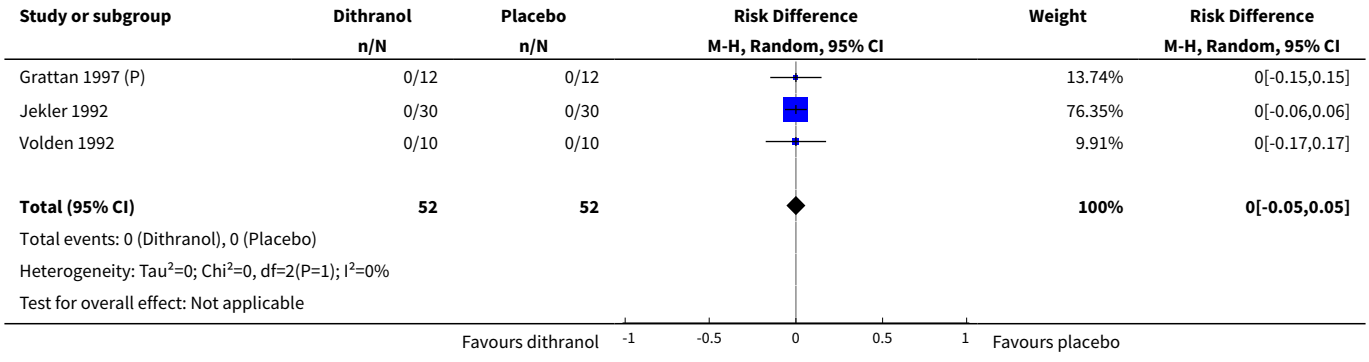




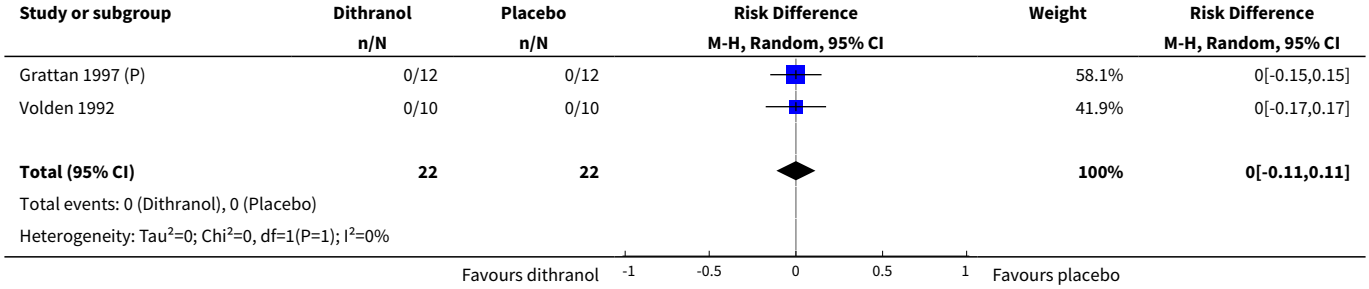
Analysis 4.6. Comparison 4 Dithranol versus placebo, Outcome 6 Total withdrawals.

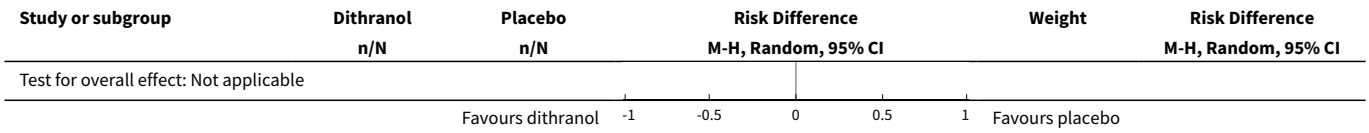


Analysis 4.7. Comparison 4 Dithranol versus placebo, Outcome 7 Withdrawals due to adverse events.

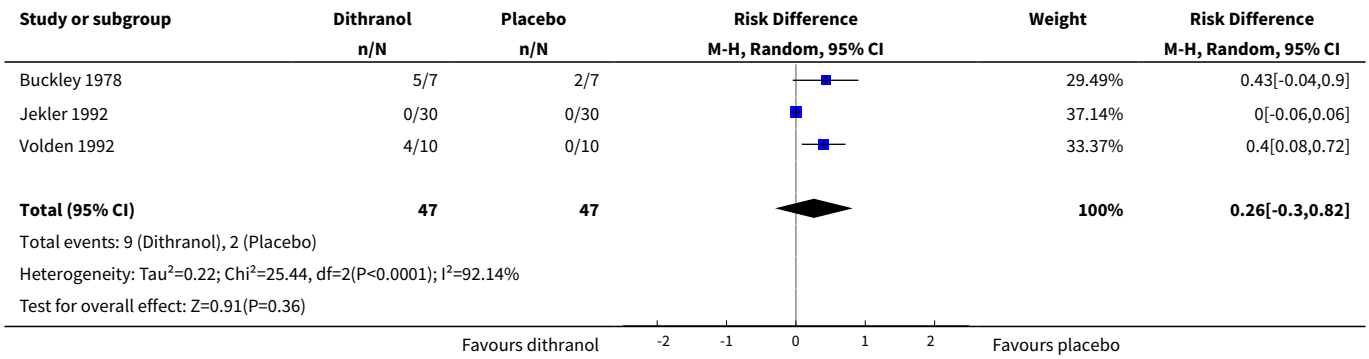


Analysis 4.8. Comparison 4 Dithranol versus placebo, Outcome 8 Withdrawals due to treatment failure.

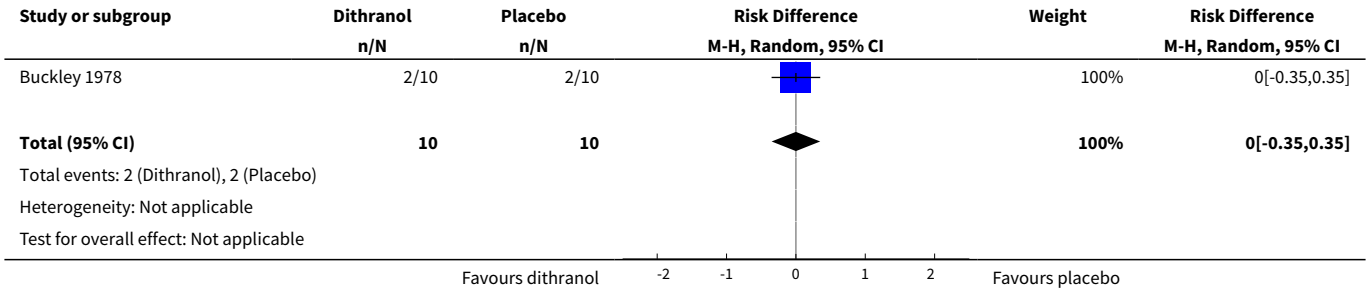




Analysis 4.9. Comparison 4 Dithranol versus placebo, Outcome 9 Adverse events (local).



Analysis 4.10. Comparison 4 Dithranol versus placebo, Outcome 10 Adverse events (systemic).



Comparison 5. Vitamin D combination products versus placebo

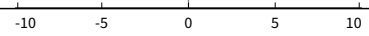
Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 IAGI	5	2264	Std. Mean Difference (IV, Random, 95% CI)	-1.44 [-1.76, -1.12]
1.1 Combination calcipotriol/betamethasone dipropionate, once daily	4	1416	Std. Mean Difference (IV, Random, 95% CI)	-1.21 [-1.50, -0.91]
1.2 Combination calcipotriol/betamethasone dipropionate, twice daily	2	848	Std. Mean Difference (IV, Random, 95% CI)	-1.90 [-2.09, -1.71]
2 TSS	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
2.1 Combination calcipotriol/betamethasone dipropionate, once daily	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
2.2 Combination calcipotriol/betamethasone dipropionate, twice daily	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
3 PASI	5	2263	Std. Mean Difference (IV, Random, 95% CI)	-1.24 [-1.53, -0.95]
3.1 Combination calcipotriol/betamethasone dipropionate, once daily	4	1414	Std. Mean Difference (IV, Random, 95% CI)	-1.14 [-1.57, -0.70]
3.2 Combination calcipotriol/betamethasone dipropionate, twice daily	2	849	Std. Mean Difference (IV, Random, 95% CI)	-1.41 [-1.86, -0.97]
4 PAGI	1		Std. Mean Difference (IV, Random, 95% CI)	Totals not selected
4.1 Combination calcipotriol/betamethasone dipropionate, once daily	1		Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
4.2 Combination calcipotriol/betamethasone dipropionate, twice daily	0		Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
5 Combined end point (IAGI/TSS/PASI/PAGI)	5	2264	Std. Mean Difference (IV, Random, 95% CI)	-1.44 [-1.76, -1.12]
5.1 Combination calcipotriol/betamethasone dipropionate, once daily	4	1416	Std. Mean Difference (IV, Random, 95% CI)	-1.21 [-1.50, -0.91]
5.2 Combination calcipotriol/betamethasone dipropionate, twice daily	2	848	Std. Mean Difference (IV, Random, 95% CI)	-1.90 [-2.09, -1.71]
6 Total withdrawals	5	2340	Risk Difference (M-H, Random, 95% CI)	-0.12 [-0.17, -0.07]
6.1 Combination calcipotriol/betamethasone dipropionate, once daily	4	1483	Risk Difference (M-H, Random, 95% CI)	-0.15 [-0.22, -0.09]
6.2 Combination calcipotriol/betamethasone dipropionate, twice daily	2	857	Risk Difference (M-H, Random, 95% CI)	-0.07 [-0.12, -0.03]
7 Withdrawals due to adverse events	3	1723	Risk Difference (M-H, Random, 95% CI)	-0.07 [-0.11, -0.04]
7.1 Combination calcipotriol/betamethasone dipropionate, once daily	3	1280	Risk Difference (M-H, Random, 95% CI)	-0.07 [-0.11, -0.03]
7.2 Combination calcipotriol/betamethasone dipropionate, twice daily	1	443	Risk Difference (M-H, Random, 95% CI)	-0.10 [-0.14, -0.05]
8 Withdrawals due to treatment failure	1	802	Risk Difference (M-H, Random, 95% CI)	-0.09 [-0.12, -0.06]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
8.1 Combination calcipotriol/betamethasone dipropionate, once daily	1	359	Risk Difference (M-H, Random, 95% CI)	-0.09 [-0.13, -0.05]
8.2 Combination calcipotriol/betamethasone dipropionate, twice daily	1	443	Risk Difference (M-H, Random, 95% CI)	-0.09 [-0.13, -0.05]
9 Adverse events (local)	5	2334	Risk Difference (M-H, Random, 95% CI)	-0.05 [-0.08, -0.02]
9.1 Combination calcipotriol/betamethasone dipropionate, once daily	4	1479	Risk Difference (M-H, Random, 95% CI)	-0.07 [-0.11, -0.02]
9.2 Combination calcipotriol/betamethasone dipropionate, twice daily	2	855	Risk Difference (M-H, Random, 95% CI)	-0.03 [-0.08, 0.01]
10 Adverse events (systemic)	1	412	Risk Difference (M-H, Random, 95% CI)	0.0 [-0.01, 0.01]
10.1 Combination calcipotriol/betamethasone dipropionate, once daily	0	0	Risk Difference (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
10.2 Combination calcipotriol/betamethasone dipropionate, twice daily	1	412	Risk Difference (M-H, Random, 95% CI)	0.0 [-0.01, 0.01]

Analysis 5.1. Comparison 5 Vitamin D combination products versus placebo, Outcome 1 IAGI.

Study or subgroup	Vitamin D combination N	Vitamin D combination Mean(SD)	Placebo N	Placebo Mean(SD)	Std. Mean Difference Random, 95% CI	Weight	Std. Mean Difference Random, 95% CI
5.1.1 Combination calcipotriol/betamethasone dipropionate, once daily							
Fleming 2010 (P)	150	1.9 (1.1)	28	2.6 (0.6)		14.5%	-0.79[-1.2,-0.38]
Guenther 2002 (P)	150	-3.6 (1)	206	-1.9 (1.1)		17.17%	-1.58[-1.82,-1.33]
Kaufmann 2002 (P)	490	1.5 (0.9)	157	2.7 (0.9)		17.76%	-1.31[-1.51,-1.12]
Langley 2011 (P)	171	1.8 (0.9)	64	2.8 (0.8)		16.28%	-1.02[-1.32,-0.72]
Subtotal ***	**961**		**455**			**65.7%**	**-1.21[-1.5,-0.91]**
Heterogeneity: Tau^2=0.07; Chi^2=14.26, df=3(P=0); I^2=78.97%							
Test for overall effect: Z=7.96(P<0.0001)							
5.1.2 Combination calcipotriol/betamethasone dipropionate, twice daily							
Guenther 2002 (P)	234	-3.8 (1)	206	-1.9 (1.1)		17.41%	-1.81[-2.03,-1.59]
Papp 2003 (P)	301	-3.8 (0.9)	107	-1.9 (1.1)		16.89%	-2.01[-2.27,-1.75]
Subtotal ***	**535**		**313**			**34.3%**	**-1.9[-2.09,-1.71]**
Heterogeneity: Tau^2=0; Chi^2=1.27, df=1(P=0.26); I^2=21.54%							
Test for overall effect: Z=19.38(P<0.0001)							
Total ***	**1496**		**768**			**100%**	**-1.44[-1.76,-1.12]**
Heterogeneity: Tau^2=0.14; Chi^2=47.32, df=5(P<0.0001); I^2=89.43%							
Test for overall effect: Z=8.73(P<0.0001)							
Test for subgroup differences: Chi^2=14.67, df=1 (P=0), I^2=93.19%							



Favours vitamin D combination

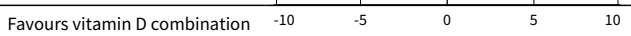
Favours placebo

Analysis 5.3. Comparison 5 Vitamin D combination products versus placebo, Outcome 3 PASI.

Study or subgroup	Vitamin D combination N	Mean(SD)	Placebo N	Mean(SD)	Std. Mean Difference Random, 95% CI	Weight	Std. Mean Difference Random, 95% CI
5.3.1 Combination calcipotriol/betamethasone dipropionate, once daily							
Fleming 2010 (P)	147	3.1 (2.8)	28	5.5 (3.5)		13.92%	-0.82[-1.23,-0.4]
Guenther 2002 (P)	150	3 (2.5)	207	7.7 (5.5)		17.43%	-1.04[-1.27,-0.82]
Kaufmann 2002 (P)	490	-0.7 (0.3)	157	-0.2 (0.3)		17.76%	-1.7[-1.91,-1.5]
Langley 2011 (P)	171	3.6 (3)	64	6.5 (3.6)		16.11%	-0.92[-1.21,-0.62]
Subtotal ***	**958**		**456**			**65.22%**	**-1.14[-1.57,-0.7]**
Heterogeneity: Tau²=0.17; Chi²=31.51, df=3(P<0.0001); I²=90.48%							
Test for overall effect: Z=5.13(P<0.0001)							
5.3.2 Combination calcipotriol/betamethasone dipropionate, twice daily							
Guenther 2002 (P)	234	2.7 (2.5)	207	7.7 (5.5)		17.76%	-1.19[-1.4,-0.99]
Papp 2003 (P)	301	-0.7 (0.3)	107	-0.3 (0.3)		17.02%	-1.65[-1.89,-1.4]
Subtotal ***	**535**		**314**			**34.78%**	**-1.41[-1.86,-0.97]**
Heterogeneity: Tau²=0.09; Chi²=7.65, df=1(P=0.01); I²=86.93%							
Test for overall effect: Z=6.25(P<0.0001)							
Total ***	**1493**		**770**			**100%**	**-1.24[-1.53,-0.95]**
Heterogeneity: Tau²=0.11; Chi²=40.35, df=5(P<0.0001); I²=87.61%							
Test for overall effect: Z=8.39(P<0.0001)							
Test for subgroup differences: Chi²=0.76, df=1 (P=0.38), I²=0%							

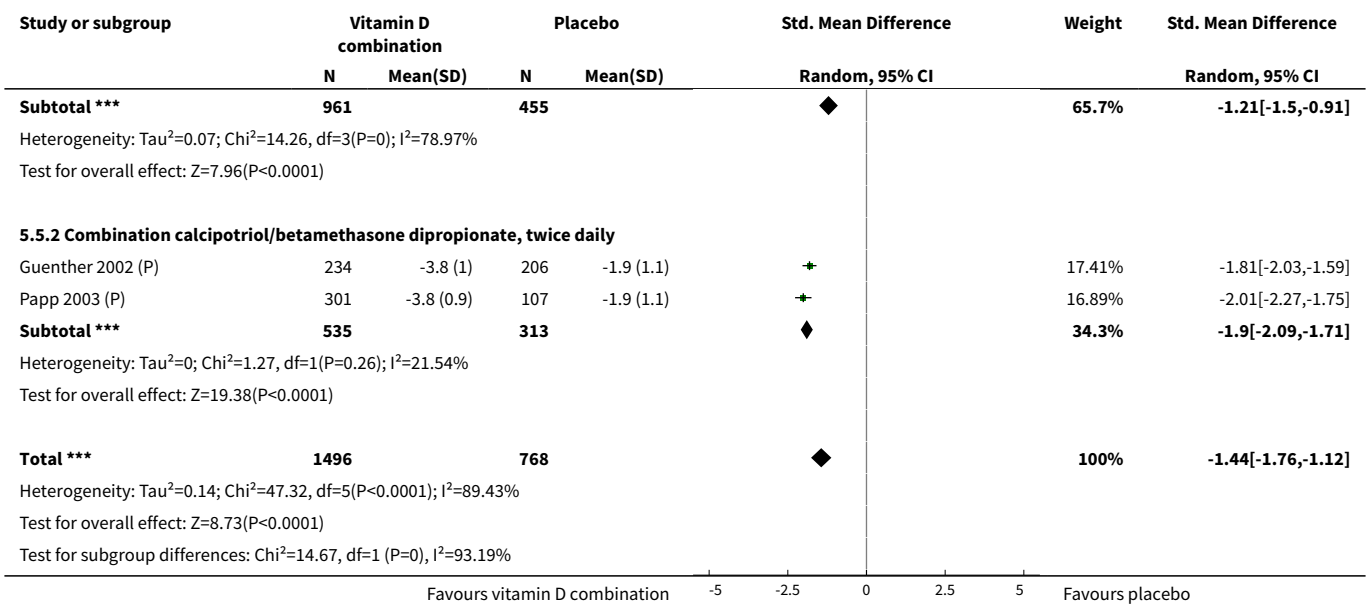
Analysis 5.4. Comparison 5 Vitamin D combination products versus placebo, Outcome 4 PAGI.

Study or subgroup	Vitamin D combination N	Mean(SD)	Placebo N	Mean(SD)	Std. Mean Difference Random, 95% CI	Std. Mean Difference Random, 95% CI
5.4.1 Combination calcipotriol/betamethasone dipropionate, once daily						
Langley 2011 (P)	171	1.8 (0.9)	64	2.5 (1)		-0.69[-0.98,-0.4]
5.4.2 Combination calcipotriol/betamethasone dipropionate, twice daily						

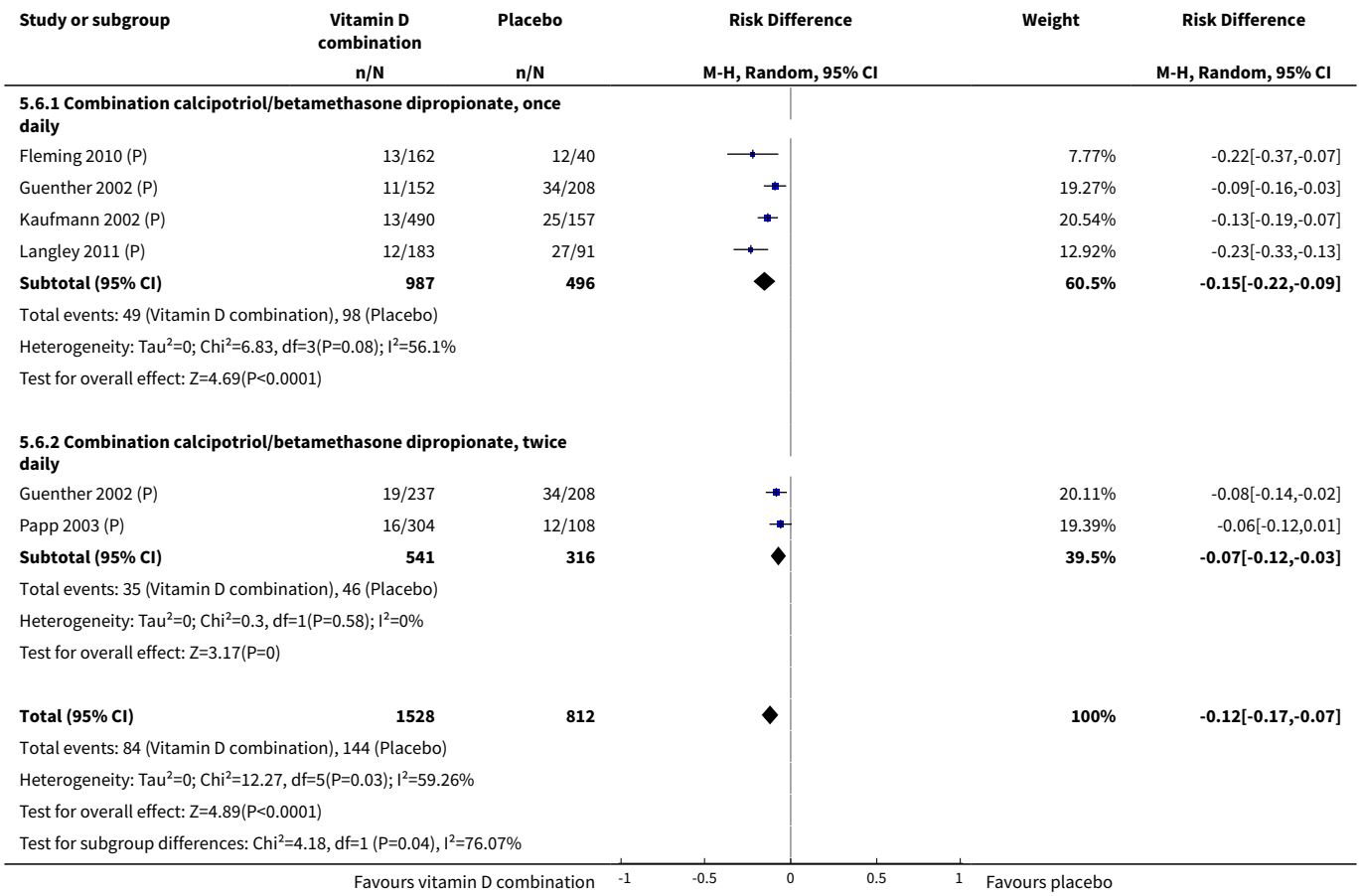


Analysis 5.5. Comparison 5 Vitamin D combination products versus placebo, Outcome 5 Combined end point (IAGI/TSS/PASI/PAGI).

Study or subgroup	Vitamin D combination N	Mean(SD)	Placebo N	Mean(SD)	Std. Mean Difference Random, 95% CI	Weight	Std. Mean Difference Random, 95% CI
5.5.1 Combination calcipotriol/betamethasone dipropionate, once daily							
Fleming 2010 (P)	150	1.9 (1.1)	28	2.6 (0.6)		14.5%	-0.79[-1.2,-0.38]
Guenther 2002 (P)	150	-3.6 (1)	206	-1.9 (1.1)		17.17%	-1.58[-1.82,-1.33]
Kaufmann 2002 (P)	490	1.5 (0.9)	157	2.7 (0.9)		17.76%	-1.31[-1.51,-1.12]
Langley 2011 (P)	171	1.8 (0.9)	64	2.8 (0.8)		16.28%	-1.02[-1.32,-0.72]

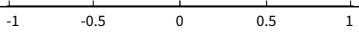


Analysis 5.6. Comparison 5 Vitamin D combination products versus placebo, Outcome 6 Total withdrawals.



Analysis 5.7. Comparison 5 Vitamin D combination products versus placebo, Outcome 7 Withdrawals due to adverse events.

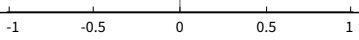
Study or subgroup	Vitamin D combination n/N	Placebo n/N	Risk Difference M-H, Random, 95% CI	Weight	Risk Difference M-H, Random, 95% CI
5.7.1 Combination calcipotriol/betamethasone dipropionate, once daily					
Guenther 2002 (P)	0/151	21/208		25.42%	-0.1[-0.14,-0.06]
Kaufmann 2002 (P)	3/490	12/157		25.45%	-0.07[-0.11,-0.03]
Langley 2011 (P)	3/183	4/91		23.49%	-0.03[-0.07,0.02]
Subtotal (95% CI)	**824**	**456**		**74.36%**	**-0.07[-0.11,-0.03]**
Total events: 6 (Vitamin D combination), 37 (Placebo)					
Heterogeneity: Tau^2=0; Chi^2=5.36, df=2(P=0.07); I^2=62.68%					
Test for overall effect: Z=3.21(P=0)					
5.7.2 Combination calcipotriol/betamethasone dipropionate, twice daily					
Guenther 2002 (P)	1/235	21/208		25.64%	-0.1[-0.14,-0.05]
Subtotal (95% CI)	**235**	**208**		**25.64%**	**-0.1[-0.14,-0.05]**
Total events: 1 (Vitamin D combination), 21 (Placebo)					
Heterogeneity: Not applicable					
Test for overall effect: Z=4.54(P<0.0001)					
Total (95% CI)	**1059**	**664**		**100%**	**-0.07[-0.11,-0.04]**
Total events: 7 (Vitamin D combination), 58 (Placebo)					
Heterogeneity: Tau^2=0; Chi^2=6.67, df=3(P=0.08); I^2=55.03%					
Test for overall effect: Z=4.58(P<0.0001)					
Test for subgroup differences: Chi^2=0.98, df=1 (P=0.32), I^2=0%					



Favours vitamin D combination — Favours placebo

Analysis 5.8. Comparison 5 Vitamin D combination products versus placebo, Outcome 8 Withdrawals due to treatment failure.

Study or subgroup	Vitamin D combination n/N	Placebo n/N	Risk Difference M-H, Random, 95% CI	Weight	Risk Difference M-H, Random, 95% CI
5.8.1 Combination calcipotriol/betamethasone dipropionate, once daily					
Guenther 2002 (P)	0/151	19/208		49.45%	-0.09[-0.13,-0.05]
Subtotal (95% CI)	**151**	**208**		**49.45%**	**-0.09[-0.13,-0.05]**
Total events: 0 (Vitamin D combination), 19 (Placebo)					
Heterogeneity: Not applicable					
Test for overall effect: Z=4.42(P<0.0001)					
5.8.2 Combination calcipotriol/betamethasone dipropionate, twice daily					
Guenther 2002 (P)	1/235	19/208		50.55%	-0.09[-0.13,-0.05]
Subtotal (95% CI)	**235**	**208**		**50.55%**	**-0.09[-0.13,-0.05]**
Total events: 1 (Vitamin D combination), 19 (Placebo)					
Heterogeneity: Not applicable					
Test for overall effect: Z=4.26(P<0.0001)					



Favours vitamin D combination — Favours placebo

Study or subgroup	Vitamin D combination n/N	Placebo n/N	Risk Difference M-H, Random, 95% CI	Weight	Risk Difference M-H, Random, 95% CI
Total (95% CI)	**386**	**416**	◆	**100%**	**-0.09[-0.12,-0.06]**
Total events: 1 (Vitamin D combination), 38 (Placebo)					
Heterogeneity: Tau^2=0; Chi^2=0.02, df=1(P=0.88); I^2=0%					
Test for overall effect: Z=6.14(P<0.0001)					
Test for subgroup differences: Chi^2=0.02, df=1 (P=0.88), I^2=0%					

Favours vitamin D combination -1 -0.5 0 0.5 1 Favours placebo

Analysis 5.9. Comparison 5 Vitamin D combination products versus placebo, Outcome 9 Adverse events (local).

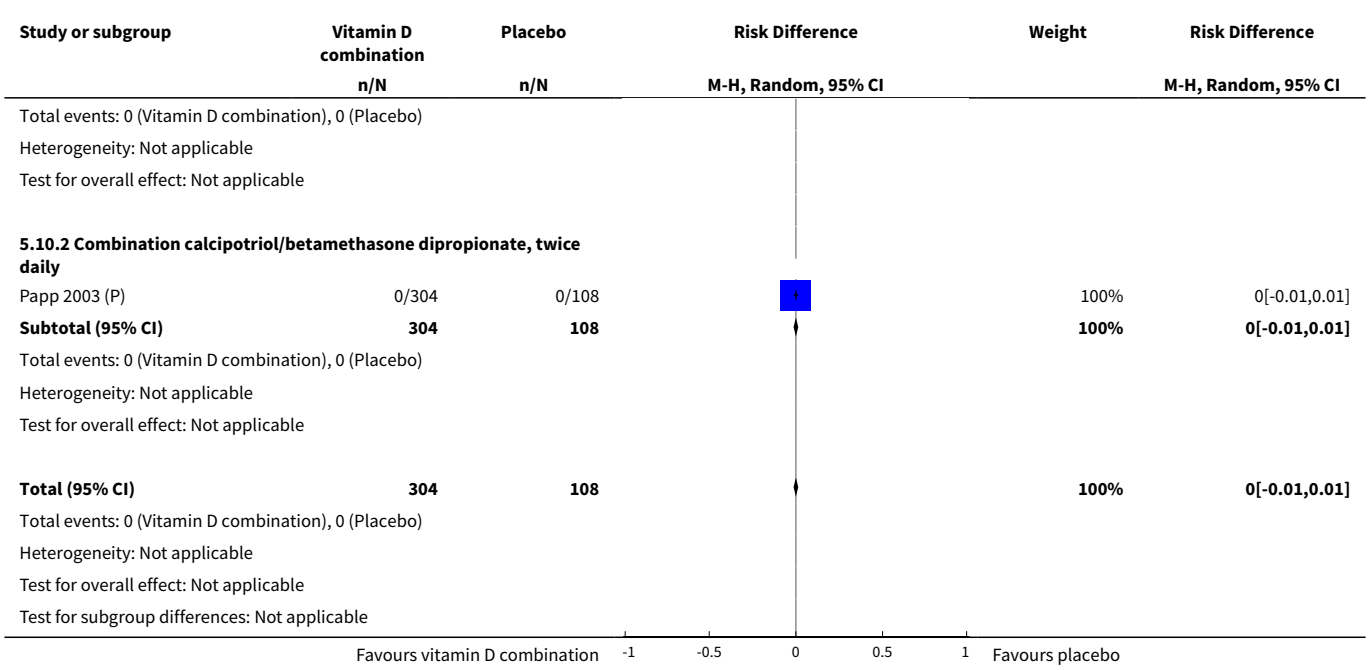
Study or subgroup	Vitamin D combination n/N	Placebo n/N	Risk Difference M-H, Random, 95% CI	Weight	Risk Difference M-H, Random, 95% CI
5.9.1 Combination calcipotriol/betamethasone dipropionate, once daily					
Fleming 2010 (P)	12/160	10/40	▪	4.76%	-0.17[-0.32,-0.03]
Guenther 2002 (P)	15/151	26/208	▪	19.73%	-0.03[-0.09,0.04]
Kaufmann 2002 (P)	29/490	21/157	▪	24.97%	-0.07[-0.13,-0.02]
Langley 2011 (P)	16/182	14/91	▪	12.4%	-0.07[-0.15,0.02]
Subtotal (95% CI)	**983**	**496**	◆	**61.85%**	**-0.07[-0.11,-0.02]**
Total events: 72 (Vitamin D combination), 71 (Placebo)					
Heterogeneity: Tau^2=0; Chi^2=3.92, df=3(P=0.27); I^2=23.51%					
Test for overall effect: Z=2.95(P=0)					
5.9.2 Combination calcipotriol/betamethasone dipropionate, twice daily					
Guenther 2002 (P)	25/235	26/208	▪	23.15%	-0.02[-0.08,0.04]
Papp 2003 (P)	30/304	17/108	▪	14.99%	-0.06[-0.14,0.02]
Subtotal (95% CI)	**539**	**316**	◆	**38.15%**	**-0.03[-0.08,0.01]**
Total events: 55 (Vitamin D combination), 43 (Placebo)					
Heterogeneity: Tau^2=0; Chi^2=0.66, df=1(P=0.42); I^2=0%					
Test for overall effect: Z=1.41(P=0.16)					
Total (95% CI)	**1522**	**812**	◆	**100%**	**-0.05[-0.08,-0.02]**
Total events: 127 (Vitamin D combination), 114 (Placebo)					
Heterogeneity: Tau^2=0; Chi^2=5.56, df=5(P=0.35); I^2=10.02%					
Test for overall effect: Z=3.36(P=0)					
Test for subgroup differences: Chi^2=0.97, df=1 (P=0.32), I^2=0%					

Favours vitamin D combination -1 -0.5 0 0.5 1 Favours placebo

Analysis 5.10. Comparison 5 Vitamin D combination products versus placebo, Outcome 10 Adverse events (systemic).

Study or subgroup	Vitamin D combination n/N	Placebo n/N	Risk Difference M-H, Random, 95% CI	Weight	Risk Difference M-H, Random, 95% CI
5.10.1 Combination calcipotriol/betamethasone dipropionate, once daily					
Subtotal (95% CI)	**0**	**0**			**Not estimable**

Favours vitamin D combination -1 -0.5 0 0.5 1 Favours placebo



Comparison 6. Other treatment versus placebo

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 IAGI	8		Std. Mean Difference (IV, Random, 95% CI)	Totals not selected
1.1 Aloe vera extract 0.5% hydrophilic cream, three times per day	0		Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
1.2 Anti-IL-8 monoclonal antibody cream	1		Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
1.3 Betamethasone 17-valerate 21-acetate plus tretinoin plus salicylic acid	1		Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
1.4 Caffeine (topical) 10%, TD	0		Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
1.5 Calcipotriene 0.005% ointment + nicotinamide 0.05% or 0.1% or 0.7% or 1.4%, twice daily	0		Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
1.6 Dead Sea salts emollient lotion	0		Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
1.7 Fish oil plus occlusion	0		Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1.8 Herbal skin care (Dr Michaels® cleansing gel, ointment and skin conditioner), twice daily	0		Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
1.9 Hexafluoro-1,25-dihydroxyvitamin D3	1		Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
1.10 Indigo naturalis 1.4% ointment	1		Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
1.11 Kukui nut oil, TD	1		Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
1.12 *Mahonia aquifolium* (Reliéva™), twice daily	0		Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
1.13 Methotrexate gel	1		Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
1.14 Mycophenolic acid ointment	0		Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
1.15 NG-monomethyl-L-arginine (L-NMMA) cream	0		Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
1.16 Nicotinamide 1.4%, twice daily	0		Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
1.17 Oleum horwathiensis (Psoricur®)	1		Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
1.18 Omega-3-polyunsaturated fatty acids ointment	0		Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
1.19 Platelet aggregation activating factor (PAF)(Ro 24-0238)	1		Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
1.20 Polymyxin B cream 200,000 U/g	0		Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
1.21 PTH (1-34) in Novasome A® liposomal cream, twice daily	0		Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
1.22 Sirolimus (topical), 2.2% for 6 wks, then 8% for a further 6 wks	0		Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
1.23 Tacrolimus ointment	0		Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
1.24 Tar	0		Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
1.25 Tazarotene	0		Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1.26 Theophylline 1% ointment, twice daily	0		Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
2 TSS	17		Std. Mean Difference (IV, Random, 95% CI)	Subtotals only
2.1 Aloe vera extract 0.5% hydrophilic cream, three times per day	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
2.2 Anti-IL-8 monoclonal antibody cream	1	89	Std. Mean Difference (IV, Random, 95% CI)	-0.70 [-1.13, -0.27]
2.3 Betamethasone 17-valerate 21-acetate plus tretinoin plus salicylic acid	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
2.4 Caffeine (topical) 10%, TD	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
2.5 Calcipotriene 0.005% ointment + nicotinamide 0.05% or 0.1% or 0.7% or 1.4%, twice daily	1	192	Std. Mean Difference (IV, Random, 95% CI)	-0.48 [-0.81, -0.15]
2.6 Dead Sea salts emollient lotion	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
2.7 Fish oil plus occlusion	1	50	Std. Mean Difference (IV, Random, 95% CI)	-1.05 [-1.64, -0.46]
2.8 Herbal skin care (Dr Michaels® cleansing gel, ointment and skin conditioner), twice daily	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
2.9 Hexafluoro-1,25-dihydroxyvitamin D3, twice daily	1	30	Std. Mean Difference (IV, Random, 95% CI)	-1.13 [-1.91, -0.35]
2.10 Indigo naturalis 1.4% ointment	2	88	Std. Mean Difference (IV, Random, 95% CI)	-1.64 [-2.13, -1.15]
2.11 Kukui nut oil, TD	1	24	Std. Mean Difference (IV, Random, 95% CI)	0.33 [-0.48, 1.14]
2.12 *Mahonia aquifolium* (Reliéva™), twice daily	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
2.13 Methotrexate gel	1	82	Std. Mean Difference (IV, Random, 95% CI)	-0.48 [-0.92, -0.04]
2.14 Mycophenolic acid ointment	1	14	Std. Mean Difference (IV, Random, 95% CI)	-1.44 [-2.67, -0.22]
2.15 NG-monomethyl-L-arginine (L-NMMA) cream	1	34	Std. Mean Difference (IV, Random, 95% CI)	0.08 [-0.60, 0.75]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
2.16 Nicotinamide 1.4%, twice daily	1	96	Std. Mean Difference (IV, Random, 95% CI)	-0.20 [-0.60, 0.20]
2.17 Oleum horwathiensis (Psoricur®)	1	42	Std. Mean Difference (IV, Random, 95% CI)	-0.77 [-1.40, -0.14]
2.18 Omega-3-polyunsaturated fatty acids ointment	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
2.19 Platelet aggregation activating factor (PAF)(Ro 24-0238)	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
2.20 Polymyxin B cream 200,000 U/g	1	30	Std. Mean Difference (IV, Random, 95% CI)	0.13 [-0.59, 0.85]
2.21 PTH (1-34) in Novasome A® liposomal cream, twice daily	1	30	Std. Mean Difference (IV, Random, 95% CI)	-2.31 [-3.26, -1.36]
2.22 Sirolimus (topical), 2.2% for 6 wks, then 8% for a further 6 wks	1	44	Std. Mean Difference (IV, Random, 95% CI)	-0.39 [-0.98, 0.21]
2.23 Tacrolimus ointment	1	47	Std. Mean Difference (IV, Random, 95% CI)	0.06 [-0.52, 0.63]
2.24 Tar	1	36	Std. Mean Difference (IV, Random, 95% CI)	-0.45 [-1.11, 0.22]
2.25 Tazarotene	1	318	Std. Mean Difference (IV, Random, 95% CI)	-0.86 [-1.11, -0.62]
2.26 Theophylline 1% ointment, twice daily	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
3 PASI	9		Std. Mean Difference (IV, Random, 95% CI)	Totals not selected
3.1 Aloe vera extract 0.5% hydrophilic cream, three times per day	1		Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
3.2 Anti-IL-8 monoclonal antibody cream	0		Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
3.3 Betamethasone 17-valerate 21-acetate plus tretinoin plus salicylic acid	1		Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
3.4 Caffeine (topical) 10%, TD	1		Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
3.5 Calcipotriene 0.005% ointment + nicotinamide 0.05% or 0.1% or 0.7% or 1.4%, twice daily	0		Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
3.6 Dead Sea salts emollient lotion, 30%	1		Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
3.7 Fish oil plus occlusion	0		Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
3.8 Herbal skin care (Dr Michaels® cleansing gel, ointment and skin conditioner), twice daily	1		Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
3.9 Hexafluoro-1,25-dihydroxyvitamin D3, twice daily	0		Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
3.10 Indigo naturalis 1.4% ointment	0		Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
3.11 Kukui nut oil, twice daily	1		Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
3.12 *Mahonia aquifolium* (Reliéva™), twice daily	1		Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
3.13 Methotrexate gel	1		Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
3.14 Mycophenolic acid ointment	0		Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
3.15 NG-monomethyl-L-arginine (L-NMMA) cream	0		Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
3.16 Nicotinamide 1.4%, twice daily	0		Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
3.17 Oleum horwathiensis (Psoricur®)	0		Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
3.18 Omega-3-polyunsaturated fatty acids ointment	0		Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
3.19 Platelet aggregation activating factor (PAF)(Ro 24-0238)	0		Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
3.20 Polymyxin B cream 200,000 U/g	0		Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
3.21 PTH (1-34) in Novasome A® liposomal cream, twice daily	0		Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
3.22 Sirolimus (topical), 2.2% for 6 wks, then 8% for a further 6 wks	0		Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
3.23 Tacrolimus ointment	0		Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
3.24 Tar	0		Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
3.25 Tazarotene	0		Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
3.26 Theophylline 1% ointment, twice daily	1		Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
4 PAGI	2		Std. Mean Difference (IV, Random, 95% CI)	Totals not selected
4.1 Aloe vera extract 0.5% hydrophilic cream, three times per day	0		Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
4.2 Anti-IL-8 monoclonal antibody cream	0		Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
4.3 Betamethasone 17-valerate 21-acetate plus tretinoin plus salicylic acid	1		Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
4.4 Caffeine (topical) 10%, TD	0		Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
4.5 Calcipotriene 0.005% ointment + nicotinamide 0.05% or 0.1% or 0.7% or 1.4%, twice daily	0		Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
4.6 Dead Sea salts emollient lotion, 30%	0		Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
4.7 Fish oil plus occlusion	0		Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
4.8 Herbal skin care (Dr Michaels® cleansing gel, ointment and skin conditioner), twice daily	0		Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
4.9 Hexafluoro-1,25-dihydroxyvitamin D3, twice daily	0		Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
4.10 Indigo naturalis 1.4% ointment	0		Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
4.11 Kukui nut oil, TD	1		Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
4.12 *Mahonia aquifolium* (Reliéva™), twice daily	0		Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
4.13 Methotrexate gel	0		Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
4.14 Mycophenolic acid ointment	0		Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
4.15 NG-monomethyl-L-arginine (L-NMMA) cream	0		Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
4.16 Nicotinamide 1.4%, twice daily	0		Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
4.17 Oleum horwathiensis (Psoricur®)	0		Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
4.18 Omega-3-polyunsaturated fatty acids ointment	0		Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
4.19 Platelet aggregation activating factor (PAF)(Ro 24-0238)	0		Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
4.20 Polymyxin B cream 200,000 U/g	0		Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
4.21 PTH (1-34) in Novasome A® liposomal cream, twice daily	0		Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
4.22 Sirolimus (topical), 2.2% for 6 wks, then 8% for a further 6 wks	0		Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
4.23 Tacrolimus ointment	0		Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
4.24 Tar	0		Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
4.25 Tazarotene	0		Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
4.26 Theophylline 1% ointment, twice daily	0		Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
5 Combined end point (IAGI/TSS/PASI/PAGI)	26		Std. Mean Difference (IV, Random, 95% CI)	Subtotals only
5.1 Aloe vera extract 0.5% hydrophilic cream, three times per day	1	60	Std. Mean Difference (IV, Random, 95% CI)	-1.58 [-2.16, -0.99]
5.2 Anti-IL-8 monoclonal antibody cream	1	89	Std. Mean Difference (IV, Random, 95% CI)	-0.59 [-1.01, -0.16]
5.3 Betamethasone 17-valerate 21-acetate plus tretinoin plus salicylic acid	1	81	Std. Mean Difference (IV, Random, 95% CI)	-0.76 [-1.21, -0.31]
5.4 Caffeine (topical) 10%, TD	1	78	Std. Mean Difference (IV, Random, 95% CI)	-0.39 [-0.84, 0.06]
5.5 Calcipotriene 0.005% ointment + nicotinamide 0.05% or 0.1% or 0.7% or 1.4%, twice daily	1	192	Std. Mean Difference (IV, Random, 95% CI)	-0.48 [-0.81, -0.15]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
5.6 Dead Sea salts emollient lotion, 30%	1	19	Std. Mean Difference (IV, Random, 95% CI)	0.57 [-0.36, 1.51]
5.7 Fish oil plus occlusion	1	50	Std. Mean Difference (IV, Random, 95% CI)	-1.05 [-1.64, -0.46]
5.8 Herbal skin care (Dr Michaels® cleansing gel, ointment and skin conditioner), twice daily	1	24	Std. Mean Difference (IV, Random, 95% CI)	-2.96 [-4.19, -1.74]
5.9 Hexafluoro-1,25-dihydroxyvitamin D3	1	30	Std. Mean Difference (IV, Random, 95% CI)	-0.62 [-1.35, 0.12]
5.10 Indigo naturalis 1.4% ointment	2	88	Std. Mean Difference (IV, Random, 95% CI)	-2.09 [-2.62, -1.56]
5.11 Kukui nut oil, TD	1	24	Std. Mean Difference (IV, Random, 95% CI)	0.0 [-0.80, 0.80]
5.12 *Mahonia aquifolium* (Reliéva™), twice daily	1	200	Std. Mean Difference (IV, Random, 95% CI)	-0.77 [-1.06, -0.48]
5.13 Methotrexate gel	2	142	Std. Mean Difference (IV, Random, 95% CI)	-1.05 [-2.04, -0.06]
5.14 Mycophenolic acid ointment	1	14	Std. Mean Difference (IV, Random, 95% CI)	-1.44 [-2.67, -0.22]
5.15 NG-monomethyl-L-arginine (L-NMMA) cream	1	34	Std. Mean Difference (IV, Random, 95% CI)	0.08 [-0.60, 0.75]
5.16 Nicotinamide 1.4%, twice daily	1	96	Std. Mean Difference (IV, Random, 95% CI)	-0.20 [-0.60, 0.20]
5.17 Oleum horwathiensis (Psoricur®)	1	42	Std. Mean Difference (IV, Random, 95% CI)	-0.02 [-0.63, 0.58]
5.18 Omega-3-polyunsaturated fatty acids ointment	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
5.19 Platelet aggregation activating factor (PAF)(Ro 24-0238)	1	80	Std. Mean Difference (IV, Random, 95% CI)	-0.07 [-0.50, 0.37]
5.20 Polymyxin B cream 200,000 U/g	1	30	Std. Mean Difference (IV, Random, 95% CI)	0.13 [-0.59, 0.85]
5.21 PTH (1-34) in Novasome A® liposomal cream, twice daily	1	30	Std. Mean Difference (IV, Random, 95% CI)	-2.31 [-3.26, -1.36]
5.22 Sirolimus (topical), 2.2% for 6 wks, then 8% for a further 6 wks	1	44	Std. Mean Difference (IV, Random, 95% CI)	-0.39 [-0.98, 0.21]
5.23 Tacrolimus ointment	1	47	Std. Mean Difference (IV, Random, 95% CI)	0.06 [-0.52, 0.63]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
5.24 Tar	1	36	Std. Mean Difference (IV, Random, 95% CI)	-0.45 [-1.11, 0.22]
5.25 Tazarotene	1	318	Std. Mean Difference (IV, Random, 95% CI)	-0.86 [-1.11, -0.62]
5.26 Theophylline 1% ointment, twice daily	1	22	Std. Mean Difference (IV, Random, 95% CI)	-2.87 [-4.13, -1.62]
6 Total withdrawals	23		Risk Difference (M-H, Random, 95% CI)	Subtotals only
6.1 Aloe vera extract 0.5% hydrophilic cream, three times per day	1	60	Risk Difference (M-H, Random, 95% CI)	0.0 [-0.06, 0.06]
6.2 Anti-IL-8 monoclonal antibody cream	1	96	Risk Difference (M-H, Random, 95% CI)	-0.02 [-0.12, 0.08]
6.3 Betamethasone 17-valerate 21-acetate plus tretinoin plus salicylic acid	1	85	Risk Difference (M-H, Random, 95% CI)	-0.00 [-0.09, 0.09]
6.4 Caffeine (topical) 10%, TD	1	78	Risk Difference (M-H, Random, 95% CI)	0.0 [-0.12, 0.12]
6.5 Calcipotriene 0.005% ointment + nicotinamide 0.05% or 0.1% or 0.7% or 1.4%, twice daily	1	192	Risk Difference (M-H, Random, 95% CI)	0.03 [-0.01, 0.08]
6.6 Dead Sea salts emollient lotion	1	24	Risk Difference (M-H, Random, 95% CI)	0.25 [-0.06, 0.56]
6.7 Fish oil plus occlusion	1	50	Risk Difference (M-H, Random, 95% CI)	0.0 [-0.07, 0.07]
6.8 Herbal skin care (Dr Michaels® cleansing gel, ointment and skin conditioner), twice daily	0	0	Risk Difference (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
6.9 Hexafluoro-1,25-dihydroxyvitamin D3	1	30	Risk Difference (M-H, Random, 95% CI)	0.0 [-0.12, 0.12]
6.10 Indigo naturalis 1.4% ointment	2	112	Risk Difference (M-H, Random, 95% CI)	0.0 [-0.15, 0.15]
6.11 Kukui nut oil, TD	1	30	Risk Difference (M-H, Random, 95% CI)	-0.13 [-0.42, 0.15]
6.12 *Mahonia aquifolium* (Reliéva™), twice daily	1	200	Risk Difference (M-H, Random, 95% CI)	-0.23 [-0.32, -0.14]
6.13 Methotrexate gel	1	60	Risk Difference (M-H, Random, 95% CI)	0.0 [-0.06, 0.06]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
6.14 Mycophenolic acid ointment	1	14	Risk Difference (M-H, Random, 95% CI)	0.0 [-0.24, 0.24]
6.15 NG-monomethyl-L-arginine (L-NMMA) cream	1	34	Risk Difference (M-H, Random, 95% CI)	0.0 [-0.11, 0.11]
6.16 Nicotinamide 1.4%, twice daily	1	96	Risk Difference (M-H, Random, 95% CI)	0.02 [-0.04, 0.08]
6.17 Oleum horwathiensis	1	50	Risk Difference (M-H, Random, 95% CI)	0.16 [-0.04, 0.36]
6.18 Omega-3-polyunsaturated fatty acids ointment	1	146	Risk Difference (M-H, Random, 95% CI)	0.0 [-0.15, 0.15]
6.19 Platelet aggregation activating factor (PAF)(Ro 24-0238)	1	104	Risk Difference (M-H, Random, 95% CI)	0.0 [-0.16, 0.16]
6.20 Polymyxin B cream 200,000 U/g	1	30	Risk Difference (M-H, Random, 95% CI)	0.0 [-0.24, 0.24]
6.21 PTH (1-34) in Novasome A® liposomal cream, twice daily	1	30	Risk Difference (M-H, Random, 95% CI)	0.0 [-0.12, 0.12]
6.22 Sirolimus (topical)	0	0	Risk Difference (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
6.23 Tacrolimus ointment	0	0	Risk Difference (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
6.24 Tar	0	0	Risk Difference (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
6.25 Tazarotene	2	1627	Risk Difference (M-H, Random, 95% CI)	0.04 [-0.01, 0.09]
6.26 Theophylline 1% ointment, twice daily	1	22	Risk Difference (M-H, Random, 95% CI)	0.0 [-0.16, 0.16]
7 Withdrawals due to adverse events	19		Risk Difference (M-H, Random, 95% CI)	Subtotals only
7.1 Aloe vera extract 0.5% hydrophilic cream, three times per day	1	60	Risk Difference (M-H, Random, 95% CI)	0.0 [-0.06, 0.06]
7.2 Anti-IL-8 monoclonal antibody cream	0	0	Risk Difference (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
7.3 Betamethasone 17-valerate 21-acetate plus tretinoin plus salicylic acid	1	85	Risk Difference (M-H, Random, 95% CI)	-0.00 [-0.07, 0.06]
7.4 Caffeine (topical) 10%, TD	1	78	Risk Difference (M-H, Random, 95% CI)	0.0 [-0.05, 0.05]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
7.5 Calcipotriene 0.005% ointment + nicotinamide 0.05% or 0.1% or 0.7% or 1.4%, twice daily	1	192	Risk Difference (M-H, Random, 95% CI)	0.0 [-0.03, 0.03]
7.6 Dead Sea salts emollient lotion	1	24	Risk Difference (M-H, Random, 95% CI)	0.08 [-0.18, 0.35]
7.7 Fish oil plus occlusion	1	50	Risk Difference (M-H, Random, 95% CI)	0.0 [-0.07, 0.07]
7.8 Herbal skin care (Dr Michaels® cleansing gel, ointment and skin conditioner), twice daily	0	0	Risk Difference (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
7.9 Hexafluoro-1,25-dihydroxyvitamin D3	1	30	Risk Difference (M-H, Random, 95% CI)	0.0 [-0.12, 0.12]
7.10 Indigo naturalis 1.4% ointment	2	112	Risk Difference (M-H, Random, 95% CI)	0.0 [-0.04, 0.04]
7.11 Kukui nut oil, TD	1	30	Risk Difference (M-H, Random, 95% CI)	0.0 [-0.12, 0.12]
7.12 *Mahonia aquifolium* (Reliéva™), twice daily	0	0	Risk Difference (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
7.13 Methotrexate gel	1	60	Risk Difference (M-H, Random, 95% CI)	0.0 [-0.06, 0.06]
7.14 Mycophenolic acid ointment	1	14	Risk Difference (M-H, Random, 95% CI)	0.0 [-0.24, 0.24]
7.15 NG-monomethyl-L-arginine (L-NMMA) cream	1	34	Risk Difference (M-H, Random, 95% CI)	0.0 [-0.11, 0.11]
7.16 Nicotinamide 1.4%, twice daily	1	96	Risk Difference (M-H, Random, 95% CI)	0.0 [-0.04, 0.04]
7.17 Oleum horwathiensis	1	50	Risk Difference (M-H, Random, 95% CI)	0.0 [-0.07, 0.07]
7.18 Omega-3-polyunsaturated fatty acids ointment	1	146	Risk Difference (M-H, Random, 95% CI)	0.0 [-0.03, 0.03]
7.19 Platelet aggregation activating factor (PAF)(Ro 24-0238)	0	0	Risk Difference (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
7.20 Polymyxin B cream 200,000 U/g	0	0	Risk Difference (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
7.21 PTH (1-34) in Novasome A® liposomal cream, twice daily	1	30	Risk Difference (M-H, Random, 95% CI)	0.0 [-0.12, 0.12]
7.22 Sirolimus (topical)	0	0	Risk Difference (M-H, Random, 95% CI)	0.0 [0.0, 0.0]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
7.23 Tacrolimus ointment	0	0	Risk Difference (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
7.24 Tar	0	0	Risk Difference (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
7.25 Tazarotene	2	1627	Risk Difference (M-H, Random, 95% CI)	0.07 [0.05, 0.10]
7.26 Theophylline 1% ointment, twice daily	1	22	Risk Difference (M-H, Random, 95% CI)	0.0 [-0.16, 0.16]
8 Withdrawals due to treatment failure	18		Risk Difference (M-H, Random, 95% CI)	Subtotals only
8.1 Aloe vera extract 0.5% hydrophilic cream, three times per day	1	60	Risk Difference (M-H, Random, 95% CI)	0.0 [-0.06, 0.06]
8.2 Anti-IL-8 monoclonal antibody cream	0	0	Risk Difference (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
8.3 Betamethasone 17-valerate 21-acetate plus tretinoin plus salicylic acid	1	85	Risk Difference (M-H, Random, 95% CI)	0.02 [-0.04, 0.08]
8.4 Caffeine (topical) 10%, TD	1	78	Risk Difference (M-H, Random, 95% CI)	0.0 [-0.05, 0.05]
8.5 Calcipotriene 0.005% ointment + nicotinamide 0.05% or 0.1% or 0.7% or 1.4%, twice daily	1	192	Risk Difference (M-H, Random, 95% CI)	0.0 [-0.03, 0.03]
8.6 Dead Sea salts emollient lotion	1	24	Risk Difference (M-H, Random, 95% CI)	0.08 [-0.12, 0.29]
8.7 Fish oil plus occlusion	1	50	Risk Difference (M-H, Random, 95% CI)	0.0 [-0.07, 0.07]
8.8 Herbal skin care (Dr Michaels® cleansing gel, ointment and skin conditioner), twice daily	0	0	Risk Difference (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
8.9 Hexafluoro-1,25-dihydroxyvitamin D3	1	30	Risk Difference (M-H, Random, 95% CI)	0.0 [-0.12, 0.12]
8.10 Indigo naturalis 1.4% ointment	1	28	Risk Difference (M-H, Random, 95% CI)	0.0 [-0.13, 0.13]
8.11 Kukui nut oil, TD	1	30	Risk Difference (M-H, Random, 95% CI)	0.0 [-0.12, 0.12]
8.12 *Mahonia aquifolium* (Reliéva™), twice daily	0	0	Risk Difference (M-H, Random, 95% CI)	0.0 [0.0, 0.0]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
8.13 Methotrexate gel	1	60	Risk Difference (M-H, Random, 95% CI)	0.0 [-0.06, 0.06]
8.14 Mycophenolic acid ointment	1	14	Risk Difference (M-H, Random, 95% CI)	0.0 [-0.24, 0.24]
8.15 NG-monomethyl-L-arginine (L-NMMA) cream	1	34	Risk Difference (M-H, Random, 95% CI)	0.0 [-0.11, 0.11]
8.16 Nicotinamide 1.4%, twice daily	1	96	Risk Difference (M-H, Random, 95% CI)	0.0 [-0.04, 0.04]
8.17 Oleum horwathiensis	1	50	Risk Difference (M-H, Random, 95% CI)	0.0 [-0.07, 0.07]
8.18 Omega-3-polyunsaturated fatty acids ointment	1	146	Risk Difference (M-H, Random, 95% CI)	0.0 [-0.03, 0.03]
8.19 Platelet aggregation activating factor (PAF)(Ro 24-0238)	0	0	Risk Difference (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
8.20 Polymyxin B cream 200,000 U/g	0	0	Risk Difference (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
8.21 PTH (1-34) in Novasome A® liposomal cream, twice daily	1	30	Risk Difference (M-H, Random, 95% CI)	0.0 [-0.12, 0.12]
8.22 Sirolimus (topical)	0	0	Risk Difference (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
8.23 Tacrolimus ointment	0	0	Risk Difference (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
8.24 Tar	0	0	Risk Difference (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
8.25 Tazarotene	2	1627	Risk Difference (M-H, Random, 95% CI)	-0.02 [-0.04, 0.01]
8.26 Theophylline 1% ointment, twice daily	1	22	Risk Difference (M-H, Random, 95% CI)	0.0 [-0.16, 0.16]
9 Adverse events (local)	21		Risk Difference (M-H, Random, 95% CI)	Subtotals only
9.1 Aloe vera extract 0.5% hydrophilic cream, three times per day	1	60	Risk Difference (M-H, Random, 95% CI)	0.0 [-0.06, 0.06]
9.2 Anti-IL-8 monoclonal antibody cream	1	92	Risk Difference (M-H, Random, 95% CI)	0.02 [-0.10, 0.14]
9.3 Betamethasone 17-valerate 21-acetate plus tretinoin plus salicylic acid	1	85	Risk Difference (M-H, Random, 95% CI)	-0.00 [-0.07, 0.06]

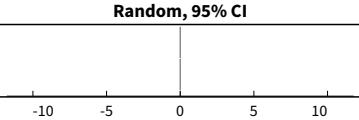
Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
9.4 Caffeine (topical) 10%, TD	1	78	Risk Difference (M-H, Random, 95% CI)	0.05 [-0.03, 0.13]
9.5 Calcipotriene 0.005% ointment + nicotinamide 0.05% or 0.1% or 0.7% or 1.4%, twice daily	1	192	Risk Difference (M-H, Random, 95% CI)	0.13 [-0.02, 0.27]
9.6 Dead Sea salts emollient lotion	1	24	Risk Difference (M-H, Random, 95% CI)	0.08 [-0.18, 0.35]
9.7 Fish oil plus occlusion	1	50	Risk Difference (M-H, Random, 95% CI)	0.04 [-0.06, 0.14]
9.8 Herbal skin care (Dr Michaels® cleansing gel, ointment and skin conditioner), twice daily	1	24	Risk Difference (M-H, Random, 95% CI)	-0.09 [-0.44, 0.27]
9.9 Hexafluoro-1,25-dihydroxyvitamin D3	1	30	Risk Difference (M-H, Random, 95% CI)	0.13 [-0.06, 0.33]
9.10 Indigo naturalis 1.4% ointment	2	88	Risk Difference (M-H, Random, 95% CI)	0.0 [-0.05, 0.05]
9.11 Kukui nut oil, TD	1	30	Risk Difference (M-H, Random, 95% CI)	0.0 [-0.12, 0.12]
9.12 *Mahonia aquifolium* (Reliéva™), twice daily	1	200	Risk Difference (M-H, Random, 95% CI)	-0.02 [-0.06, 0.02]
9.13 Methotrexate gel	1	60	Risk Difference (M-H, Random, 95% CI)	0.0 [-0.06, 0.06]
9.14 Mycophenolic acid ointment	1	14	Risk Difference (M-H, Random, 95% CI)	0.0 [-0.24, 0.24]
9.15 NG-monomethyl-L-arginine (L-NMMA) cream	1	34	Risk Difference (M-H, Random, 95% CI)	0.0 [-0.11, 0.11]
9.16 Nicotinamide 1.4%, twice daily	1	96	Risk Difference (M-H, Random, 95% CI)	0.10 [-0.07, 0.28]
9.17 Oleum horwathiensis	1	50	Risk Difference (M-H, Random, 95% CI)	0.04 [-0.06, 0.14]
9.18 Omega-3-polyunsaturated fatty acids ointment	1	146	Risk Difference (M-H, Random, 95% CI)	0.01 [-0.02, 0.05]
9.19 Platelet aggregation activating factor (PAF)(Ro 24-0238)	1	104	Risk Difference (M-H, Random, 95% CI)	0.0 [-0.19, 0.19]
9.20 Polymyxin B cream 200,000 U/g	0	0	Risk Difference (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
9.21 PTH (1-34) in Novasome A® liposomal cream, twice daily	1	30	Risk Difference (M-H, Random, 95% CI)	0.0 [-0.12, 0.12]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
9.22 Sirolimus (topical)	0	0	Risk Difference (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
9.23 Tacrolimus ointment	0	0	Risk Difference (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
9.24 Tar	0	0	Risk Difference (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
9.25 Tazarotene	0	0	Risk Difference (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
9.26 Theophylline 1% ointment, twice daily	1	22	Risk Difference (M-H, Random, 95% CI)	0.0 [-0.16, 0.16]
10 Adverse events (systemic)	12		Risk Difference (M-H, Random, 95% CI)	Subtotals only
10.1 Aloe vera extract 0.5% hydrophilic cream, three times per day	0	0	Risk Difference (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
10.2 Anti-IL-8 monoclonal antibody cream	0	0	Risk Difference (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
10.3 Betamethasone 17-valerate 21-acetate plus tretinoin plus salicylic acid	1	85	Risk Difference (M-H, Random, 95% CI)	0.0 [-0.04, 0.04]
10.4 Caffeine (topical) 10%, TD	0	0	Risk Difference (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
10.5 Calcipotriene 0.005% ointment + nicotinamide 0.05% or 0.1% or 0.7% or 1.4%, twice daily	0	0	Risk Difference (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
10.6 Dead Sea salts emollient lotion	0	0	Risk Difference (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
10.7 Fish oil plus occlusion	0	0	Risk Difference (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
10.8 Herbal skin care (Dr Michaels® cleansing gel, ointment and skin conditioner), twice daily	0	0	Risk Difference (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
10.9 Hexafluoro-1,25-dihydroxyvitamin D3	1	30	Risk Difference (M-H, Random, 95% CI)	0.0 [-0.12, 0.12]
10.10 Indigo naturalis 1.4% ointment	2	88	Risk Difference (M-H, Random, 95% CI)	0.0 [-0.05, 0.05]
10.11 Kukui nut oil, TD	0	0	Risk Difference (M-H, Random, 95% CI)	0.0 [0.0, 0.0]

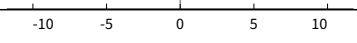
Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
10.12 *Mahonia aquifolium* (Reliéva™), twice daily	0	0	Risk Difference (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
10.13 Methotrexate gel	2	166	Risk Difference (M-H, Random, 95% CI)	0.0 [-0.03, 0.03]
10.14 Mycophenolic acid ointment	0	0	Risk Difference (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
10.15 NG-monomethyl-L-arginine (L-NMMA) cream	1	34	Risk Difference (M-H, Random, 95% CI)	0.0 [-0.11, 0.11]
10.16 Nicotinamide 1.4%, twice daily	0	0	Risk Difference (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
10.17 Oleum horwathiensis	1	50	Risk Difference (M-H, Random, 95% CI)	0.0 [-0.07, 0.07]
10.18 Omega-3-polyunsaturated fatty acids ointment	0	0	Risk Difference (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
10.19 Platelet aggregation activating factor (PAF)(Ro 24-0238)	1	104	Risk Difference (M-H, Random, 95% CI)	0.0 [-0.04, 0.04]
10.20 Polymyxin B cream 200,000 U/g	0	0	Risk Difference (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
10.21 PTH (1-34) in Novasome A® liposomal cream, twice daily	1	30	Risk Difference (M-H, Random, 95% CI)	0.0 [-0.12, 0.12]
10.22 Sirolimus (topical)	0	0	Risk Difference (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
10.23 Tacrolimus ointment	0	0	Risk Difference (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
10.24 Tar	0	0	Risk Difference (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
10.25 Tazarotene	2	414	Risk Difference (M-H, Random, 95% CI)	0.0 [-0.01, 0.01]
10.26 Theophylline 1% ointment, twice daily	0	0	Risk Difference (M-H, Random, 95% CI)	0.0 [0.0, 0.0]

Analysis 6.1. Comparison 6 Other treatment versus placebo, Outcome 1 IAGI.

Study or subgroup	Other treatment N	Other treatment Mean(SD)	Placebo N	Placebo Mean(SD)	Std. Mean Difference Random, 95% CI	Std. Mean Difference Random, 95% CI
6.1.1 Aloe vera extract 0.5% hydrophilic cream, three times per day						



Study or subgroup	Other treatment N	Other treatment Mean(SD)	Placebo N	Placebo Mean(SD)	Std. Mean Difference Random, 95% CI	Std. Mean Difference Random, 95% CI
6.1.2 Anti-IL-8 monoclonal antibody cream						
Jin 2001	45	-1.3 (1)	44	-0.7 (0.8)		-0.59[-1.01,-0.16]
6.1.3 Betamethasone 17-valerate 21-acetate plus tretinoin plus salicylic acid						
Santoianni 2001	42	-2.4 (0.7)	39	-1.8 (0.8)		-0.76[-1.21,-0.31]
6.1.4 Caffeine (topical) 10%, TD						
6.1.5 Calcipotriene 0.005% ointment + nicotinamide 0.05% or 0.1% or 0.7% or 1.4%, twice daily						
6.1.6 Dead Sea salts emollient lotion						
6.1.7 Fish oil plus occlusion						
6.1.8 Herbal skin care (Dr Michaels® cleansing gel, ointment and skin conditioner), twice daily						
6.1.9 Hexafluoro-1,25-dihydroxyvitamin D3						
Durakovic 2001	15	-3.3 (0.7)	15	-2.8 (0.9)		-0.62[-1.35,0.12]
6.1.10 Indigo naturalis 1.4% ointment						
Lin 2008	34	-4.2 (1.2)	34	-1.7 (1.1)		-2.14[-2.74,-1.53]
6.1.11 Kukui nut oil, TD						
Brown 2005	13	1.7 (0.9)	11	1.7 (0.8)		0[-0.8,0.8]
6.1.12 Mahonia aquifolium (Reliéva™), twice daily						
6.1.13 Methotrexate gel						
Sutton 2001	39	-2.3 (1.2)	41	-1.8 (0.7)		-0.56[-1.01,-0.12]
6.1.14 Mycophenolic acid ointment						
6.1.15 NG-monomethyl-L-arginine (L-NMMA) cream						
6.1.16 Nicotinamide 1.4%, twice daily						
6.1.17 Oleum horwathiensis (Psoricur®)						
Lassus 1991	19	-2.2 (1.7)	23	-2.2 (1.7)		-0.02[-0.63,0.58]
6.1.18 Omega-3-polyunsaturated fatty acids ointment						
6.1.19 Platelet aggregation activating factor (PAF)(Ro 24-0238)						
Wolska 1995	40	-3.1 (0.8)	40	-3.1 (0.7)		-0.07[-0.5,0.37]
6.1.20 Polymyxin B cream 200,000 U/g						
6.1.21 PTH (1-34) in Novasome A® liposomal cream, twice daily						
6.1.22 Sirolimus (topical), 2.2% for 6 wks, then 8% for a further 6 wks						

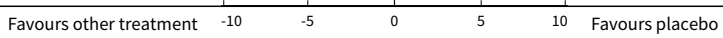


Favours other treatment Favours placebo

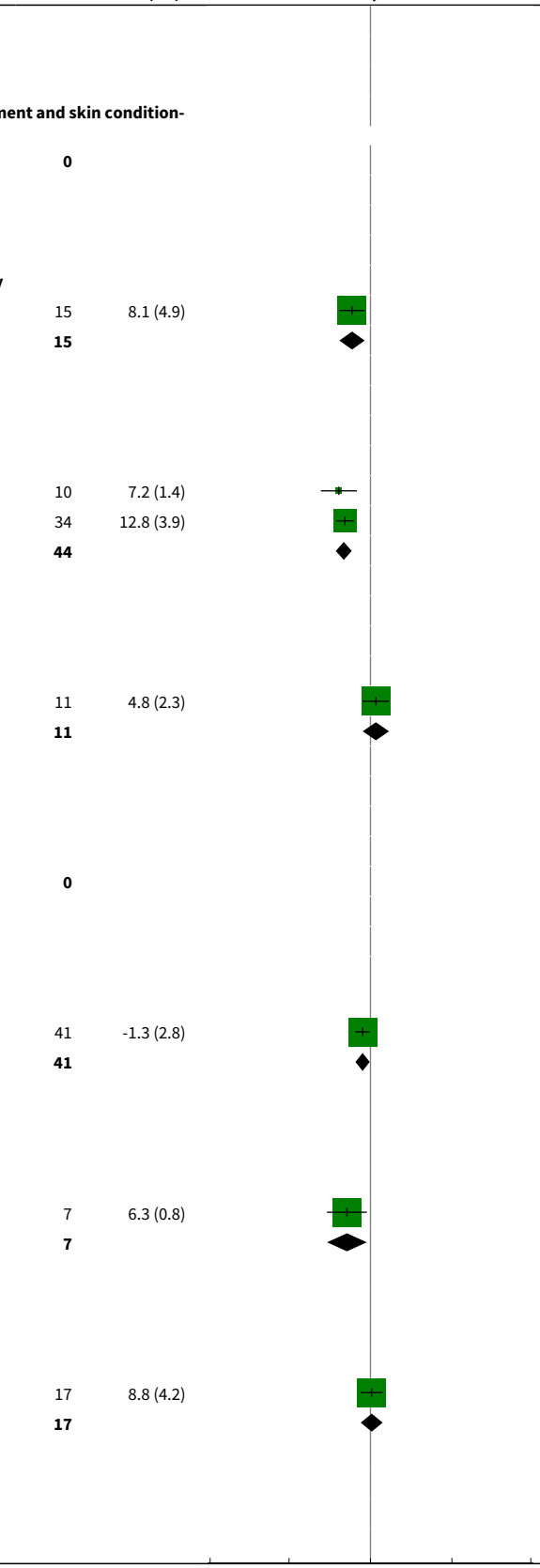
Study or subgroup	Other treatment N	Other treatment Mean(SD)	Placebo N	Placebo Mean(SD)	Std. Mean Difference Random, 95% CI	Std. Mean Difference Random, 95% CI
6.1.23 Tacrolimus ointment						
6.1.24 Tar						
6.1.25 Tazarotene						
6.1.26 Theophylline 1% ointment, twice daily						

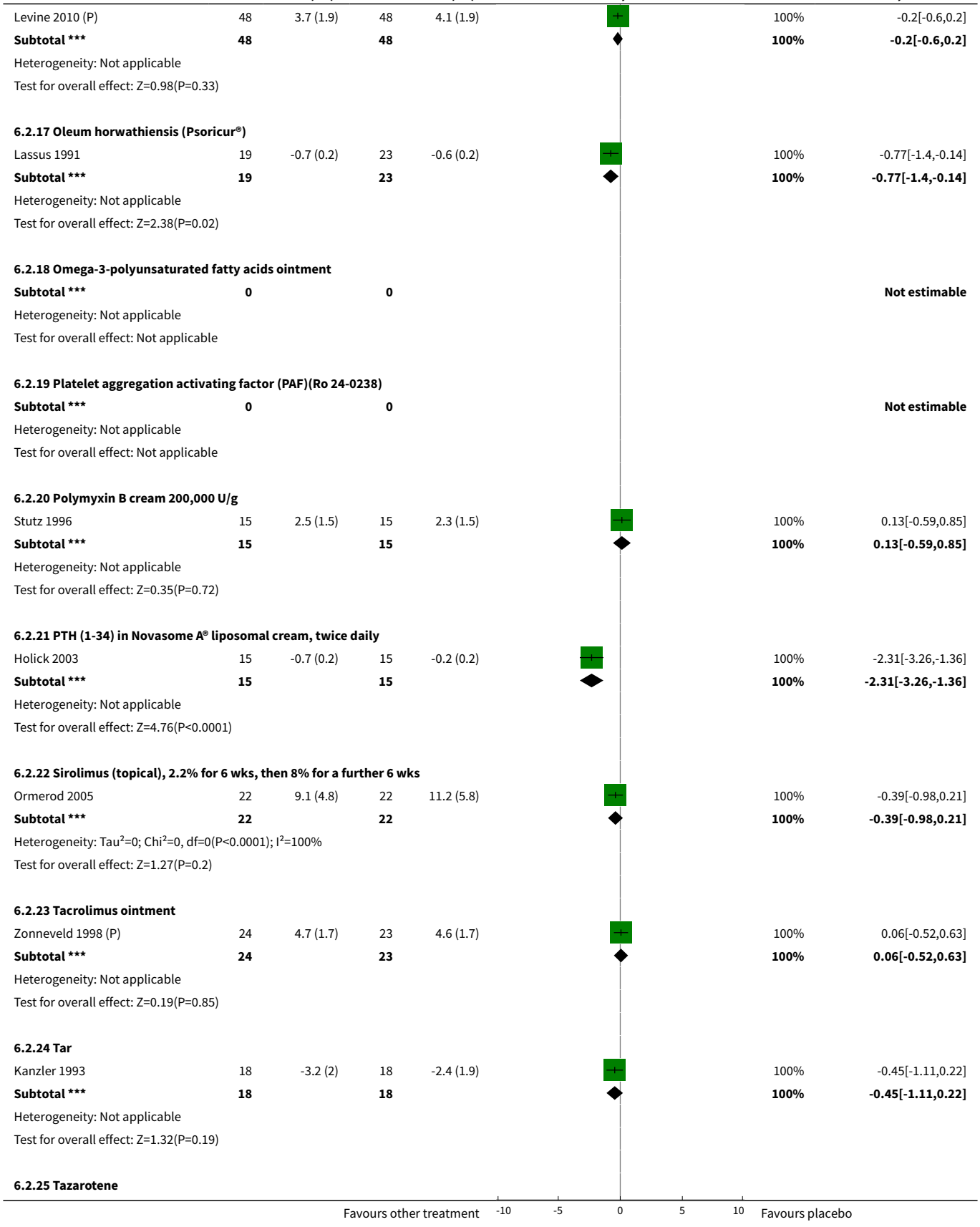
Analysis 6.2. Comparison 6 Other treatment versus placebo, Outcome 2 TSS.

Study or subgroup	Other treatment N	Other treatment Mean(SD)	Placebo N	Placebo Mean(SD)	Std. Mean Difference Random, 95% CI	Weight	Std. Mean Difference Random, 95% CI
6.2.1 Aloe vera extract 0.5% hydrophilic cream, three times per day							
Subtotal ***	**0**		**0**				**Not estimable**
Heterogeneity: Not applicable							
Test for overall effect: Not applicable							
6.2.2 Anti-IL-8 monoclonal antibody cream							
Jin 2001	45	4.8 (3.2)	44	7.1 (3.3)		100%	-0.7[-1.13,-0.27]
Subtotal ***	**45**		**44**			**100%**	**-0.7[-1.13,-0.27]**
Heterogeneity: Not applicable							
Test for overall effect: Z=3.22(P=0)							
6.2.3 Betamethasone 17-valerate 21-acetate plus tretinoin plus salicylic acid							
Subtotal ***	**0**		**0**				**Not estimable**
Heterogeneity: Not applicable							
Test for overall effect: Not applicable							
6.2.4 Caffeine (topical) 10%, TD							
Subtotal ***	**0**		**0**				**Not estimable**
Heterogeneity: Not applicable							
Test for overall effect: Not applicable							
6.2.5 Calcipotriene 0.005% ointment + nicotinamide 0.05% or 0.1% or 0.7% or 1.4%, twice daily							
Levine 2010 (P)	144	3.2 (1.9)	48	4.1 (1.9)		100%	-0.48[-0.81,-0.15]
Subtotal ***	**144**		**48**			**100%**	**-0.48[-0.81,-0.15]**
Heterogeneity: Tau^2=0; Chi^2=0, df=0(P<0.0001); I^2=100%							
Test for overall effect: Z=2.84(P=0)							
6.2.6 Dead Sea salts emollient lotion							
Subtotal ***	**0**		**0**				**Not estimable**
Heterogeneity: Not applicable							
Test for overall effect: Not applicable							
6.2.7 Fish oil plus occlusion							
Escobar 1992	25	1.7 (1.9)	25	3.8 (1.9)		100%	-1.05[-1.64,-0.46]
Subtotal ***	**25**		**25**			**100%**	**-1.05[-1.64,-0.46]**



Study or subgroup	Other treatment N	Other treatment Mean(SD)	Placebo N	Placebo Mean(SD)	Std. Mean Difference Random, 95% CI	Weight	Std. Mean Difference Random, 95% CI
Heterogeneity: Not applicable							
Test for overall effect: Z=3.46(P=0)							
6.2.8 Herbal skin care (Dr Michaels® cleansing gel, ointment and skin conditioner), twice daily							
Subtotal ***	**0**		**0**				**Not estimable**
Heterogeneity: Not applicable							
Test for overall effect: Not applicable							
6.2.9 Hexafluoro-1,25-dihydroxyvitamin D3, twice daily							
Durakovic 2001	15	2.4 (4.9)	15	8.1 (4.9)		100%	-1.13[-1.91,-0.35]
Subtotal ***	**15**		**15**			**100%**	**-1.13[-1.91,-0.35]**
Heterogeneity: Not applicable							
Test for overall effect: Z=2.85(P=0)							
6.2.10 Indigo naturalis 1.4% ointment							
Lin 2007	10	3.7 (2)	10	7.2 (1.4)		19.72%	-1.94[-3.05,-0.84]
Lin 2008	34	6.3 (4.3)	34	12.8 (3.9)		80.28%	-1.57[-2.11,-1.02]
Subtotal ***	**44**		**44**			**100%**	**-1.64[-2.13,-1.15]**
Heterogeneity: Tau^2=0; Chi^2=0.36, df=1(P=0.55); I^2=0%							
Test for overall effect: Z=6.56(P<0.0001)							
6.2.11 Kukui nut oil, TD							
Brown 2005	13	5.6 (2.3)	11	4.8 (2.3)		100%	0.33[-0.48,1.14]
Subtotal ***	**13**		**11**			**100%**	**0.33[-0.48,1.14]**
Heterogeneity: Not applicable							
Test for overall effect: Z=0.81(P=0.42)							
6.2.12 Mahonia aquifolium (Reliéva™), twice daily							
Subtotal ***	**0**		**0**				**Not estimable**
Heterogeneity: Not applicable							
Test for overall effect: Not applicable							
6.2.13 Methotrexate gel							
Sutton 2001	41	-3 (3.9)	41	-1.3 (2.8)		100%	-0.48[-0.92,-0.04]
Subtotal ***	**41**		**41**			**100%**	**-0.48[-0.92,-0.04]**
Heterogeneity: Not applicable							
Test for overall effect: Z=2.16(P=0.03)							
6.2.14 Mycophenolic acid ointment							
Geilen 2000	7	5.1 (0.7)	7	6.3 (0.8)		100%	-1.44[-2.67,-0.22]
Subtotal ***	**7**		**7**			**100%**	**-1.44[-2.67,-0.22]**
Heterogeneity: Not applicable							
Test for overall effect: Z=2.32(P=0.02)							
6.2.15 NG-monomethyl-L-arginine (L-NMMA) cream							
Ormerod 2000	17	9.1 (3.6)	17	8.8 (4.2)		100%	0.08[-0.6,0.75]
Subtotal ***	**17**		**17**			**100%**	**0.08[-0.6,0.75]**
Heterogeneity: Not applicable							
Test for overall effect: Z=0.22(P=0.83)							
6.2.16 Nicotinamide 1.4%, twice daily							





Study or subgroup	Other treatment N	Other treatment Mean(SD)	Placebo N	Placebo Mean(SD)	Std. Mean Difference Random, 95% CI	Weight	Std. Mean Difference Random, 95% CI
Weinstein 1996	211	3.8 (1.7)	107	5.3 (1.7)		100%	-0.86[-1.11,-0.62]
Subtotal ***	**211**		**107**			**100%**	**-0.86[-1.11,-0.62]**
Heterogeneity: Not applicable							
Test for overall effect: Z=7(P<0.0001)							
6.2.26 Theophylline 1% ointment, twice daily							
Subtotal ***	**0**		**0**				**Not estimable**
Heterogeneity: Not applicable							
Test for overall effect: Not applicable							
Test for subgroup differences: Chi^2=63.44, df=1 (P<0.0001), I^2=74.78%							

Favours other treatment -10 -5 0 5 10 Favours placebo

Analysis 6.3. Comparison 6 Other treatment versus placebo, Outcome 3 PASI.

Study or subgroup	Other treatment N	Other treatment Mean(SD)	Placebo N	Placebo Mean(SD)	Std. Mean Difference Random, 95% CI	Std. Mean Difference Random, 95% CI
6.3.1 Aloe vera extract 0.5% hydrophilic cream, three times per day						
Syed 1996	30	2.2 (3.8)	30	8.2 (3.8)		-1.58[-2.16,-0.99]
6.3.2 Anti-IL-8 monoclonal antibody cream						
6.3.3 Betamethasone 17-valerate 21-acetate plus tretinoin plus salicylic acid						
Santoianni 2001	42	2.3 (3)	39	3.9 (3)		-0.54[-0.99,-0.1]
6.3.4 Caffeine (topical) 10%, TD						
Vali 2005	39	4.4 (4.8)	39	6.3 (4.7)		-0.39[-0.84,0.06]
6.3.5 Calcipotriene 0.005% ointment + nicotinamide 0.05% or 0.1% or 0.7% or 1.4%, twice daily						
6.3.6 Dead Sea salts emollient lotion, 30%						
Cheesbrough 1992	8	24 (11.1)	11	18.5 (7.5)		0.57[-0.36,1.51]
6.3.7 Fish oil plus occlusion						
6.3.8 Herbal skin care (Dr Michaels® cleansing gel, ointment and skin conditioner), twice daily						
Maier 2004	14	-0.9 (0.2)	10	-0.2 (0.3)		-2.96[-4.19,-1.74]
6.3.9 Hexafluoro-1,25-dihydroxyvitamin D3, twice daily						
6.3.10 Indigo naturalis 1.4% ointment						
6.3.11 Kukui nut oil, twice daily						
Brown 2005	13	3.9 (3)	11	4 (2.7)		-0.03[-0.84,0.77]
6.3.12 Mahonia aquifolium (Reliéva™), twice daily						
Bernstein 2006	100	-3.4 (3.6)	100	-0.1 (4.9)		-0.77[-1.06,-0.48]
6.3.13 Methotrexate gel						

Favours other treatment -10 -5 0 5 10 Favours placebo

Study or subgroup	Other treatment N	Other treatment Mean(SD)	Placebo N	Placebo Mean(SD)	Std. Mean Difference Random, 95% CI	Std. Mean Difference Random, 95% CI
Syed 2001b	30	2.2 (3.8)	30	8.2 (3.8)		-1.58[-2.16,-0.99]
6.3.14 Mycophenolic acid ointment						
6.3.15 NG-monomethyl-L-arginine (L-NMMA) cream						
6.3.16 Nicotinamide 1.4%, twice daily						
6.3.17 Oleum horwathiensis (Psoricur®)						
6.3.18 Omega-3-polyunsaturated fatty acids ointment						
6.3.19 Platelet aggregation activating factor (PAF)(Ro 24-0238)						
6.3.20 Polymyxin B cream 200,000 U/g						
6.3.21 PTH (1-34) in Novasome A® liposomal cream, twice daily						
6.3.22 Sirolimus (topical), 2.2% for 6 wks, then 8% for a further 6 wks						
6.3.23 Tacrolimus ointment						
6.3.24 Tar						
6.3.25 Tazarotene						
6.3.26 Theophylline 1% ointment, twice daily						
Papakostantinou 2005	11	-0.5 (0.2)	11	-0.1 (0)		-2.87[-4.13,-1.62]

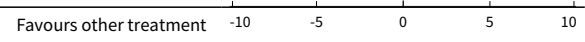
Favours other treatment -10 -5 0 5 10 Favours placebo

Analysis 6.4. Comparison 6 Other treatment versus placebo, Outcome 4 PAGI.

Study or subgroup	Other treatment N	Other treatment Mean(SD)	Placebo N	Placebo Mean(SD)	Std. Mean Difference Random, 95% CI	Std. Mean Difference Random, 95% CI
6.4.1 Aloe vera extract 0.5% hydrophilic cream, three times per day						
6.4.2 Anti-IL-8 monoclonal antibody cream						
6.4.3 Betamethasone 17-valerate 21-acetate plus tretinoin plus salicylic acid						
Santoianni 2001	42	-2.5 (1)	39	-1.7 (1.1)		-0.8[-1.26,-0.35]
6.4.4 Caffeine (topical) 10%, TD						
6.4.5 Calcipotriene 0.005% ointment + nicotinamide 0.05% or 0.1% or 0.7% or 1.4%, twice daily						
6.4.6 Dead Sea salts emollient lotion, 30%						
6.4.7 Fish oil plus occlusion						

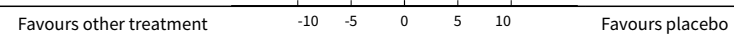
Favours other treatment -10 -5 0 5 10 Favours placebo

Study or subgroup	Other treatment N	Other treatment Mean(SD)	Placebo N	Placebo Mean(SD)	Std. Mean Difference Random, 95% CI	Std. Mean Difference Random, 95% CI
6.4.8 Herbal skin care (Dr Michaels® cleansing gel, ointment and skin conditioner), twice daily						
6.4.9 Hexafluoro-1,25-dihydroxyvitamin D3, twice daily						
6.4.10 Indigo naturalis 1.4% ointment						
6.4.11 Kukui nut oil, TD						
Brown 2005	13	1.7 (0.9)	11	1.7 (0.9)		0[-0.8,0.8]
6.4.12 Mahonia aquifolium (Reliéva™), twice daily						
6.4.13 Methotrexate gel						
6.4.14 Mycophenolic acid ointment						
6.4.15 NG-monomethyl-L-arginine (L-NMMA) cream						
6.4.16 Nicotinamide 1.4%, twice daily						
6.4.17 Oleum horwathiensis (Psoricur®)						
6.4.18 Omega-3-polyunsaturated fatty acids ointment						
6.4.19 Platelet aggregation activating factor (PAF)(Ro 24-0238)						
6.4.20 Polymyxin B cream 200,000 U/g						
6.4.21 PTH (1-34) in Novasome A® liposomal cream, twice daily						
6.4.22 Sirolimus (topical), 2.2% for 6 wks, then 8% for a further 6 wks						
6.4.23 Tacrolimus ointment						
6.4.24 Tar						
6.4.25 Tazarotene						
6.4.26 Theophylline 1% ointment, twice daily						

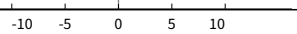


Analysis 6.5. Comparison 6 Other treatment versus placebo, Outcome 5 Combined end point (IAGI/TSS/PASI/PAGI).

Study or subgroup	Other treatment N	Other treatment Mean(SD)	Placebo N	Placebo Mean(SD)	Std. Mean Difference Random, 95% CI	Weight	Std. Mean Difference Random, 95% CI
6.5.1 Aloe vera extract 0.5% hydrophilic cream, three times per day							
Syed 1996	30	2.2 (3.8)	30	8.2 (3.8)		100%	-1.58[-2.16,-0.99]
Subtotal ***	**30**		**30**			**100%**	**-1.58[-2.16,-0.99]**



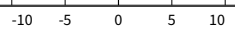
Study or subgroup	Other treatment N	Other treatment Mean(SD)	Placebo N	Placebo Mean(SD)	Std. Mean Difference Random, 95% CI	Weight	Std. Mean Difference Random, 95% CI
Heterogeneity: Not applicable							
Test for overall effect: Z=5.29(P<0.0001)							
6.5.2 Anti-IL-8 monoclonal antibody cream							
Jin 2001	45	-1.3 (1)	44	-0.7 (0.8)		100%	-0.59[-1.01,-0.16]
Subtotal ***	**45**		**44**			**100%**	**-0.59[-1.01,-0.16]**
Heterogeneity: Not applicable							
Test for overall effect: Z=2.72(P=0.01)							
6.5.3 Betamethasone 17-valerate 21-acetate plus tretinoin plus salicylic acid							
Santoianni 2001	42	-2.4 (0.7)	39	-1.8 (0.8)		100%	-0.76[-1.21,-0.31]
Subtotal ***	**42**		**39**			**100%**	**-0.76[-1.21,-0.31]**
Heterogeneity: Not applicable							
Test for overall effect: Z=3.29(P=0)							
6.5.4 Caffeine (topical) 10%, TD							
Vali 2005	39	4.4 (4.8)	39	6.3 (4.7)		100%	-0.39[-0.84,0.06]
Subtotal ***	**39**		**39**			**100%**	**-0.39[-0.84,0.06]**
Heterogeneity: Not applicable							
Test for overall effect: Z=1.71(P=0.09)							
6.5.5 Calcipotriene 0.005% ointment + nicotinamide 0.05% or 0.1% or 0.7% or 1.4%, twice daily							
Levine 2010 (P)	144	3.2 (1.9)	48	4.1 (1.9)		100%	-0.48[-0.81,-0.15]
Subtotal ***	**144**		**48**			**100%**	**-0.48[-0.81,-0.15]**
Heterogeneity: Tau^2=0; Chi^2=0, df=0(P<0.0001); I^2=100%							
Test for overall effect: Z=2.84(P=0)							
6.5.6 Dead Sea salts emollient lotion, 30%							
Cheesbrough 1992	8	24 (11.1)	11	18.5 (7.5)		100%	0.57[-0.36,1.51]
Subtotal ***	**8**		**11**			**100%**	**0.57[-0.36,1.51]**
Heterogeneity: Not applicable							
Test for overall effect: Z=1.2(P=0.23)							
6.5.7 Fish oil plus occlusion							
Escobar 1992	25	1.7 (1.9)	25	3.8 (1.9)		100%	-1.05[-1.64,-0.46]
Subtotal ***	**25**		**25**			**100%**	**-1.05[-1.64,-0.46]**
Heterogeneity: Not applicable							
Test for overall effect: Z=3.46(P=0)							
6.5.8 Herbal skin care (Dr Michaels® cleansing gel, ointment and skin conditioner), twice daily							
Maier 2004	14	-0.9 (0.2)	10	-0.2 (0.3)		100%	-2.96[-4.19,-1.74]
Subtotal ***	**14**		**10**			**100%**	**-2.96[-4.19,-1.74]**
Heterogeneity: Not applicable							
Test for overall effect: Z=4.74(P<0.0001)							
6.5.9 Hexafluoro-1,25-dihydroxyvitamin D3							
Durakovic 2001	15	-3.3 (0.7)	15	-2.8 (0.9)		100%	-0.62[-1.35,0.12]
Subtotal ***	**15**		**15**			**100%**	**-0.62[-1.35,0.12]**
Heterogeneity: Not applicable							
Test for overall effect: Z=1.65(P=0.1)							



Favours other treatment

Favours placebo

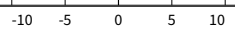
Study or subgroup	Other treatment N	Other treatment Mean(SD)	Placebo N	Placebo Mean(SD)	Std. Mean Difference Random, 95% CI	Weight	Std. Mean Difference Random, 95% CI
6.5.10 Indigo naturalis 1.4% ointment							
Lin 2007	10	3.7 (2)	10	7.2 (1.4)		22.93%	-1.94[-3.05,-0.84]
Lin 2008	34	-4.2 (1.2)	34	-1.7 (1.1)		77.07%	-2.14[-2.74,-1.53]
Subtotal ***	**44**		**44**			**100%**	**-2.09[-2.62,-1.56]**
Heterogeneity: Tau^2=0; Chi^2=0.09, df=1(P=0.76); I^2=0%							
Test for overall effect: Z=7.75(P<0.0001)							
6.5.11 Kukui nut oil, TD							
Brown 2005	13	1.7 (0.9)	11	1.7 (0.8)		100%	0[-0.8,0.8]
Subtotal ***	**13**		**11**			**100%**	**0[-0.8,0.8]**
Heterogeneity: Not applicable							
Test for overall effect: Not applicable							
6.5.12 Mahonia aquifolium (Reliéva™), twice daily							
Bernstein 2006	100	-3.4 (3.6)	100	-0.1 (4.9)		100%	-0.77[-1.06,-0.48]
Subtotal ***	**100**		**100**			**100%**	**-0.77[-1.06,-0.48]**
Heterogeneity: Not applicable							
Test for overall effect: Z=5.25(P<0.0001)							
6.5.13 Methotrexate gel							
Sutton 2001	41	-2.3 (1.2)	41	-1.8 (0.7)		51.85%	-0.56[-1,-0.12]
Syed 2001b	30	2.2 (3.8)	30	8.2 (3.8)		48.15%	-1.58[-2.16,-0.99]
Subtotal ***	**71**		**71**			**100%**	**-1.05[-2.04,-0.06]**
Heterogeneity: Tau^2=0.44; Chi^2=7.37, df=1(P=0.01); I^2=86.44%							
Test for overall effect: Z=2.07(P=0.04)							
6.5.14 Mycophenolic acid ointment							
Geilen 2000	7	5.1 (0.7)	7	6.3 (0.8)		100%	-1.44[-2.67,-0.22]
Subtotal ***	**7**		**7**			**100%**	**-1.44[-2.67,-0.22]**
Heterogeneity: Not applicable							
Test for overall effect: Z=2.32(P=0.02)							
6.5.15 NG-monomethyl-L-arginine (L-NMMA) cream							
Ormerod 2000	17	9.1 (3.6)	17	8.8 (4.2)		100%	0.08[-0.6,0.75]
Subtotal ***	**17**		**17**			**100%**	**0.08[-0.6,0.75]**
Heterogeneity: Not applicable							
Test for overall effect: Z=0.22(P=0.83)							
6.5.16 Nicotinamide 1.4%, twice daily							
Levine 2010 (P)	48	3.7 (1.9)	48	4.1 (1.9)		100%	-0.2[-0.6,0.2]
Subtotal ***	**48**		**48**			**100%**	**-0.2[-0.6,0.2]**
Heterogeneity: Not applicable							
Test for overall effect: Z=0.98(P=0.33)							
6.5.17 Oleum horwathiensis (Psoricur®)							
Lassus 1991	19	-2.2 (1.7)	23	-2.2 (1.7)		100%	-0.02[-0.63,0.58]
Subtotal ***	**19**		**23**			**100%**	**-0.02[-0.63,0.58]**
Heterogeneity: Not applicable							
Test for overall effect: Z=0.07(P=0.94)							
6.5.18 Omega-3-polyunsaturated fatty acids ointment							



Favours other treatment

Favours placebo

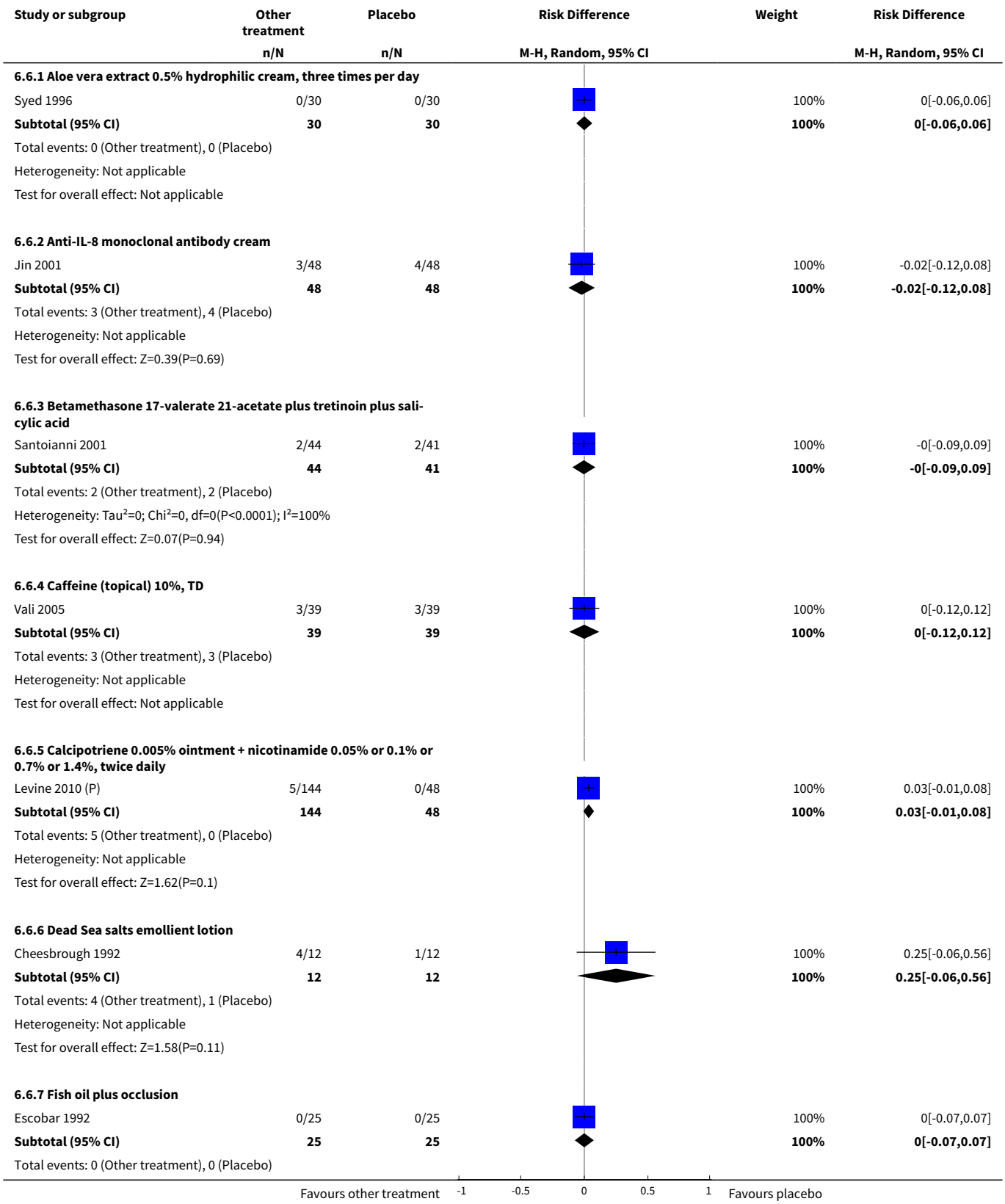
Study or subgroup	Other treatment N	Other treatment Mean(SD)	Placebo N	Placebo Mean(SD)	Std. Mean Difference Random, 95% CI	Weight	Std. Mean Difference Random, 95% CI
Subtotal ***	**0**		**0**				**Not estimable**
Heterogeneity: Not applicable							
Test for overall effect: Not applicable							
6.5.19 Platelet aggregation activating factor (PAF)(Ro 24-0238)							
Wolska 1995	40	-3.1 (0.8)	40	-3.1 (0.7)		100%	-0.07[-0.5,0.37]
Subtotal ***	**40**		**40**			**100%**	**-0.07[-0.5,0.37]**
Heterogeneity: Not applicable							
Test for overall effect: Z=0.29(P=0.77)							
6.5.20 Polymyxin B cream 200,000 U/g							
Stutz 1996	15	2.5 (1.5)	15	2.3 (1.5)		100%	0.13[-0.59,0.85]
Subtotal ***	**15**		**15**			**100%**	**0.13[-0.59,0.85]**
Heterogeneity: Not applicable							
Test for overall effect: Z=0.35(P=0.72)							
6.5.21 PTH (1-34) in Novasome A® liposomal cream, twice daily							
Holick 2003	15	-0.7 (0.2)	15	-0.2 (0.2)		100%	-2.31[-3.26,-1.36]
Subtotal ***	**15**		**15**			**100%**	**-2.31[-3.26,-1.36]**
Heterogeneity: Not applicable							
Test for overall effect: Z=4.76(P<0.0001)							
6.5.22 Sirolimus (topical), 2.2% for 6 wks, then 8% for a further 6 wks							
Ormerod 2005	22	9.1 (4.8)	22	11.2 (5.8)		100%	-0.39[-0.98,0.21]
Subtotal ***	**22**		**22**			**100%**	**-0.39[-0.98,0.21]**
Heterogeneity: Tau^2=0; Chi^2=0, df=0(P<0.0001); I^2=100%							
Test for overall effect: Z=1.27(P=0.2)							
6.5.23 Tacrolimus ointment							
Zonneveld 1998 (P)	24	4.7 (1.7)	23	4.6 (1.7)		100%	0.06[-0.52,0.63]
Subtotal ***	**24**		**23**			**100%**	**0.06[-0.52,0.63]**
Heterogeneity: Not applicable							
Test for overall effect: Z=0.19(P=0.85)							
6.5.24 Tar							
Kanzler 1993	18	-3.2 (2)	18	-2.4 (1.9)		100%	-0.45[-1.11,0.22]
Subtotal ***	**18**		**18**			**100%**	**-0.45[-1.11,0.22]**
Heterogeneity: Not applicable							
Test for overall effect: Z=1.32(P=0.19)							
6.5.25 Tazarotene							
Weinstein 1996	211	3.8 (1.7)	107	5.3 (1.7)		100%	-0.86[-1.11,-0.62]
Subtotal ***	**211**		**107**			**100%**	**-0.86[-1.11,-0.62]**
Heterogeneity: Not applicable							
Test for overall effect: Z=7(P<0.0001)							
6.5.26 Theophylline 1% ointment, twice daily							
Papakostantinou 2005	11	-0.5 (0.2)	11	-0.1 (0)		100%	-2.87[-4.13,-1.62]
Subtotal ***	**11**		**11**			**100%**	**-2.87[-4.13,-1.62]**
Heterogeneity: Not applicable							
Test for overall effect: Z=4.48(P<0.0001)							
Test for subgroup differences: Chi^2=126.78, df=1 (P<0.0001), I^2=81.07%							

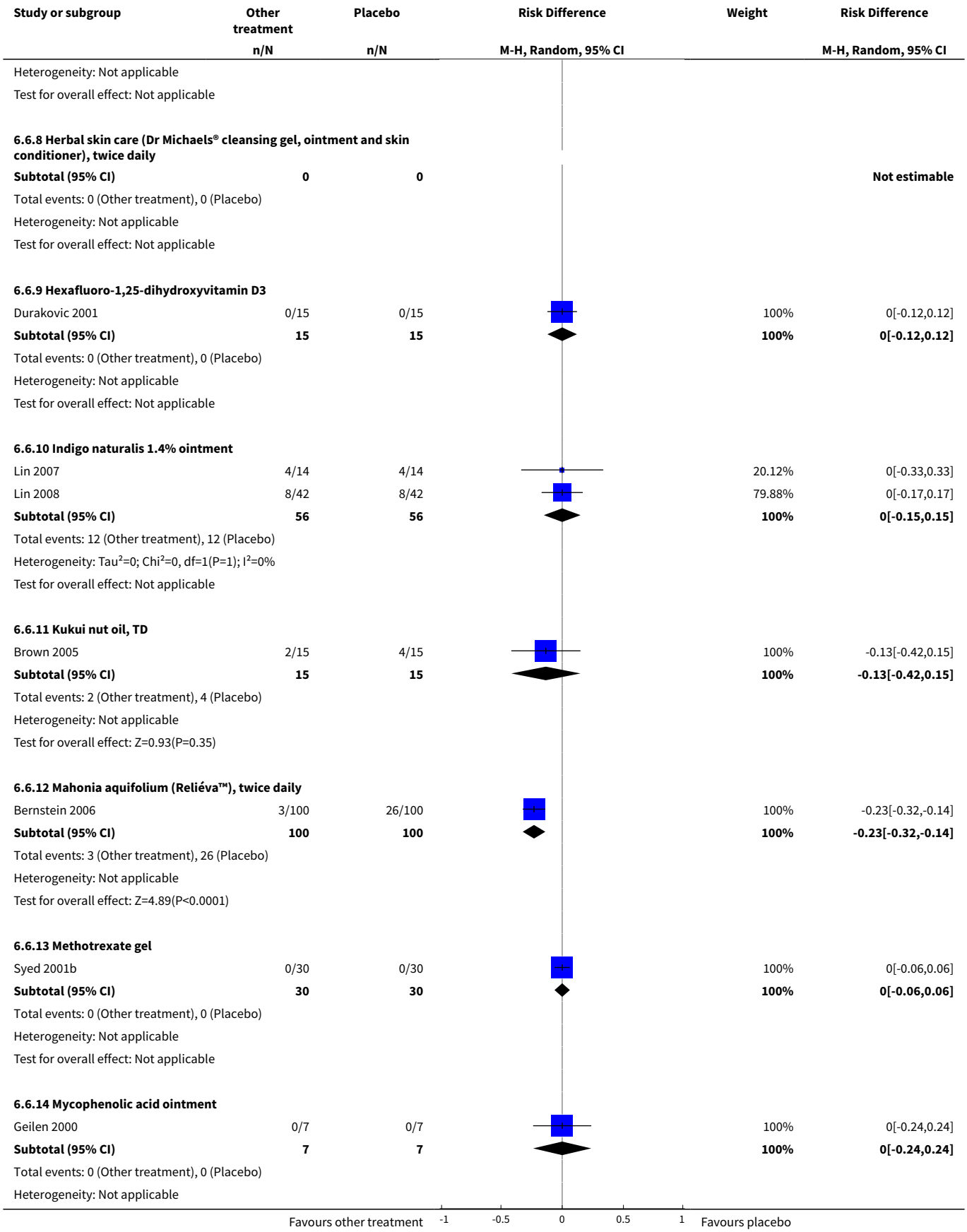


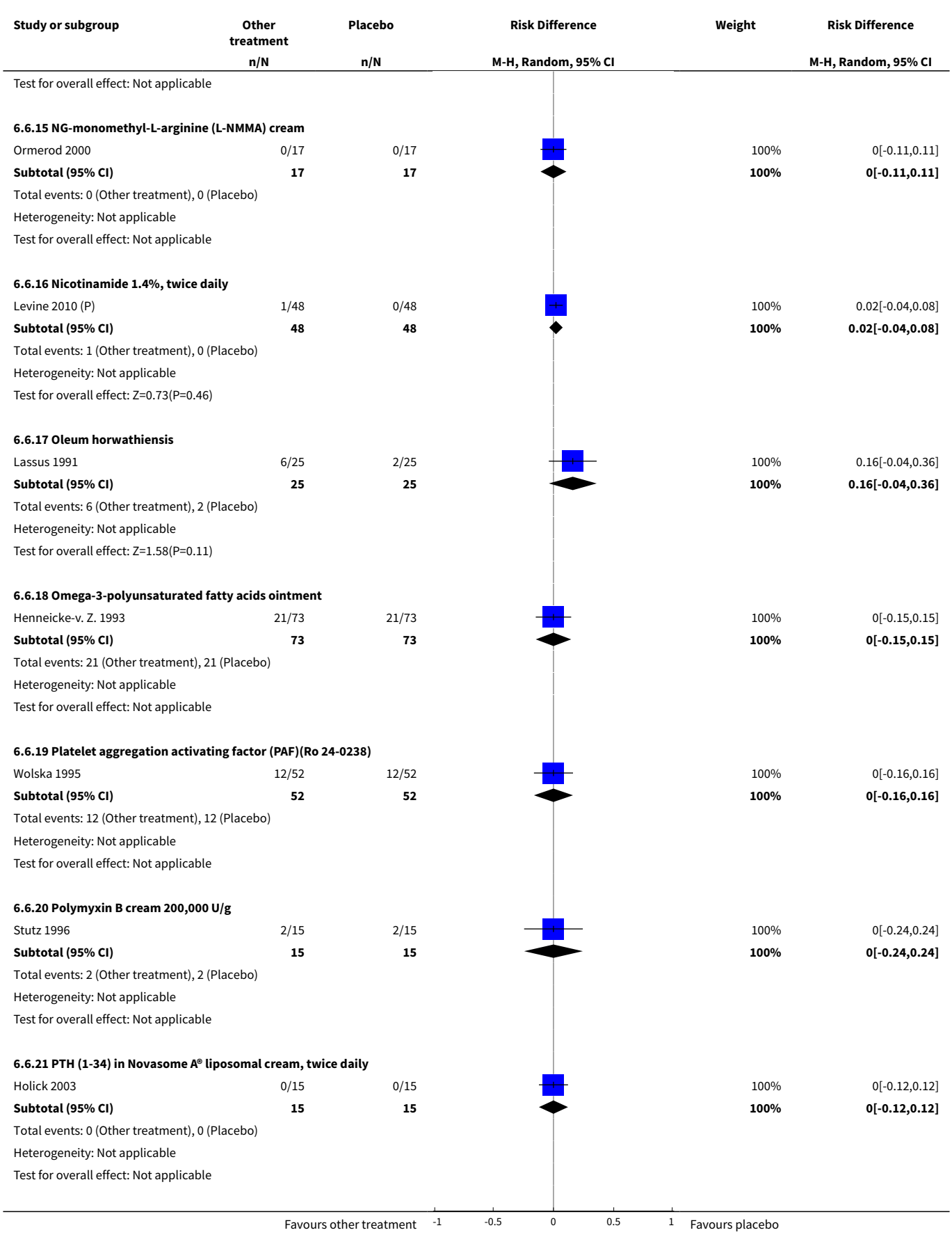
Favours other treatment

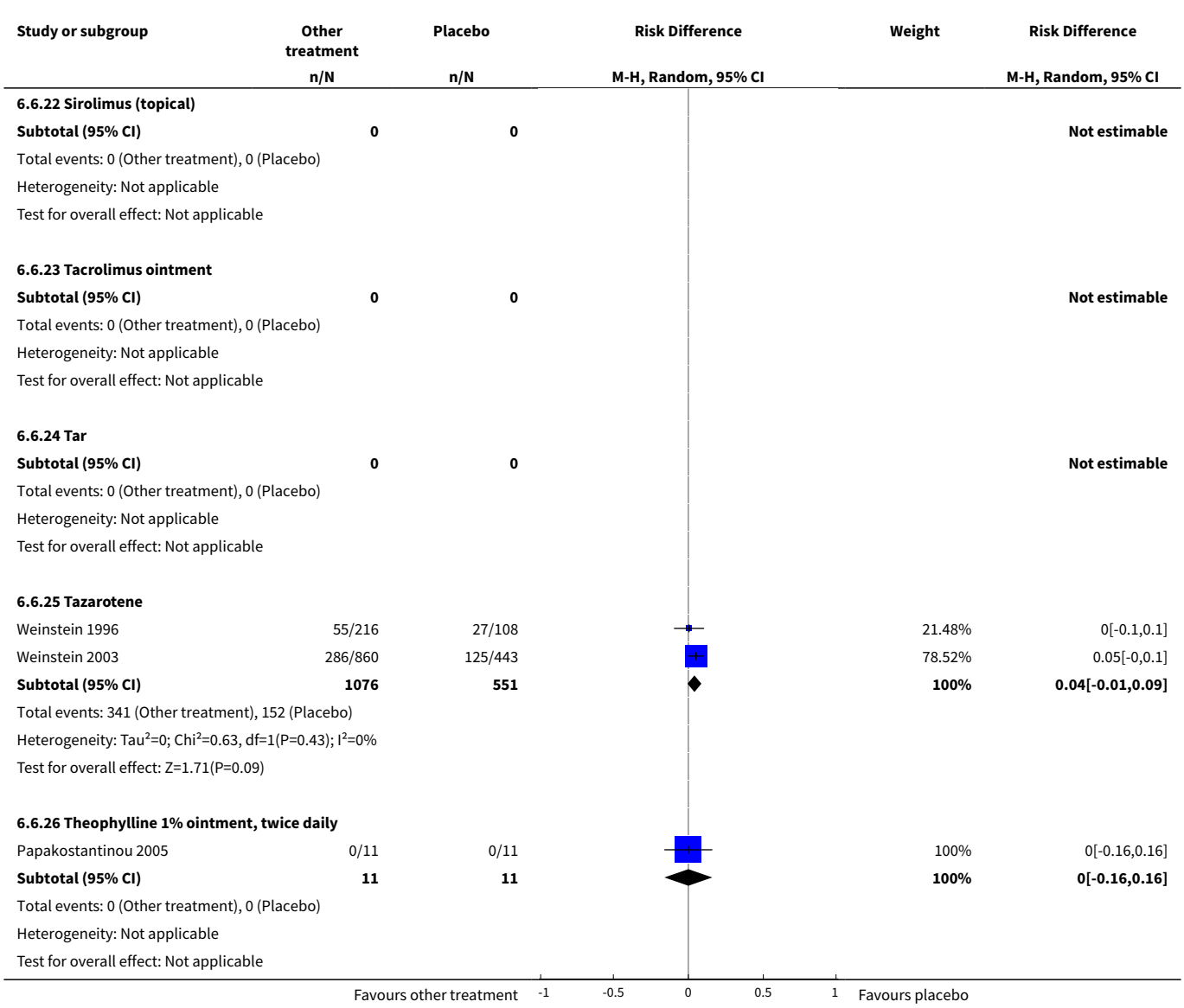
Favours placebo

Analysis 6.6. Comparison 6 Other treatment versus placebo, Outcome 6 Total withdrawals.

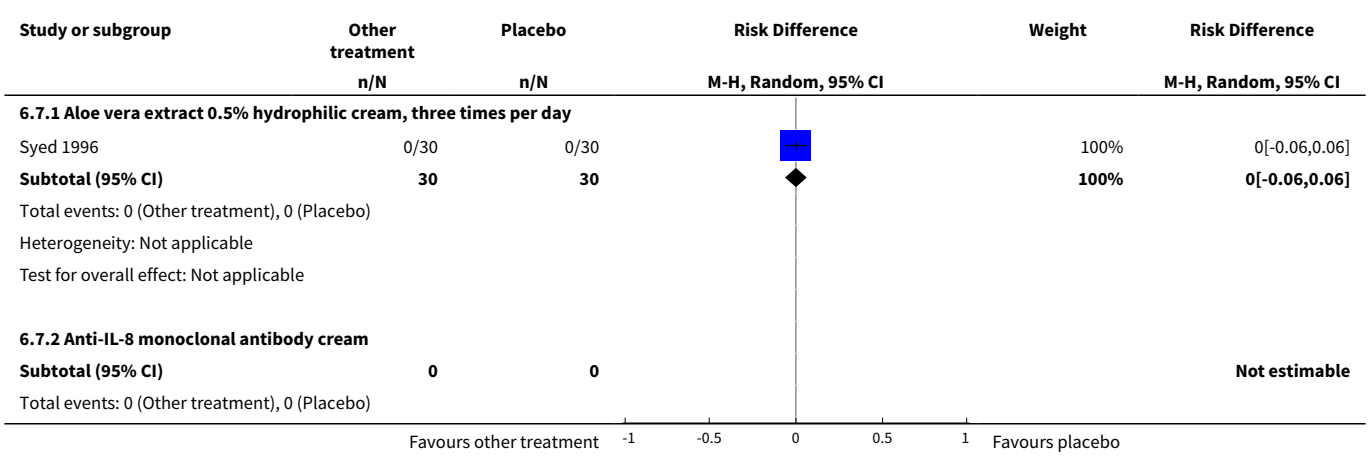


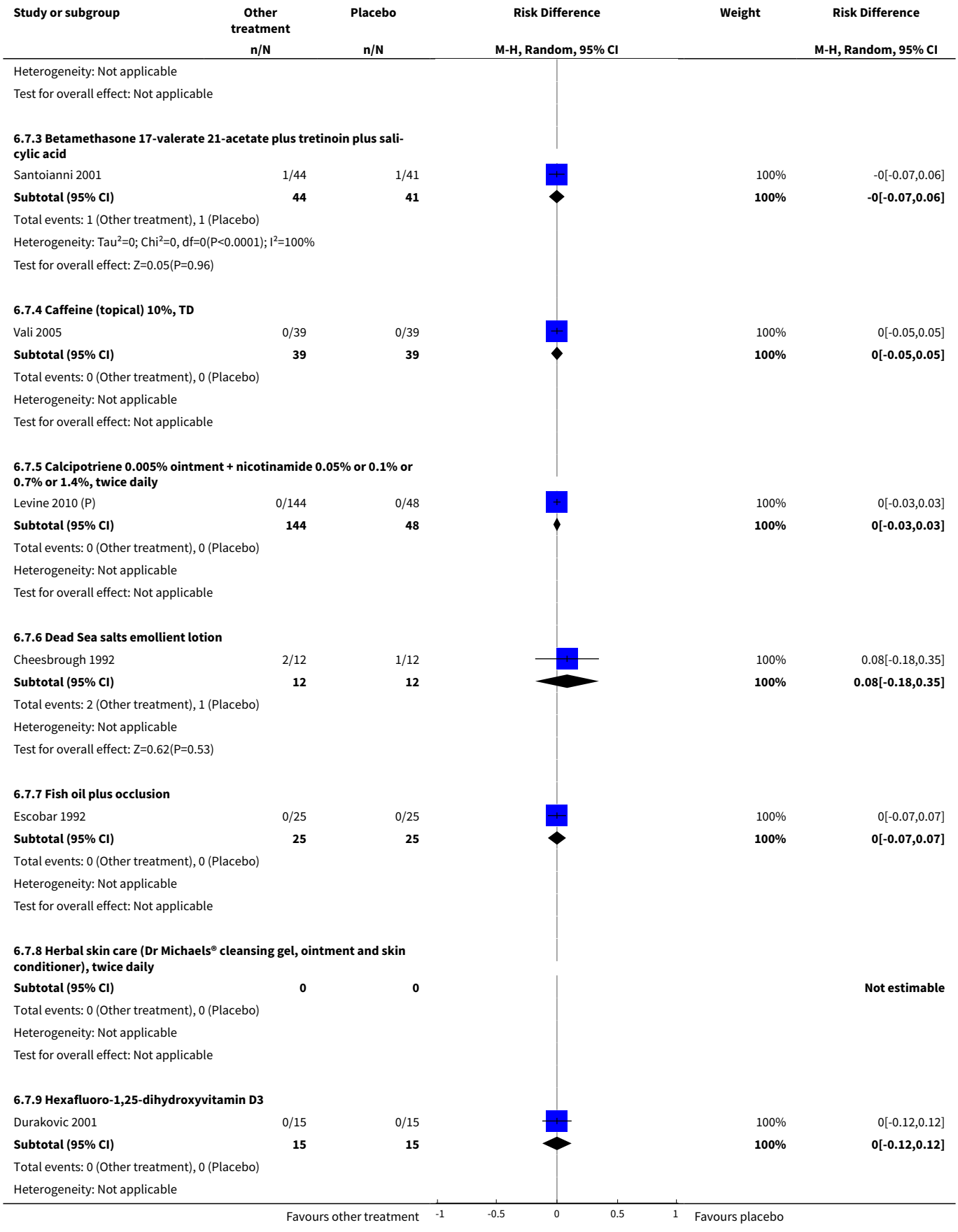




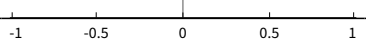


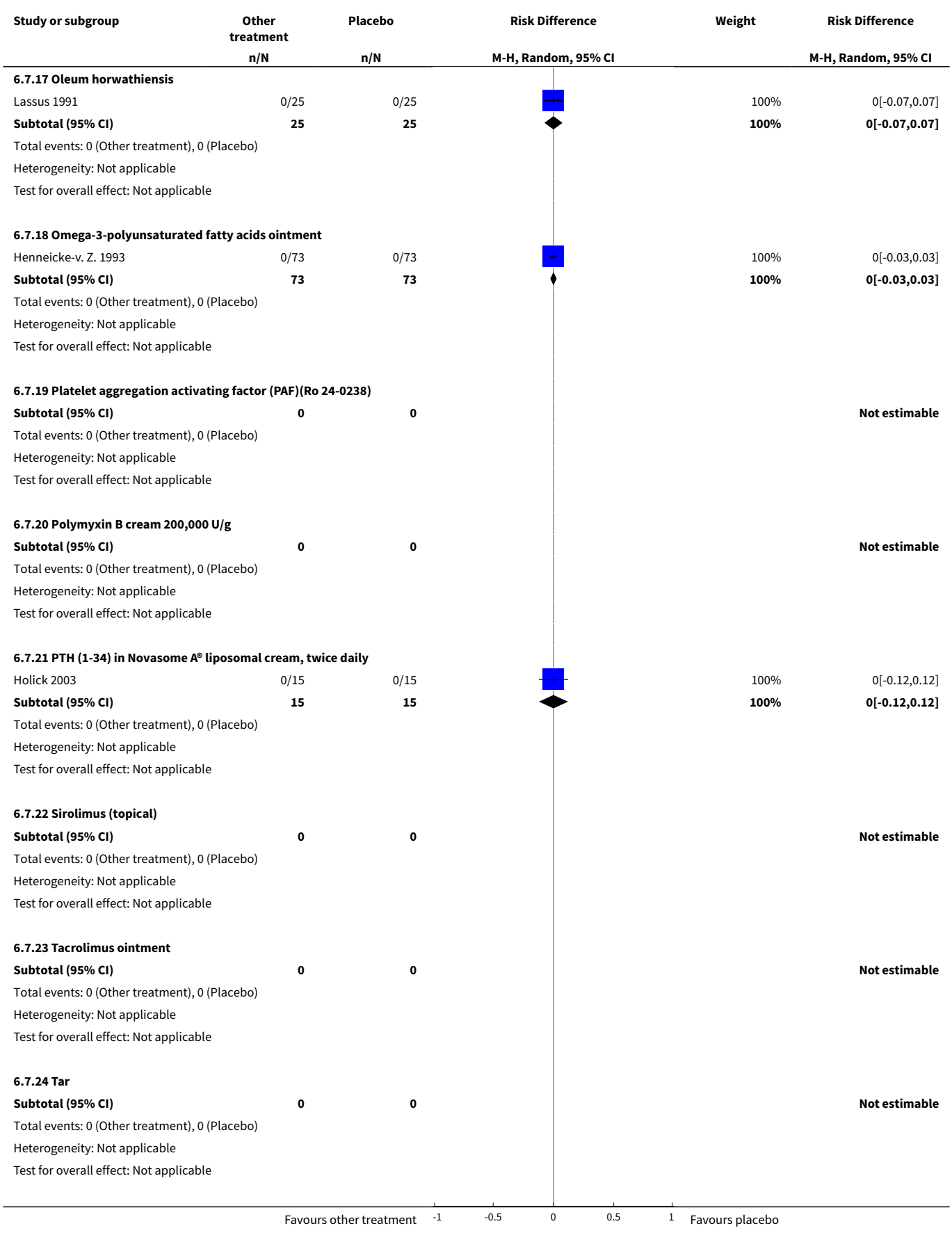
Analysis 6.7. Comparison 6 Other treatment versus placebo, Outcome 7 Withdrawals due to adverse events.

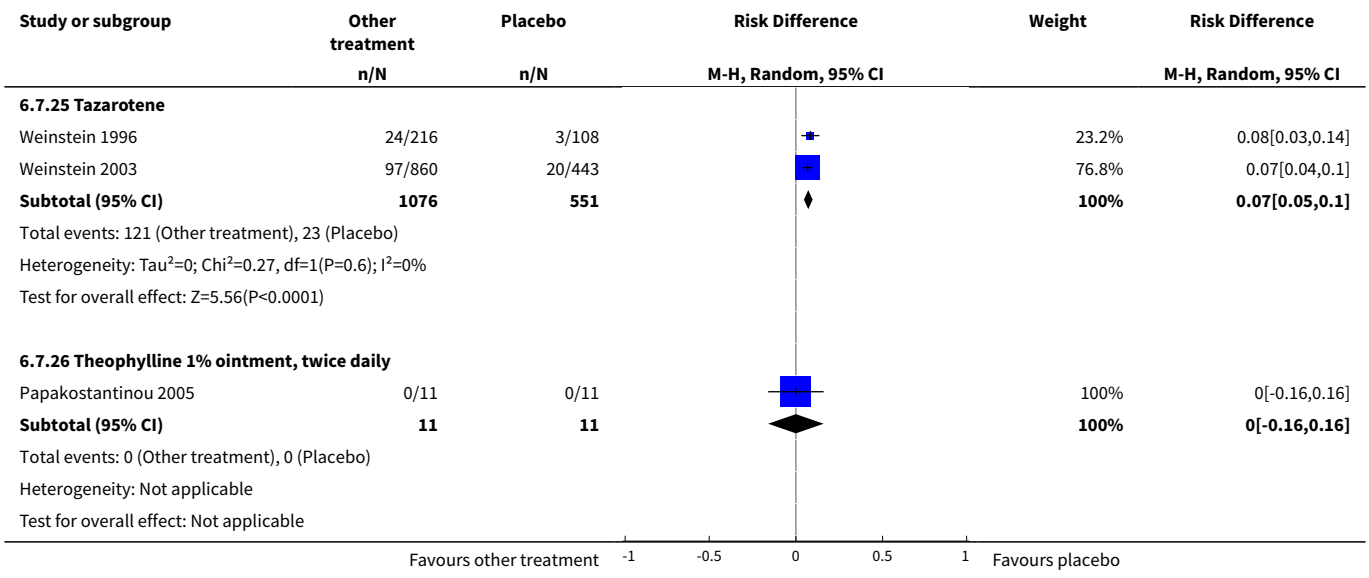




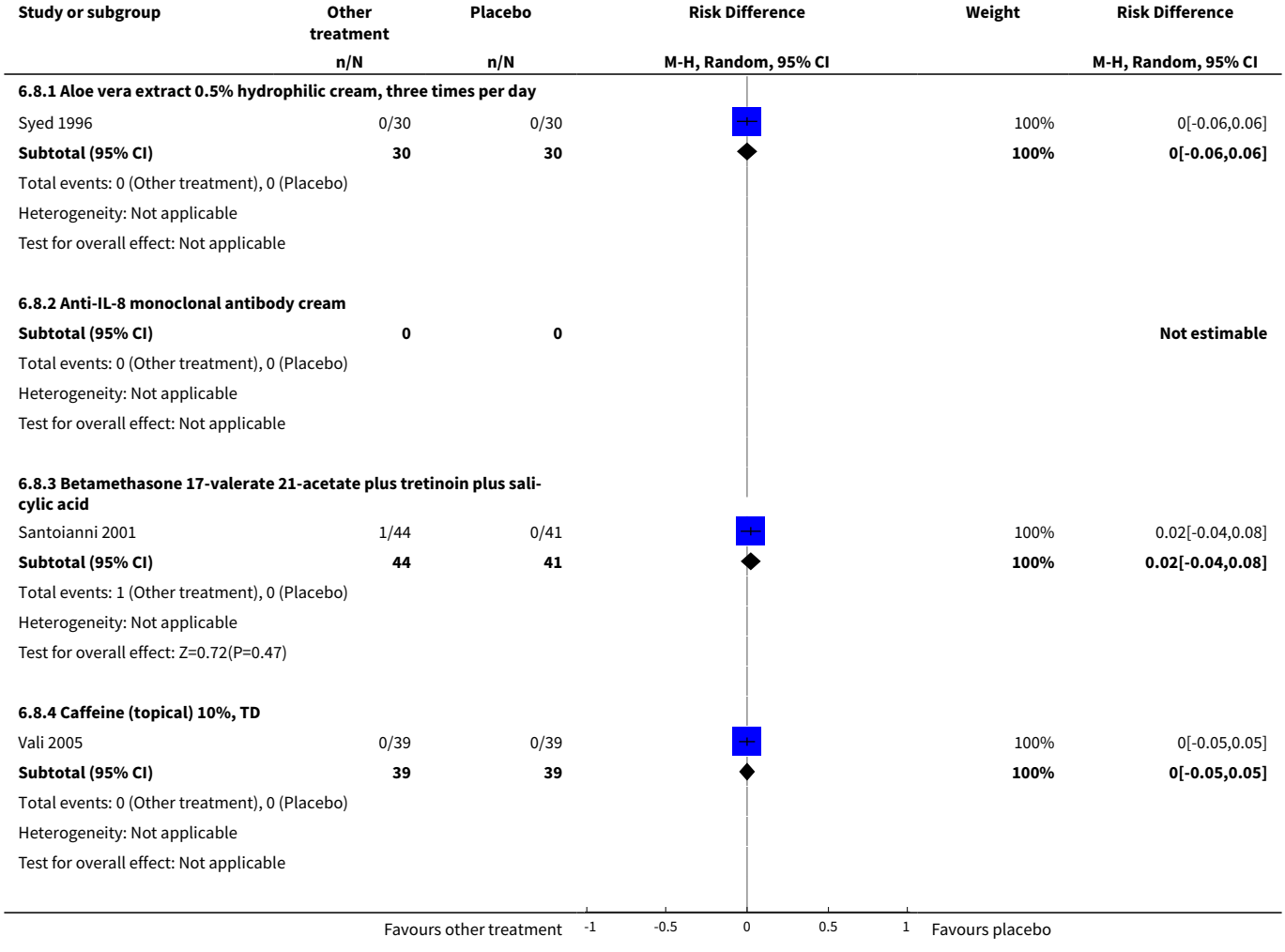
Study or subgroup	Other treatment n/N	Placebo n/N	Risk Difference M-H, Random, 95% CI	Weight	Risk Difference M-H, Random, 95% CI
Test for overall effect: Not applicable					
6.7.10 Indigo naturalis 1.4% ointment					
Lin 2007	0/14	0/14		11.07%	0[-0.13,0.13]
Lin 2008	0/42	0/42		88.93%	0[-0.05,0.05]
Subtotal (95% CI)	**56**	**56**		**100%**	**0[-0.04,0.04]**
Total events: 0 (Other treatment), 0 (Placebo)					
Heterogeneity: Tau^2=0; Chi^2=0, df=1(P=1); I^2=0%					
Test for overall effect: Not applicable					
6.7.11 Kukui nut oil, TD					
Brown 2005	0/15	0/15		100%	0[-0.12,0.12]
Subtotal (95% CI)	**15**	**15**		**100%**	**0[-0.12,0.12]**
Total events: 0 (Other treatment), 0 (Placebo)					
Heterogeneity: Not applicable					
Test for overall effect: Not applicable					
6.7.12 Mahonia aquifolium (Reliéva™), twice daily					
Subtotal (95% CI)	**0**	**0**			**Not estimable**
Total events: 0 (Other treatment), 0 (Placebo)					
Heterogeneity: Not applicable					
Test for overall effect: Not applicable					
6.7.13 Methotrexate gel					
Syed 2001b	0/30	0/30		100%	0[-0.06,0.06]
Subtotal (95% CI)	**30**	**30**		**100%**	**0[-0.06,0.06]**
Total events: 0 (Other treatment), 0 (Placebo)					
Heterogeneity: Not applicable					
Test for overall effect: Not applicable					
6.7.14 Mycophenolic acid ointment					
Geilen 2000	0/7	0/7		100%	0[-0.24,0.24]
Subtotal (95% CI)	**7**	**7**		**100%**	**0[-0.24,0.24]**
Total events: 0 (Other treatment), 0 (Placebo)					
Heterogeneity: Not applicable					
Test for overall effect: Not applicable					
6.7.15 NG-monomethyl-L-arginine (L-NMMA) cream					
Ormerod 2000	0/17	0/17		100%	0[-0.11,0.11]
Subtotal (95% CI)	**17**	**17**		**100%**	**0[-0.11,0.11]**
Total events: 0 (Other treatment), 0 (Placebo)					
Heterogeneity: Not applicable					
Test for overall effect: Not applicable					
6.7.16 Nicotinamide 1.4%, twice daily					
Levine 2010 (P)	0/48	0/48		100%	0[-0.04,0.04]
Subtotal (95% CI)	**48**	**48**		**100%**	**0[-0.04,0.04]**
Total events: 0 (Other treatment), 0 (Placebo)					
Heterogeneity: Not applicable					
Test for overall effect: Not applicable					

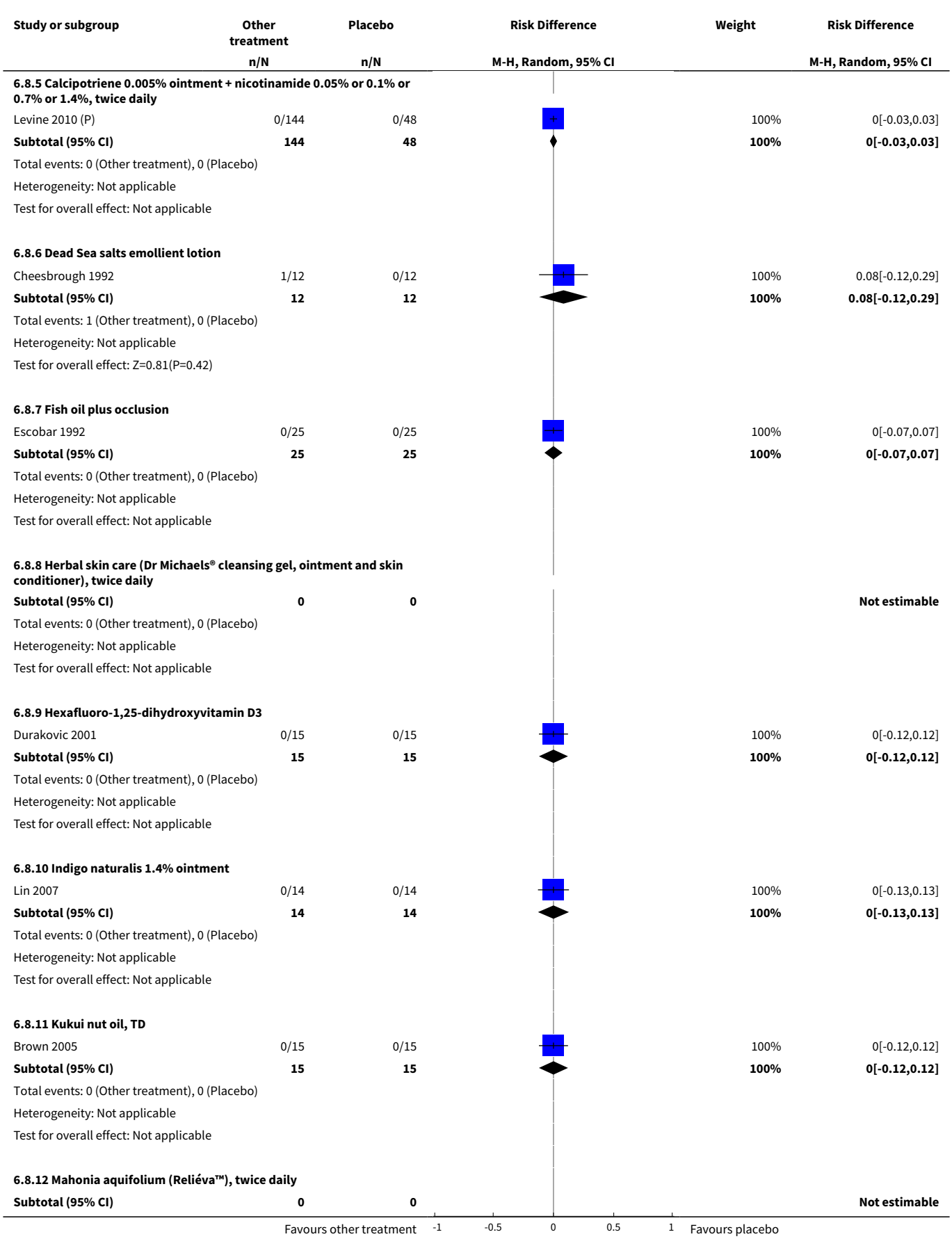


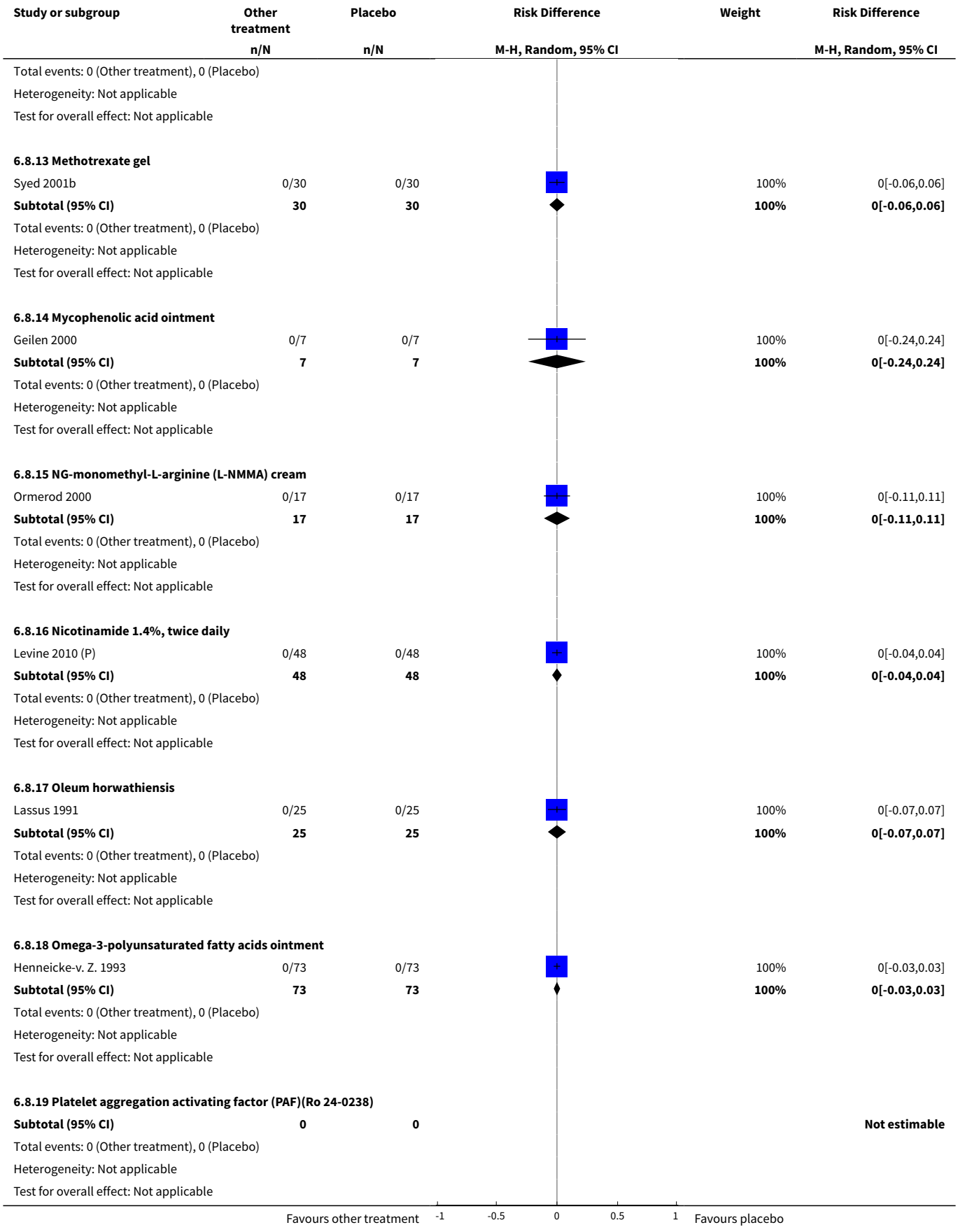


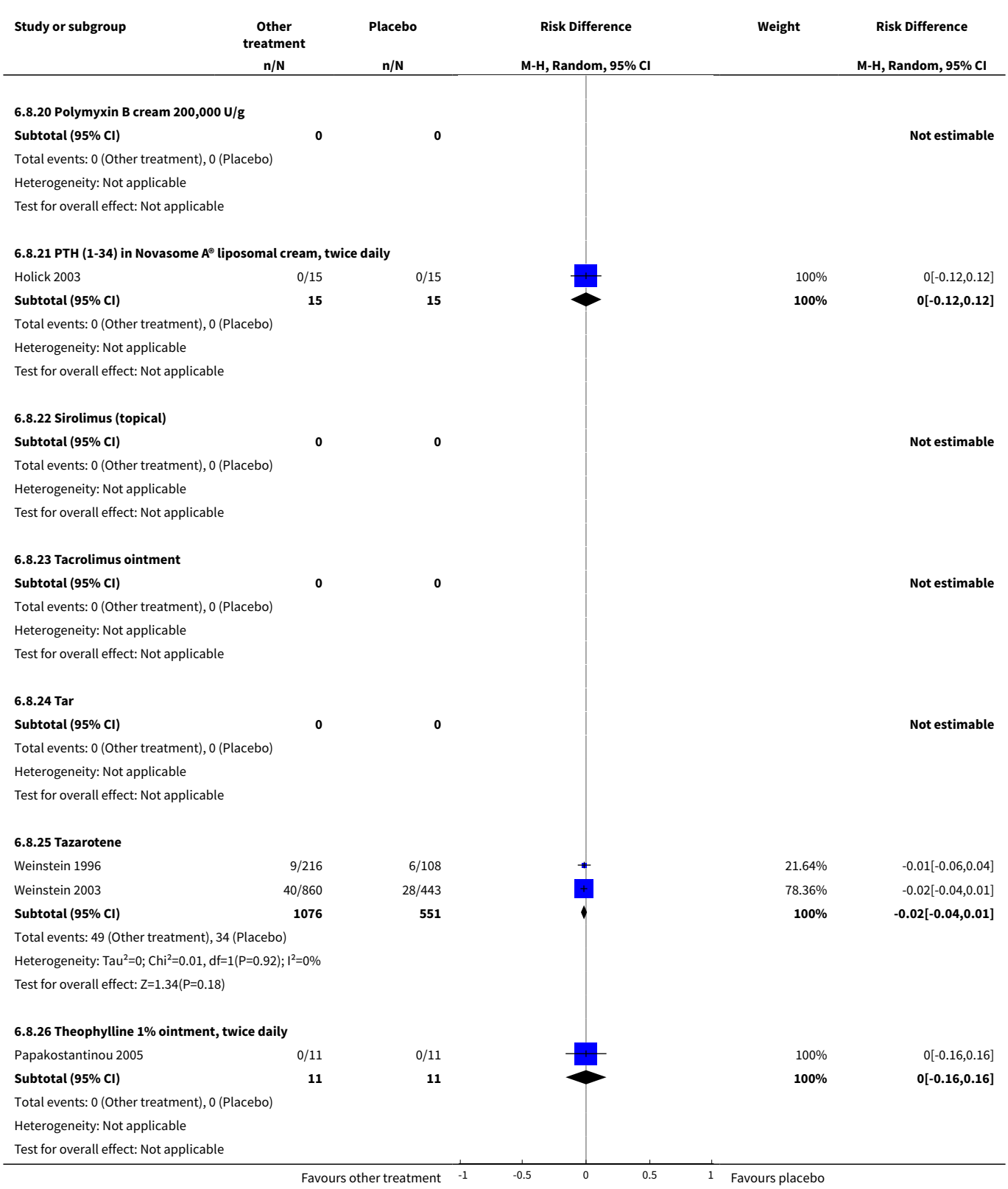


Analysis 6.8. Comparison 6 Other treatment versus placebo, Outcome 8 Withdrawals due to treatment failure.



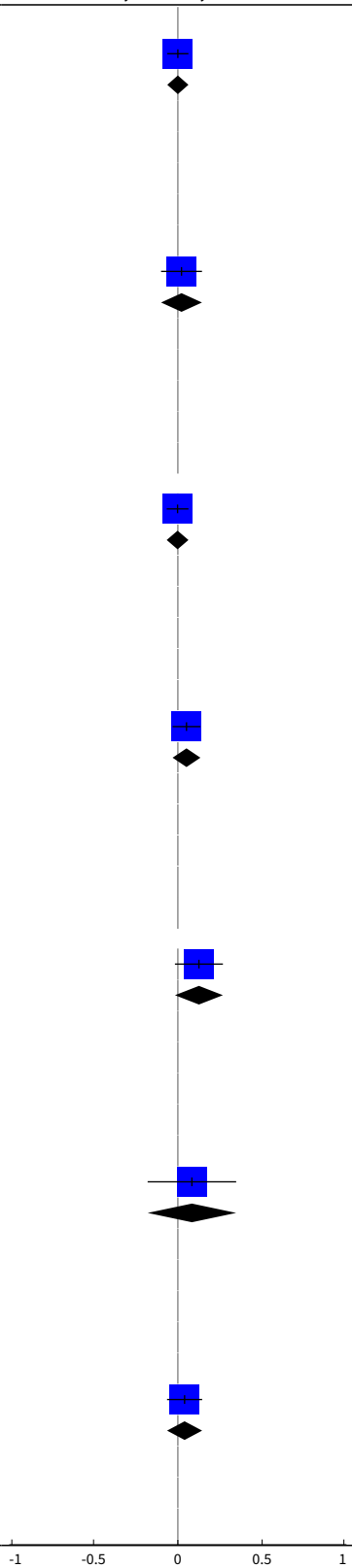


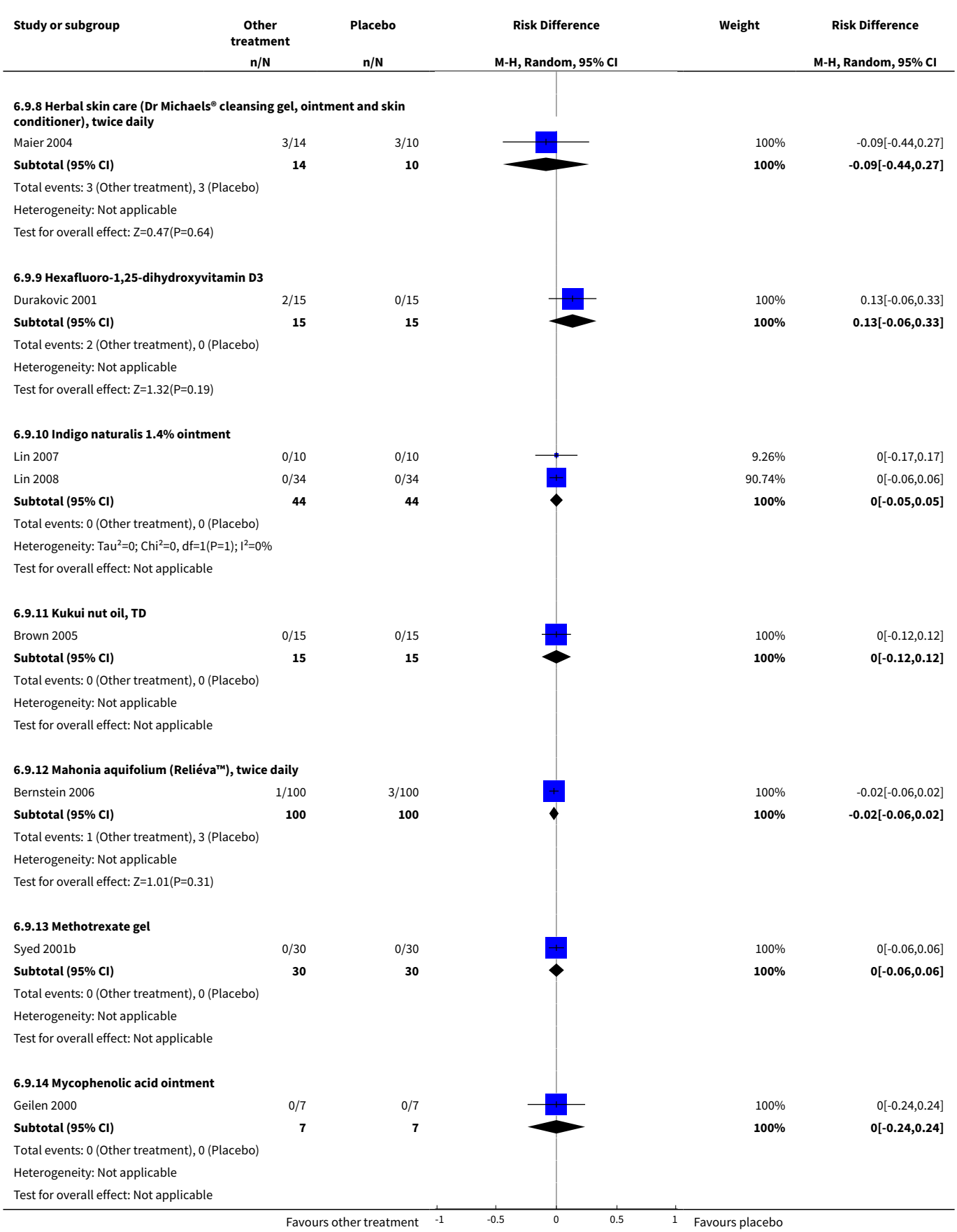


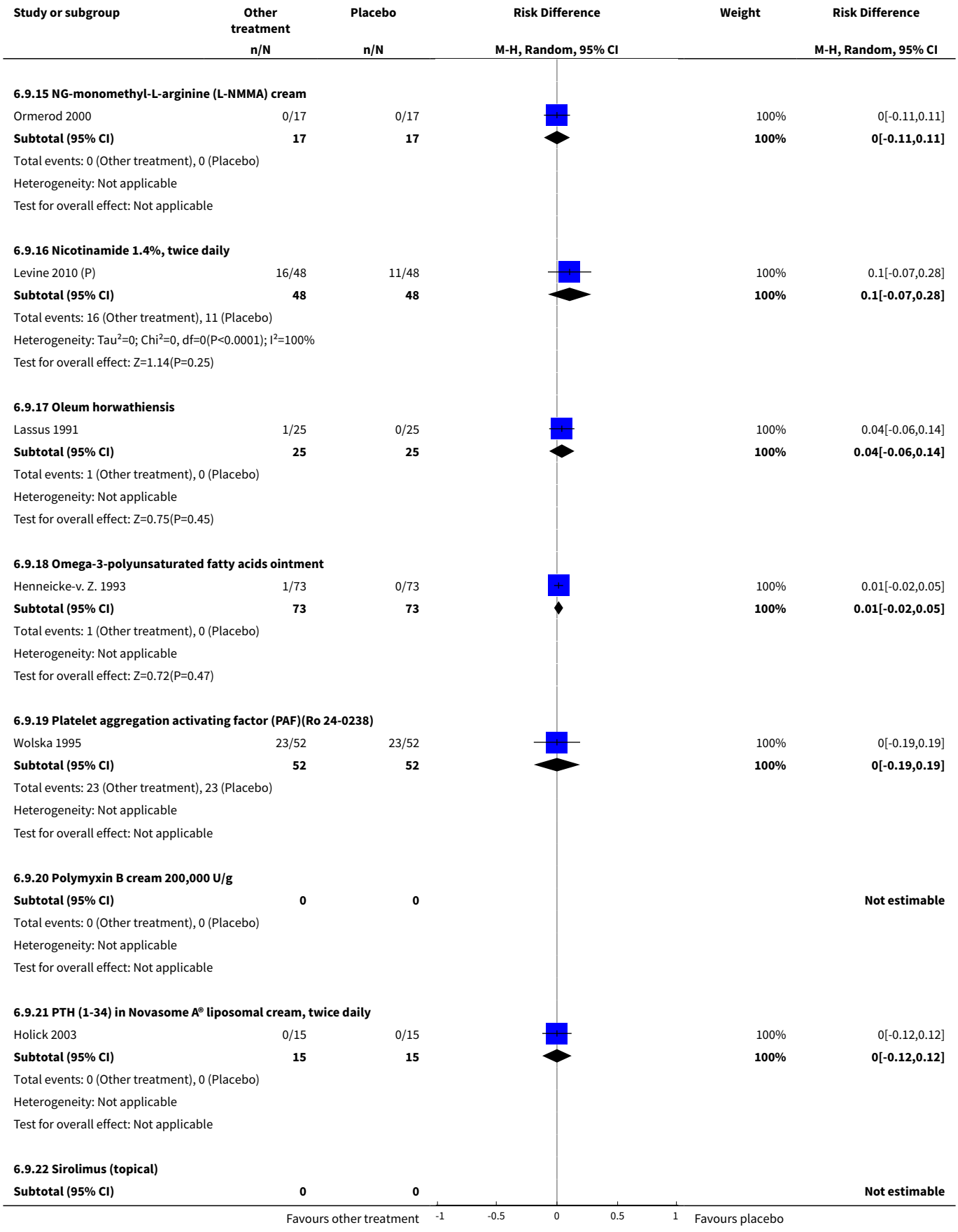


Analysis 6.9. Comparison 6 Other treatment versus placebo, Outcome 9 Adverse events (local).

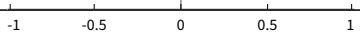
Study or subgroup	Other treatment n/N	Placebo n/N	Risk Difference M-H, Random, 95% CI	Weight	Risk Difference M-H, Random, 95% CI
6.9.1 Aloe vera extract 0.5% hydrophilic cream, three times per day					
Syed 1996	0/30	0/30		100%	0[-0.06,0.06]
Subtotal (95% CI)	**30**	**30**		**100%**	**0[-0.06,0.06]**
Total events: 0 (Other treatment), 0 (Placebo)					
Heterogeneity: Not applicable					
Test for overall effect: Not applicable					
6.9.2 Anti-IL-8 monoclonal antibody cream					
Jin 2001	5/46	4/46		100%	0.02[-0.1,0.14]
Subtotal (95% CI)	**46**	**46**		**100%**	**0.02[-0.1,0.14]**
Total events: 5 (Other treatment), 4 (Placebo)					
Heterogeneity: Not applicable					
Test for overall effect: Z=0.35(P=0.73)					
6.9.3 Betamethasone 17-valerate 21-acetate plus tretinoin plus salicylic acid					
Santoianni 2001	1/44	1/41		100%	-0[-0.07,0.06]
Subtotal (95% CI)	**44**	**41**		**100%**	**-0[-0.07,0.06]**
Total events: 1 (Other treatment), 1 (Placebo)					
Heterogeneity: Tau^2=0; Chi^2=0, df=0(P<0.0001); I^2=100%					
Test for overall effect: Z=0.05(P=0.96)					
6.9.4 Caffeine (topical) 10%, TD					
Vali 2005	2/39	0/39		100%	0.05[-0.03,0.13]
Subtotal (95% CI)	**39**	**39**		**100%**	**0.05[-0.03,0.13]**
Total events: 2 (Other treatment), 0 (Placebo)					
Heterogeneity: Not applicable					
Test for overall effect: Z=1.22(P=0.22)					
6.9.5 Calcipotriene 0.005% ointment + nicotinamide 0.05% or 0.1% or 0.7% or 1.4%, twice daily					
Levine 2010 (P)	51/144	11/48		100%	0.13[-0.02,0.27]
Subtotal (95% CI)	**144**	**48**		**100%**	**0.13[-0.02,0.27]**
Total events: 51 (Other treatment), 11 (Placebo)					
Heterogeneity: Not applicable					
Test for overall effect: Z=1.72(P=0.09)					
6.9.6 Dead Sea salts emollient lotion					
Cheesbrough 1992	2/12	1/12		100%	0.08[-0.18,0.35]
Subtotal (95% CI)	**12**	**12**		**100%**	**0.08[-0.18,0.35]**
Total events: 2 (Other treatment), 1 (Placebo)					
Heterogeneity: Not applicable					
Test for overall effect: Z=0.62(P=0.53)					
6.9.7 Fish oil plus occlusion					
Escobar 1992	1/25	0/25		100%	0.04[-0.06,0.14]
Subtotal (95% CI)	**25**	**25**		**100%**	**0.04[-0.06,0.14]**
Total events: 1 (Other treatment), 0 (Placebo)					
Heterogeneity: Not applicable					
Test for overall effect: Z=0.75(P=0.45)					





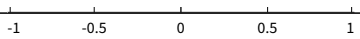


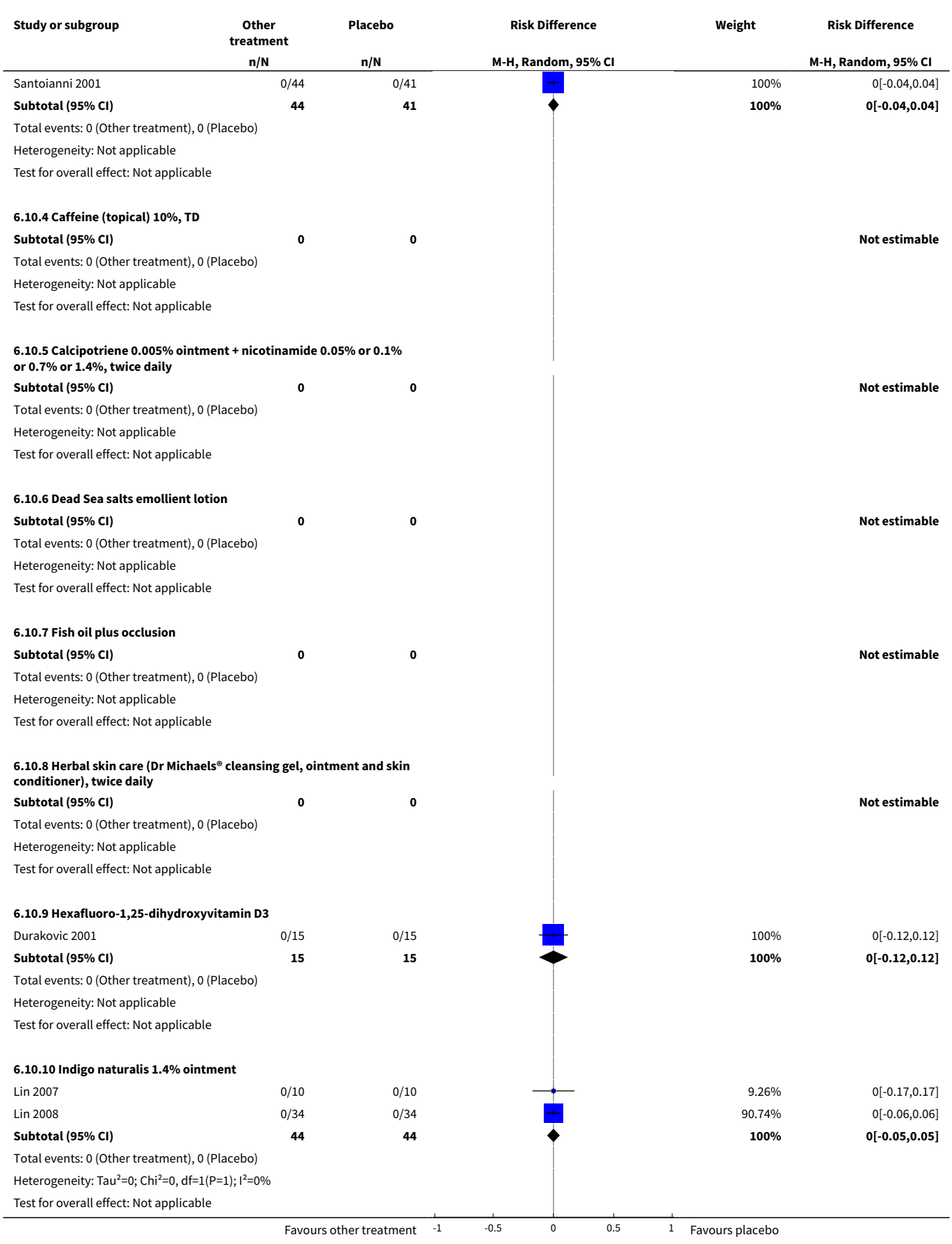
Study or subgroup	Other treatment n/N	Placebo n/N	Risk Difference M-H, Random, 95% CI	Weight	Risk Difference M-H, Random, 95% CI
Total events: 0 (Other treatment), 0 (Placebo)					
Heterogeneity: Not applicable					
Test for overall effect: Not applicable					
6.9.23 Tacrolimus ointment					
Subtotal (95% CI)	**0**	**0**			**Not estimable**
Total events: 0 (Other treatment), 0 (Placebo)					
Heterogeneity: Not applicable					
Test for overall effect: Not applicable					
6.9.24 Tar					
Subtotal (95% CI)	**0**	**0**			**Not estimable**
Total events: 0 (Other treatment), 0 (Placebo)					
Heterogeneity: Not applicable					
Test for overall effect: Not applicable					
6.9.25 Tazarotene					
Subtotal (95% CI)	**0**	**0**			**Not estimable**
Total events: 0 (Other treatment), 0 (Placebo)					
Heterogeneity: Not applicable					
Test for overall effect: Not applicable					
6.9.26 Theophylline 1% ointment, twice daily					
Papakostantinou 2005	0/11	0/11		100%	0[-0.16,0.16]
Subtotal (95% CI)	**11**	**11**		**100%**	**0[-0.16,0.16]**
Total events: 0 (Other treatment), 0 (Placebo)					
Heterogeneity: Not applicable					
Test for overall effect: Not applicable					



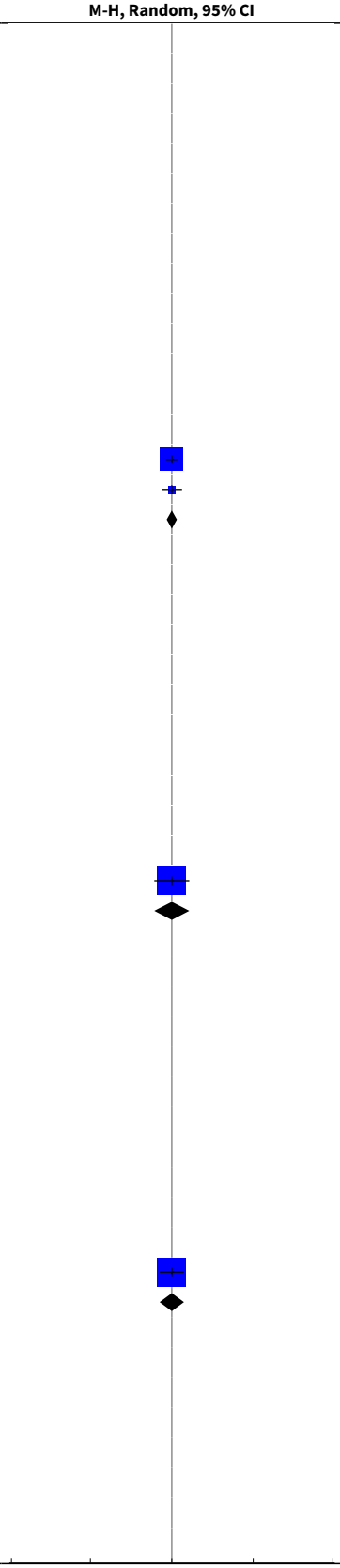
Analysis 6.10. Comparison 6 Other treatment versus placebo, Outcome 10 Adverse events (systemic).

Study or subgroup	Other treatment n/N	Placebo n/N	Risk Difference M-H, Random, 95% CI	Weight	Risk Difference M-H, Random, 95% CI
6.10.1 Aloe vera extract 0.5% hydrophilic cream, three times per day					
Subtotal (95% CI)	**0**	**0**			**Not estimable**
Total events: 0 (Other treatment), 0 (Placebo)					
Heterogeneity: Not applicable					
Test for overall effect: Not applicable					
6.10.2 Anti-IL-8 monoclonal antibody cream					
Subtotal (95% CI)	**0**	**0**			**Not estimable**
Total events: 0 (Other treatment), 0 (Placebo)					
Heterogeneity: Not applicable					
Test for overall effect: Not applicable					
6.10.3 Betamethasone 17-valerate 21-acetate plus tretinoin plus salicylic acid					

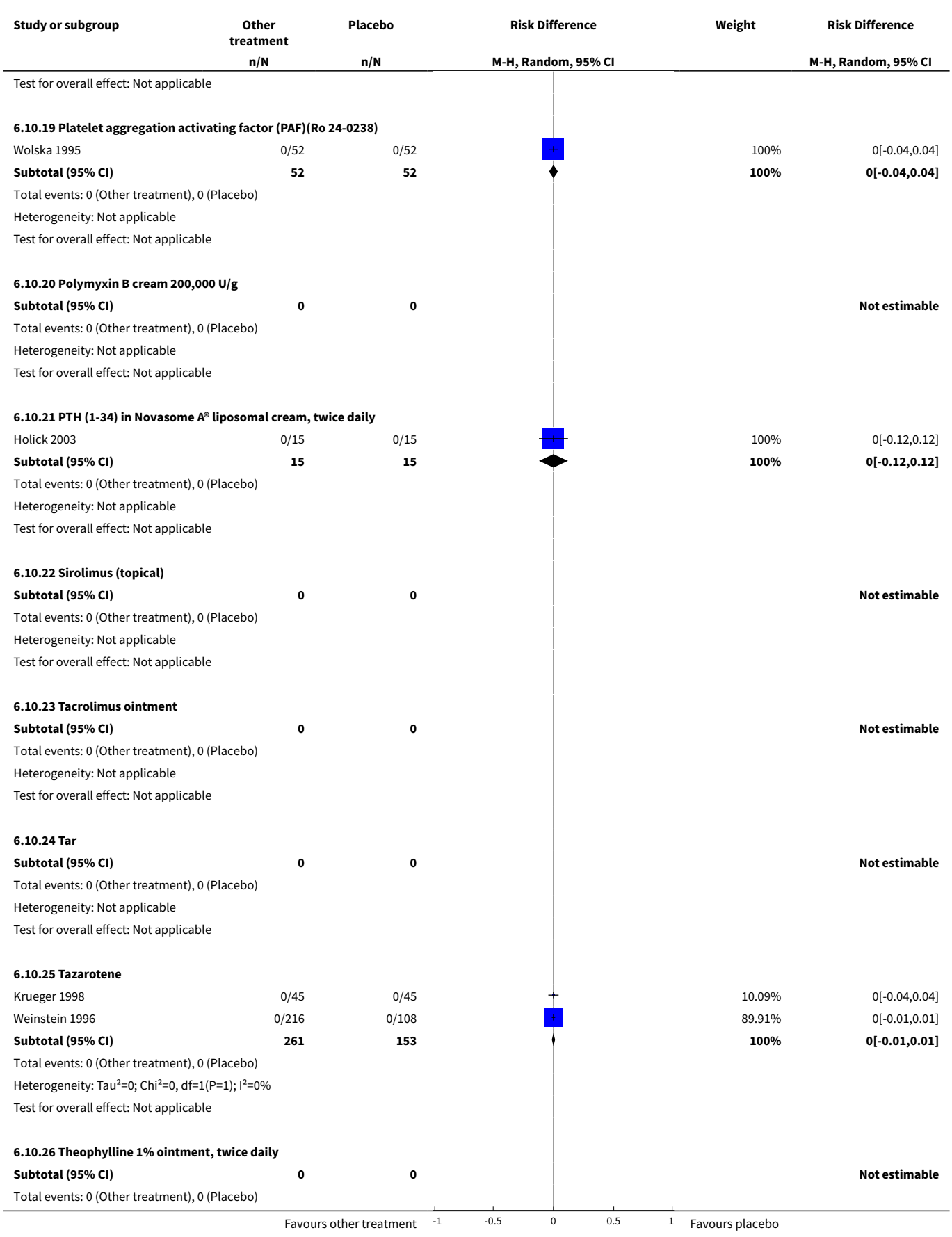


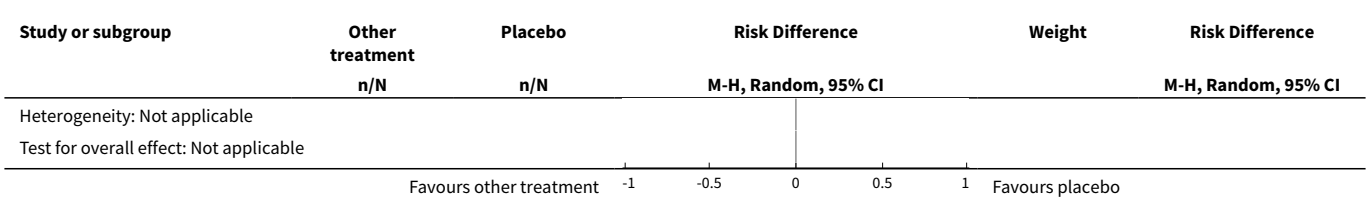


Study or subgroup	Other treatment n/N	Placebo n/N	Risk Difference M-H, Random, 95% CI	Weight	Risk Difference M-H, Random, 95% CI
6.10.11 Kukui nut oil, TD					
Subtotal (95% CI)	**0**	**0**			**Not estimable**
Total events: 0 (Other treatment), 0 (Placebo)					
Heterogeneity: Not applicable					
Test for overall effect: Not applicable					
6.10.12 Mahonia aquifolium (Reliéva™), twice daily					
Subtotal (95% CI)	**0**	**0**			**Not estimable**
Total events: 0 (Other treatment), 0 (Placebo)					
Heterogeneity: Not applicable					
Test for overall effect: Not applicable					
6.10.13 Methotrexate gel					
Sutton 2001	0/53	0/53		75.08%	0[-0.04,0.04]
Syed 2001b	0/30	0/30		24.92%	0[-0.06,0.06]
Subtotal (95% CI)	**83**	**83**		**100%**	**0[-0.03,0.03]**
Total events: 0 (Other treatment), 0 (Placebo)					
Heterogeneity: $Tau^2=0$; $Chi^2=0$, df=1(P=1); $I^2=0\%$					
Test for overall effect: Not applicable					
6.10.14 Mycophenolic acid ointment					
Subtotal (95% CI)	**0**	**0**			**Not estimable**
Total events: 0 (Other treatment), 0 (Placebo)					
Heterogeneity: Not applicable					
Test for overall effect: Not applicable					
6.10.15 NG-monomethyl-L-arginine (L-NMMA) cream					
Ormerod 2000	0/17	0/17		100%	0[-0.11,0.11]
Subtotal (95% CI)	**17**	**17**		**100%**	**0[-0.11,0.11]**
Total events: 0 (Other treatment), 0 (Placebo)					
Heterogeneity: Not applicable					
Test for overall effect: Not applicable					
6.10.16 Nicotinamide 1.4%, twice daily					
Subtotal (95% CI)	**0**	**0**			**Not estimable**
Total events: 0 (Other treatment), 0 (Placebo)					
Heterogeneity: Not applicable					
Test for overall effect: Not applicable					
6.10.17 Oleum horwathiensis					
Lassus 1991	0/25	0/25		100%	0[-0.07,0.07]
Subtotal (95% CI)	**25**	**25**		**100%**	**0[-0.07,0.07]**
Total events: 0 (Other treatment), 0 (Placebo)					
Heterogeneity: Not applicable					
Test for overall effect: Not applicable					
6.10.18 Omega-3-polyunsaturated fatty acids ointment					
Subtotal (95% CI)	**0**	**0**			**Not estimable**
Total events: 0 (Other treatment), 0 (Placebo)					
Heterogeneity: Not applicable					



Favours other treatment — Favours placebo





Comparison 7. Vitamin D analogues versus corticosteroid (potent)

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 IAGI	8		Std. Mean Difference (IV, Random, 95% CI)	Subtotals only
1.1 Calcipotriol vs. betamethasone dipropionate	3	1728	Std. Mean Difference (IV, Random, 95% CI)	0.43 [0.28, 0.58]
1.2 Calcipotriol vs. betamethasone valerate	1	412	Std. Mean Difference (IV, Random, 95% CI)	-0.02 [-0.21, 0.17]
1.3 Calcipotriol vs. desoxymetasone	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
1.4 Calcipotriol vs. diflorasone diacetate	1	256	Std. Mean Difference (IV, Random, 95% CI)	0.27 [0.02, 0.52]
1.5 Calcipotriol vs. fluocinonide	1	99	Std. Mean Difference (IV, Random, 95% CI)	-0.58 [-0.99, -0.18]
1.6 Calcitriol vs. betamethasone dipropionate	1	258	Std. Mean Difference (IV, Random, 95% CI)	0.21 [-0.04, 0.45]
1.7 Calcitriol vs. betamethasone valerate	1	30	Std. Mean Difference (IV, Random, 95% CI)	-0.19 [-0.91, 0.53]
1.8 Tacalcitol vs. betamethasone valerate	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
2 TSS	6		Std. Mean Difference (IV, Random, 95% CI)	Subtotals only
2.1 Calcipotriol vs. betamethasone dipropionate	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
2.2 Calcipotriol vs. betamethasone valerate	1	684	Std. Mean Difference (IV, Random, 95% CI)	-0.26 [-0.41, -0.11]
2.3 Calcipotriol vs. desoxymetasone	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
2.4 Calcipotriol vs. diflorasone diacetate	1	256	Std. Mean Difference (IV, Random, 95% CI)	0.40 [0.15, 0.65]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
2.5 Calcipotriol vs. fluocinonide	1	89	Std. Mean Difference (IV, Random, 95% CI)	-0.50 [-0.92, -0.07]
2.6 Calcitriol vs. betamethasone dipropionate	1	258	Std. Mean Difference (IV, Random, 95% CI)	0.27 [0.02, 0.51]
2.7 Calcitriol vs. betamethasone valerate	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
2.8 Tacalcitol vs. betamethasone valerate	2	148	Std. Mean Difference (IV, Random, 95% CI)	0.41 [0.09, 0.74]
3 PASI	9		Std. Mean Difference (IV, Random, 95% CI)	Subtotals only
3.1 Calcipotriol vs. betamethasone dipropionate	3	1728	Std. Mean Difference (IV, Random, 95% CI)	0.36 [0.22, 0.51]
3.2 Calcipotriol vs. betamethasone valerate	4	1505	Std. Mean Difference (IV, Random, 95% CI)	-0.12 [-0.22, -0.02]
3.3 Calcipotriol vs. desoxymetasone	1	20	Std. Mean Difference (IV, Random, 95% CI)	0.15 [-0.73, 1.02]
3.4 Calcipotriol vs. diflorasone diacetate	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
3.5 Calcipotriol vs. fluocinonide	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
3.6 Calcitriol vs. betamethasone dipropionate	1	258	Std. Mean Difference (IV, Random, 95% CI)	0.39 [0.14, 0.63]
3.7 Calcitriol vs. betamethasone valerate	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
3.8 Tacalcitol vs. betamethasone valerate	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
4 PAGI	2	1080	Std. Mean Difference (IV, Random, 95% CI)	-0.26 [-0.38, -0.14]
4.1 Calcipotriol vs. betamethasone dipropionate	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
4.2 Calcipotriol vs. betamethasone valerate	2	1080	Std. Mean Difference (IV, Random, 95% CI)	-0.26 [-0.38, -0.14]
4.3 Calcipotriol vs. desoxymetasone	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
4.4 Calcipotriol vs. diflorasone diacetate	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
4.5 Calcipotriol vs. fluocinonide	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
4.6 Calcitriol vs. betamethasone dipropionate	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
4.7 Calcitriol vs. betamethasone valerate	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
4.8 Tacalcitol vs. betamethasone valerate	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
5 Combined end point (IAGI/TSS/PASI/PAGI)	14		Std. Mean Difference (IV, Random, 95% CI)	Subtotals only
5.1 Calcipotriol vs. betamethasone dipropionate	3	1728	Std. Mean Difference (IV, Random, 95% CI)	0.43 [0.28, 0.58]
5.2 Calcipotriol vs. betamethasone valerate	4	1557	Std. Mean Difference (IV, Random, 95% CI)	-0.12 [-0.26, 0.02]
5.3 Calcipotriol vs. desoxymetasone	1	20	Std. Mean Difference (IV, Random, 95% CI)	0.15 [-0.73, 1.02]
5.4 Calcipotriol vs. diflorasone diacetate	1	256	Std. Mean Difference (IV, Random, 95% CI)	0.27 [0.02, 0.52]
5.5 Calcipotriol vs. fluocinonide	1	99	Std. Mean Difference (IV, Random, 95% CI)	-0.58 [-0.99, -0.18]
5.6 Calcitriol vs. betamethasone dipropionate	1	258	Std. Mean Difference (IV, Random, 95% CI)	0.21 [-0.04, 0.45]
5.7 Calcitriol vs. betamethasone valerate	1	30	Std. Mean Difference (IV, Random, 95% CI)	-0.19 [-0.91, 0.53]
5.8 Tacalcitol vs. betamethasone valerate	2	148	Std. Mean Difference (IV, Random, 95% CI)	0.41 [0.09, 0.74]
6 Total withdrawals	11	3995	Risk Difference (M-H, Random, 95% CI)	0.02 [0.00, 0.03]
6.1 Calcipotriol vs. betamethasone dipropionate	3	1739	Risk Difference (M-H, Random, 95% CI)	0.03 [0.01, 0.06]
6.2 Calcipotriol vs. betamethasone valerate	3	1520	Risk Difference (M-H, Random, 95% CI)	0.01 [-0.01, 0.04]
6.3 Calcipotriol vs. desoxymetasone	0	0	Risk Difference (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
6.4 Calcipotriol vs. diflorasone diacetate	1	268	Risk Difference (M-H, Random, 95% CI)	0.0 [-0.05, 0.05]

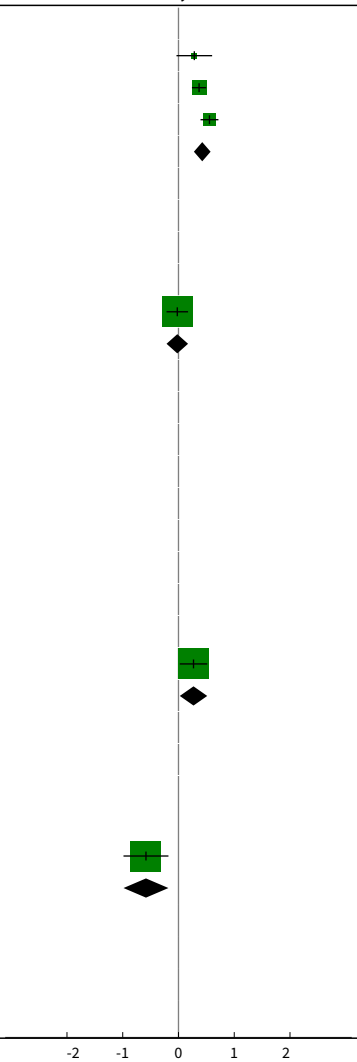
Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
6.5 Calcipotriol vs. fluocinonide	0	0	Risk Difference (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
6.6 Calcitriol vs. betamethasone dipropionate	1	258	Risk Difference (M-H, Random, 95% CI)	-0.02 [-0.08, 0.03]
6.7 Calcitriol vs. betamethasone valerate	1	30	Risk Difference (M-H, Random, 95% CI)	0.07 [-0.10, 0.23]
6.8 Tacalcitol vs. betamethasone valerate	2	180	Risk Difference (M-H, Random, 95% CI)	0.0 [-0.11, 0.11]
7 Withdrawals due to adverse events	9	3058	Risk Difference (M-H, Random, 95% CI)	0.01 [-0.00, 0.01]
7.1 Calcipotriol vs. betamethasone dipropionate	1	956	Risk Difference (M-H, Random, 95% CI)	0.02 [0.00, 0.04]
7.2 Calcipotriol vs. betamethasone valerate	3	1520	Risk Difference (M-H, Random, 95% CI)	0.00 [-0.00, 0.01]
7.3 Calcipotriol vs. desoxymetasone	0	0	Risk Difference (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
7.4 Calcipotriol vs. diflorasone diacetate	0	0	Risk Difference (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
7.5 Calcipotriol vs. fluocinonide	1	114	Risk Difference (M-H, Random, 95% CI)	-0.02 [-0.06, 0.03]
7.6 Calcitriol vs. betamethasone dipropionate	1	258	Risk Difference (M-H, Random, 95% CI)	0.01 [-0.02, 0.03]
7.7 Calcitriol vs. betamethasone valerate	1	30	Risk Difference (M-H, Random, 95% CI)	0.07 [-0.10, 0.23]
7.8 Tacalcitol vs. betamethasone valerate	2	180	Risk Difference (M-H, Random, 95% CI)	0.0 [-0.02, 0.02]
8 Withdrawals due to treatment failure	5	1500	Risk Difference (M-H, Random, 95% CI)	-0.00 [-0.01, 0.01]
8.1 Calcipotriol vs. betamethasone dipropionate	0	0	Risk Difference (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
8.2 Calcipotriol vs. betamethasone valerate	2	1099	Risk Difference (M-H, Random, 95% CI)	-0.00 [-0.01, 0.01]
8.3 Calcipotriol vs. desoxymetasone	0	0	Risk Difference (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
8.4 Calcipotriol vs. diflorasone diacetate	0	0	Risk Difference (M-H, Random, 95% CI)	0.0 [0.0, 0.0]

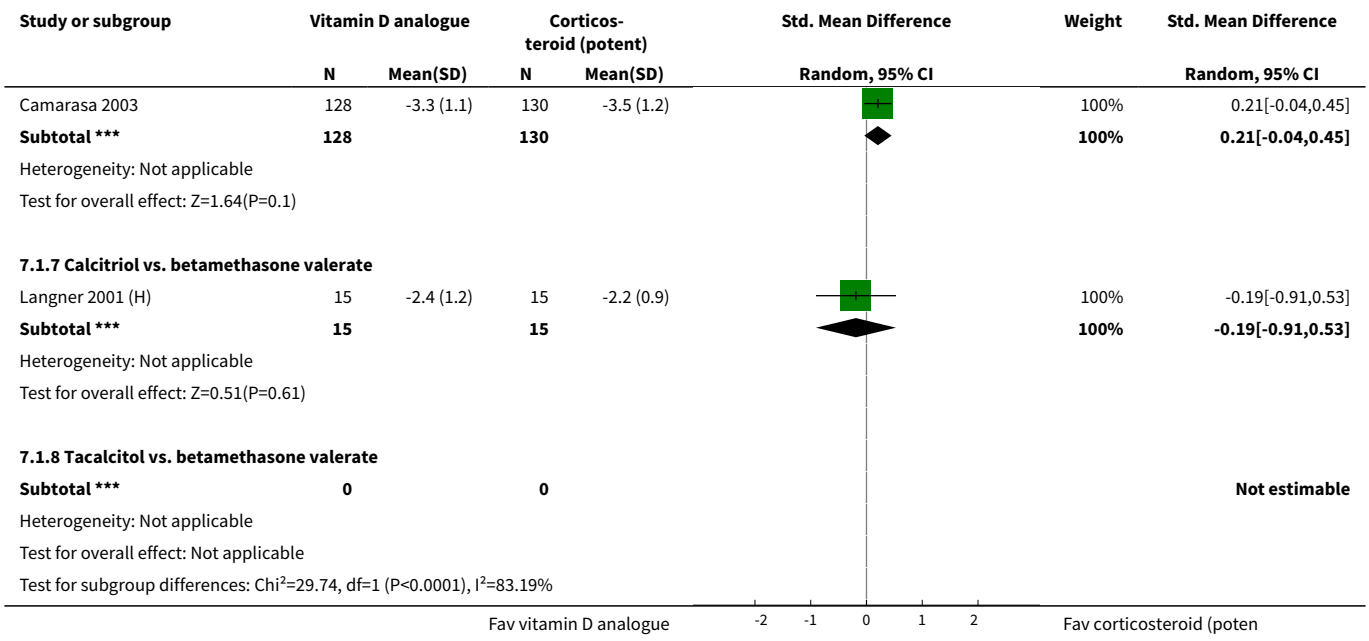
Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
8.5 Calcipotriol vs. fluocinonide	1	113	Risk Difference (M-H, Random, 95% CI)	0.0 [-0.03, 0.03]
8.6 Calcitriol vs. betamethasone dipropionate	1	258	Risk Difference (M-H, Random, 95% CI)	0.01 [-0.03, 0.05]
8.7 Calcitriol vs. betamethasone valerate	1	30	Risk Difference (M-H, Random, 95% CI)	0.0 [-0.12, 0.12]
8.8 Tacalcitol vs. betamethasone valerate	0	0	Risk Difference (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
9 Adverse events (local)	9	3778	Risk Difference (M-H, Random, 95% CI)	0.07 [0.02, 0.11]
9.1 Calcipotriol vs. betamethasone dipropionate	3	1739	Risk Difference (M-H, Random, 95% CI)	0.07 [0.04, 0.09]
9.2 Calcipotriol vs. betamethasone valerate	3	1516	Risk Difference (M-H, Random, 95% CI)	0.12 [-0.02, 0.26]
9.3 Calcipotriol vs. desoxymetasone	0	0	Risk Difference (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
9.4 Calcipotriol vs. diflorasone diacetate	0	0	Risk Difference (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
9.5 Calcipotriol vs. fluocinonide	1	113	Risk Difference (M-H, Random, 95% CI)	0.10 [-0.02, 0.22]
9.6 Calcitriol vs. betamethasone dipropionate	1	258	Risk Difference (M-H, Random, 95% CI)	0.00 [-0.05, 0.06]
9.7 Calcitriol vs. betamethasone valerate	0	0	Risk Difference (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
9.8 Tacalcitol vs. betamethasone valerate	1	152	Risk Difference (M-H, Random, 95% CI)	-0.01 [-0.07, 0.04]
10 Adverse events (systemic)	6	2547	Risk Difference (M-H, Random, 95% CI)	-0.00 [-0.00, 0.00]
10.1 Calcipotriol vs. betamethasone dipropionate	1	621	Risk Difference (M-H, Random, 95% CI)	0.0 [-0.01, 0.01]
10.2 Calcipotriol vs. betamethasone valerate	3	1516	Risk Difference (M-H, Random, 95% CI)	-0.00 [-0.00, 0.00]
10.3 Calcipotriol vs. desoxymetasone	0	0	Risk Difference (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
10.4 Calcipotriol vs. diflorasone diacetate	0	0	Risk Difference (M-H, Random, 95% CI)	0.0 [0.0, 0.0]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
10.5 Calcipotriol vs. fluocinonide	0	0	Risk Difference (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
10.6 Calcitriol vs. betamethasone dipropionate	1	258	Risk Difference (M-H, Random, 95% CI)	-0.01 [-0.04, 0.03]
10.7 Calcitriol vs. betamethasone valerate	0	0	Risk Difference (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
10.8 Tacalcitol vs. betamethasone valerate	1	152	Risk Difference (M-H, Random, 95% CI)	0.0 [-0.09, 0.09]

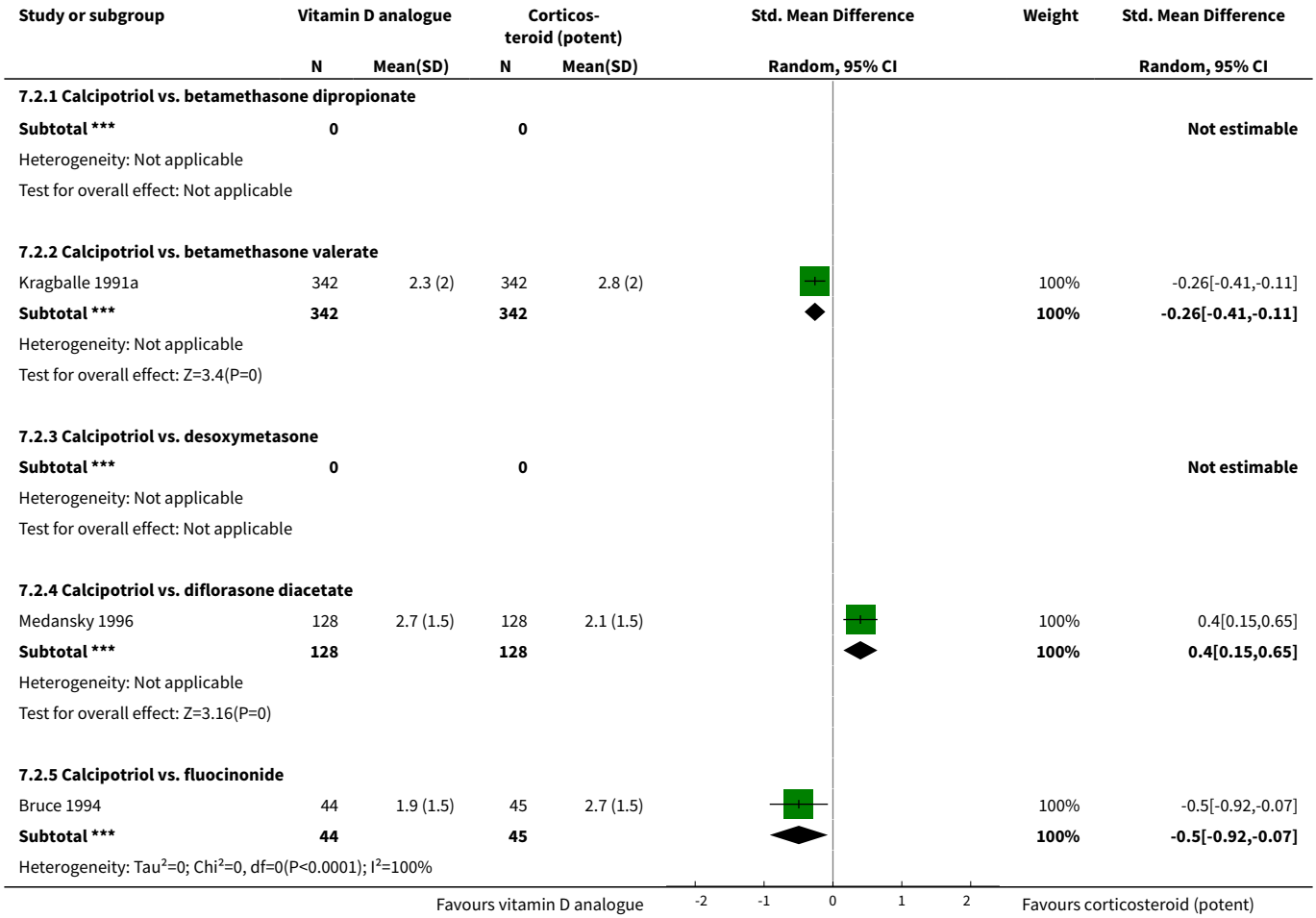
Analysis 7.1. Comparison 7 Vitamin D analogues versus corticosteroid (potent), Outcome 1 IAGI.

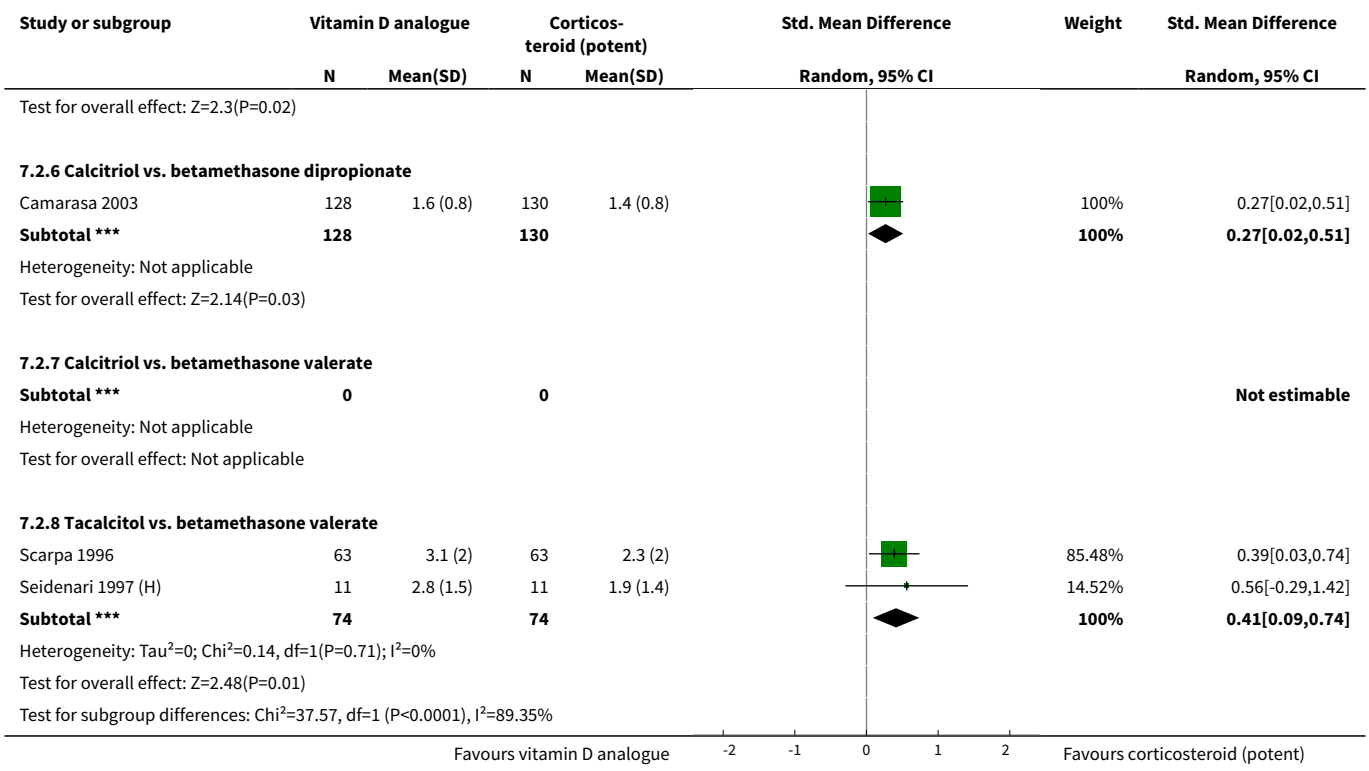
Study or subgroup	Vitamin D analogue N	Vitamin D analogue Mean(SD)	Corticosteroid (potent) N	Corticosteroid (potent) Mean(SD)	Std. Mean Difference Random, 95% CI	Weight	Std. Mean Difference Random, 95% CI
7.1.1 Calcipotriol vs. betamethasone dipropionate							
Fleming 2010 (H)	74	2.3 (0.8)	78	2 (1.1)		16.58%	0.28[-0.04,0.6]
Kaufmann 2002 (H)	480	2.2 (0.9)	476	1.9 (0.9)		45.33%	0.37[0.24,0.5]
Papp 2003 (H)	308	-2.8 (1.2)	312	-3.4 (1.1)		38.09%	0.56[0.4,0.72]
Subtotal ***	**862**		**866**			**100%**	**0.43[0.28,0.58]**
Heterogeneity: Tau^2=0.01; Chi^2=4.03, df=2(P=0.13); I^2=50.33%							
Test for overall effect: Z=5.57(P<0.0001)							
7.1.2 Calcipotriol vs. betamethasone valerate							
Molin 1997	205	-2.4 (0.9)	207	-2.4 (0.9)		100%	-0.02[-0.21,0.17]
Subtotal ***	**205**		**207**			**100%**	**-0.02[-0.21,0.17]**
Heterogeneity: Not applicable							
Test for overall effect: Z=0.22(P=0.83)							
7.1.3 Calcipotriol vs. desoxymetasone							
Subtotal ***	**0**		**0**				**Not estimable**
Heterogeneity: Not applicable							
Test for overall effect: Not applicable							
7.1.4 Calcipotriol vs. diflorasone diacetate							
Medansky 1996	128	-4.1 (1.1)	128	-4.4 (1.1)		100%	0.27[0.02,0.52]
Subtotal ***	**128**		**128**			**100%**	**0.27[0.02,0.52]**
Heterogeneity: Not applicable							
Test for overall effect: Z=2.15(P=0.03)							
7.1.5 Calcipotriol vs. fluocinonide							
Bruce 1994	52	-4 (1.3)	47	-3.3 (1.2)		100%	-0.58[-0.99,-0.18]
Subtotal ***	**52**		**47**			**100%**	**-0.58[-0.99,-0.18]**
Heterogeneity: Not applicable							
Test for overall effect: Z=2.84(P=0)							
7.1.6 Calcitriol vs. betamethasone dipropionate							



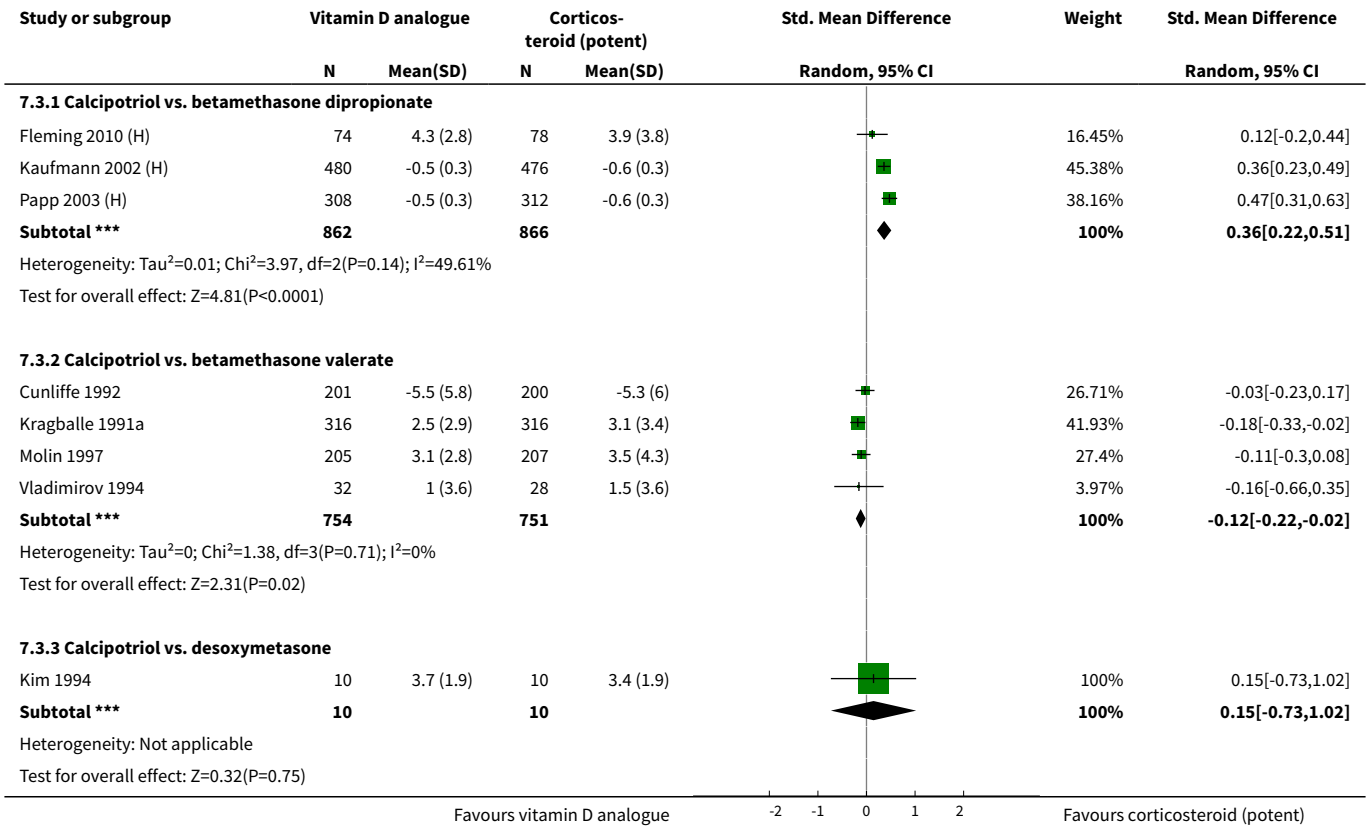


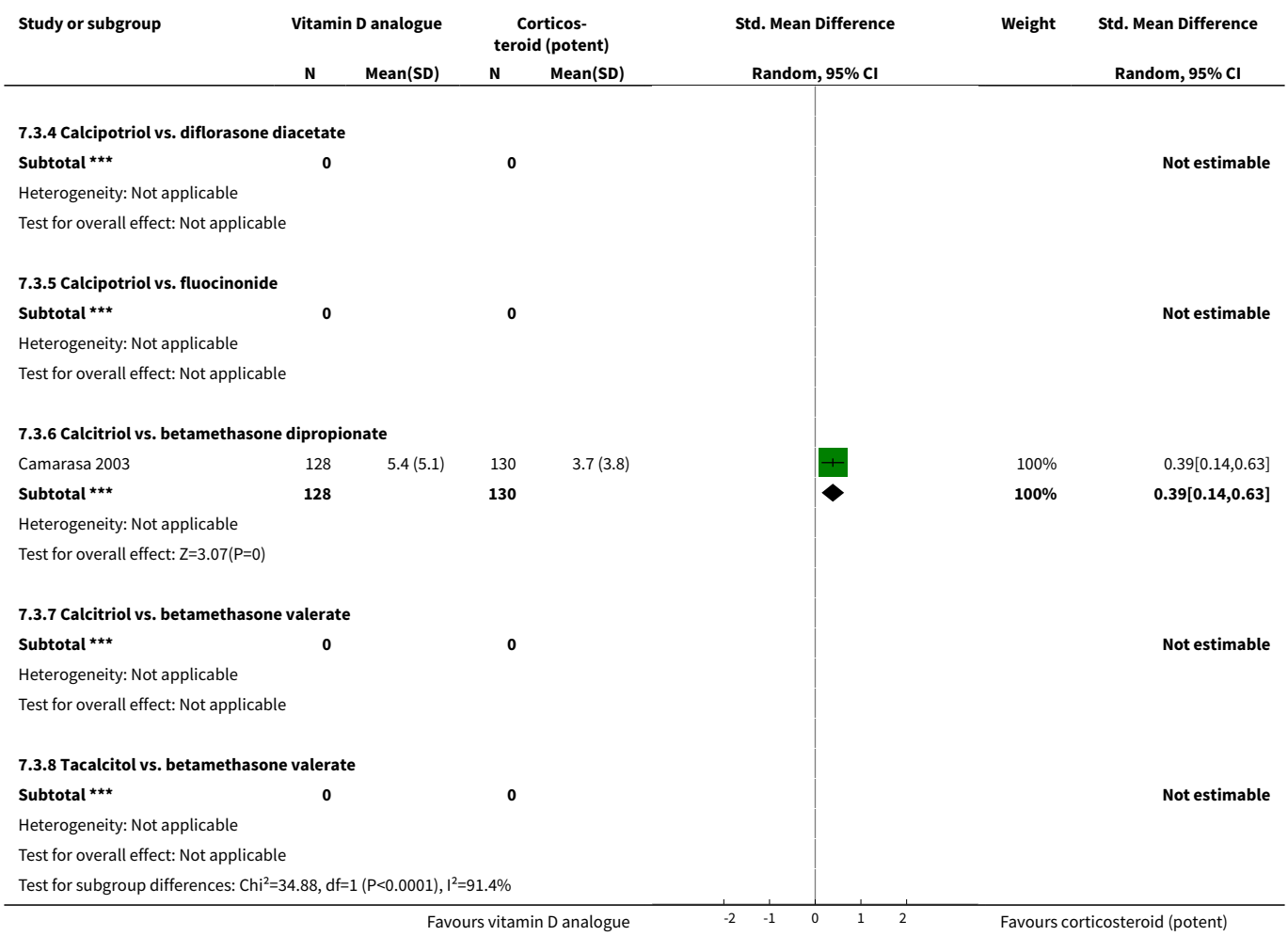
Analysis 7.2. Comparison 7 Vitamin D analogues versus corticosteroid (potent), Outcome 2 TSS.



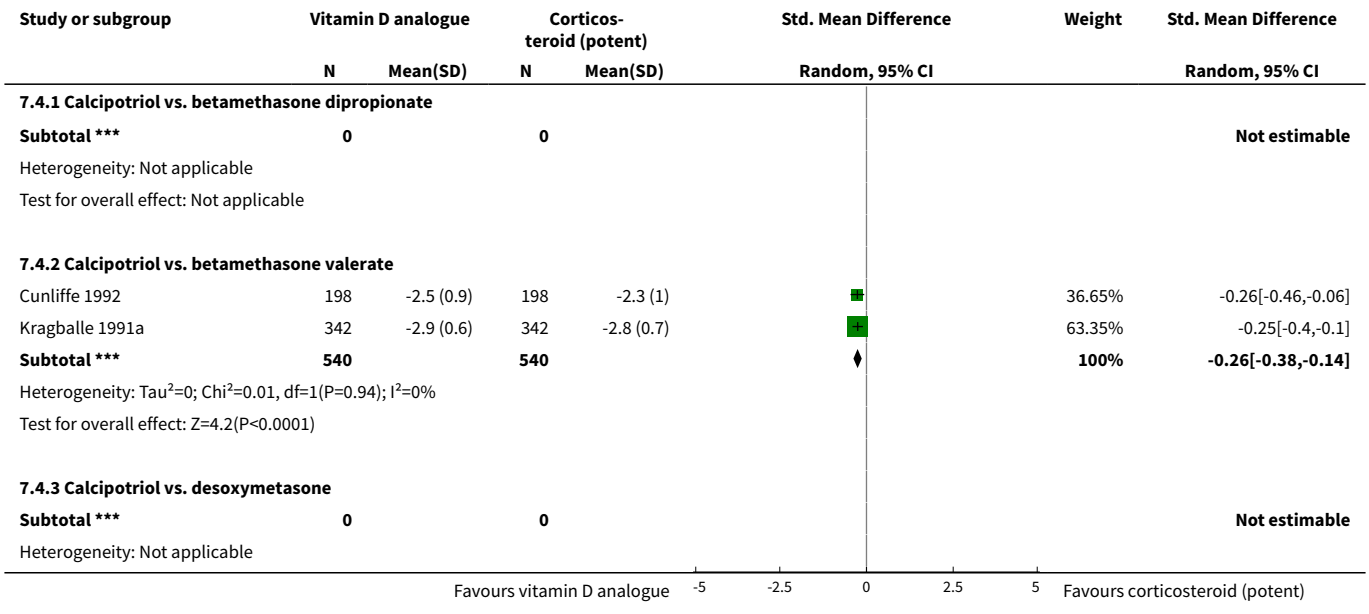


Analysis 7.3. Comparison 7 Vitamin D analogues versus corticosteroid (potent), Outcome 3 PASI.





Analysis 7.4. Comparison 7 Vitamin D analogues versus corticosteroid (potent), Outcome 4 PAGI.



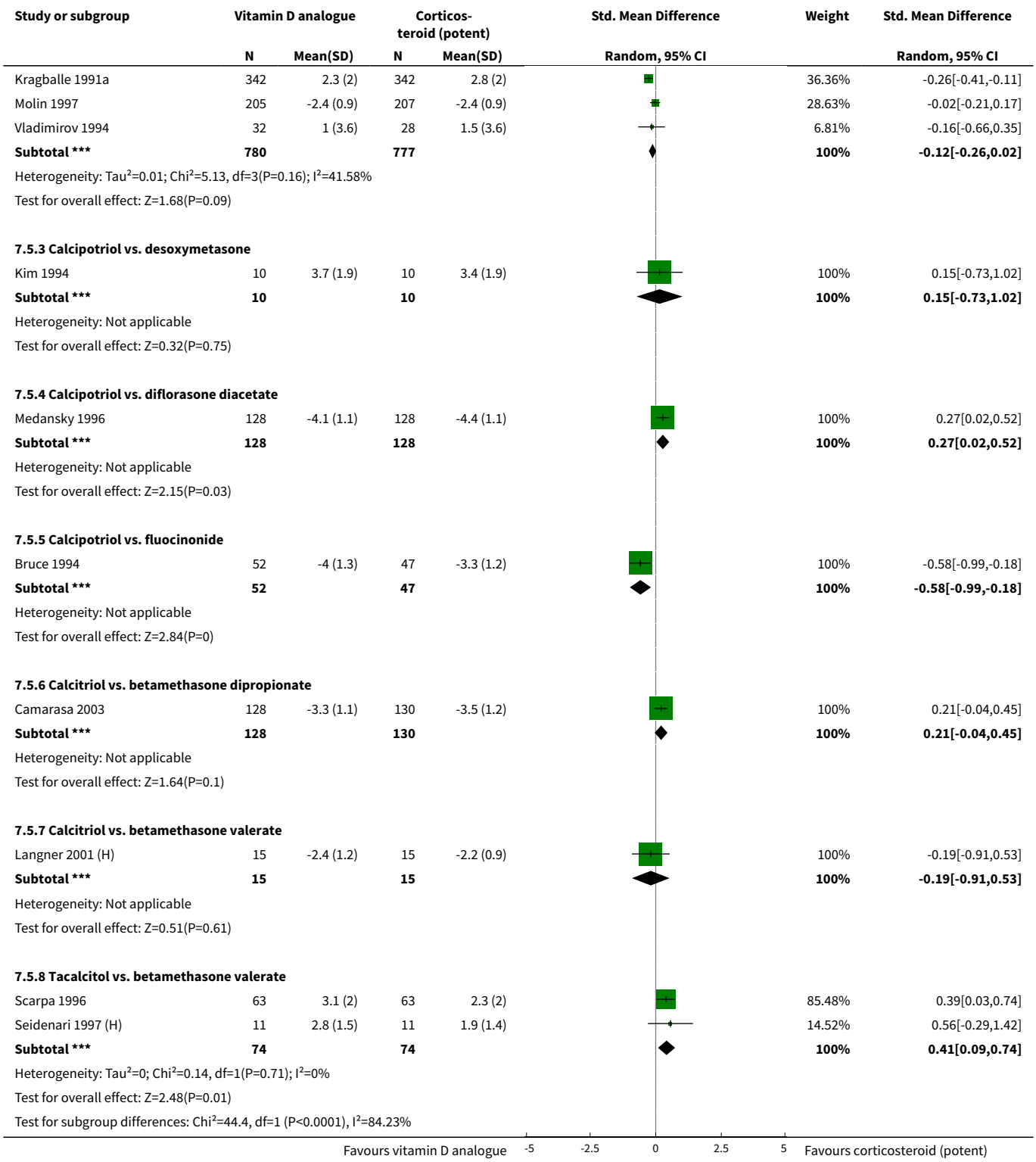
Study or subgroup	Vitamin D analogue N	Vitamin D analogue Mean(SD)	Corticosteroid (potent) N	Corticosteroid (potent) Mean(SD)	Std. Mean Difference Random, 95% CI	Weight	Std. Mean Difference Random, 95% CI
Test for overall effect: Not applicable							
7.4.4 Calcipotriol vs. diflorasone diacetate							
Subtotal ***	**0**		**0**				**Not estimable**
Heterogeneity: Not applicable							
Test for overall effect: Not applicable							
7.4.5 Calcipotriol vs. fluocinonide							
Subtotal ***	**0**		**0**				**Not estimable**
Heterogeneity: Not applicable							
Test for overall effect: Not applicable							
7.4.6 Calcitriol vs. betamethasone dipropionate							
Subtotal ***	**0**		**0**				**Not estimable**
Heterogeneity: Not applicable							
Test for overall effect: Not applicable							
7.4.7 Calcitriol vs. betamethasone valerate							
Subtotal ***	**0**		**0**				**Not estimable**
Heterogeneity: Not applicable							
Test for overall effect: Not applicable							
7.4.8 Tacalcitol vs. betamethasone valerate							
Subtotal ***	**0**		**0**				**Not estimable**
Heterogeneity: Not applicable							
Test for overall effect: Not applicable							
Total ***	**540**		**540**			**100%**	**-0.26[-0.38,-0.14]**
Heterogeneity: Tau^2=0; Chi^2=0.01, df=1(P=0.94); I^2=0%							
Test for overall effect: Z=4.2(P<0.0001)							
Test for subgroup differences: Not applicable							

Favours vitamin D analogue -5 -2.5 0 2.5 5 Favours corticosteroid (potent)

Analysis 7.5. Comparison 7 Vitamin D analogues versus corticosteroid (potent), Outcome 5 Combined end point (IAGI/TSS/PASI/PAGI).

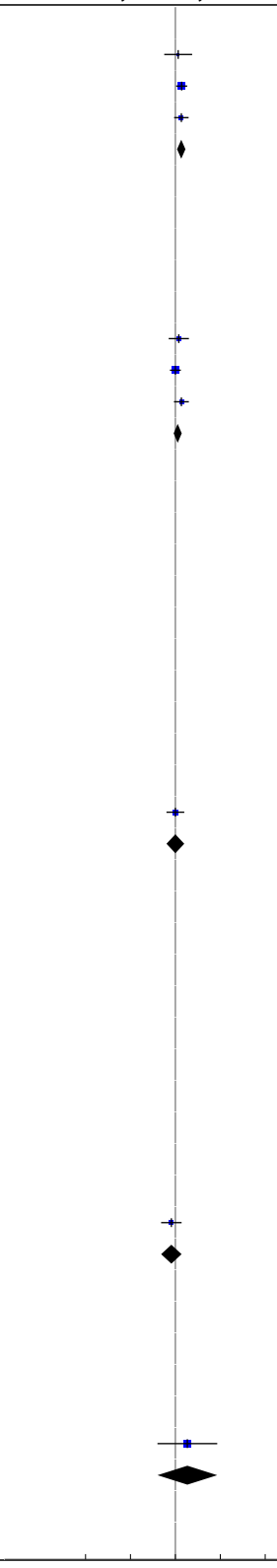
Study or subgroup	Vitamin D analogue N	Vitamin D analogue Mean(SD)	Corticosteroid (potent) N	Corticosteroid (potent) Mean(SD)	Std. Mean Difference Random, 95% CI	Weight	Std. Mean Difference Random, 95% CI
7.5.1 Calcipotriol vs. betamethasone dipropionate							
Fleming 2010 (H)	74	2.3 (0.8)	78	2 (1.1)		16.58%	0.28[-0.04,0.6]
Kaufmann 2002 (H)	480	2.2 (0.9)	476	1.9 (0.9)		45.33%	0.37[0.24,0.5]
Papp 2003 (H)	308	-2.8 (1.2)	312	-3.4 (1.1)		38.09%	0.56[0.4,0.72]
Subtotal ***	**862**		**866**			**100%**	**0.43[0.28,0.58]**
Heterogeneity: Tau^2=0.01; Chi^2=4.03, df=2(P=0.13); I^2=50.33%							
Test for overall effect: Z=5.57(P<0.0001)							
7.5.2 Calcipotriol vs. betamethasone valerate							
Cunliffe 1992	201	-5.5 (5.8)	200	-5.3 (6)		28.21%	-0.03[-0.23,0.17]

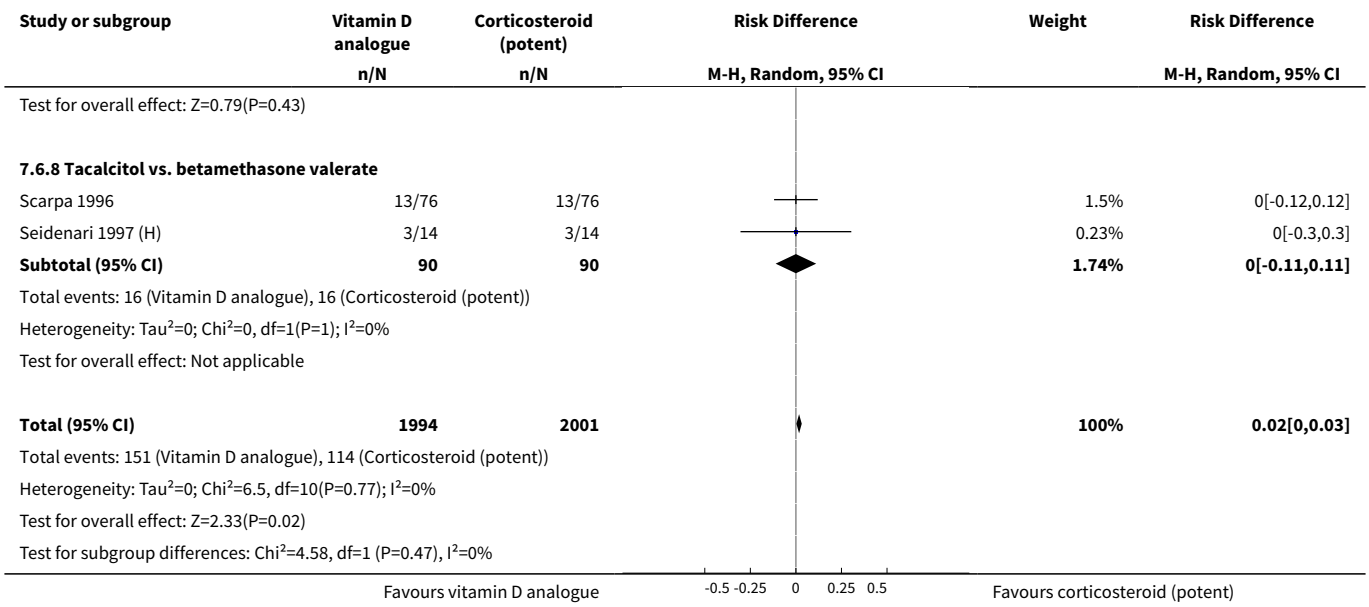
Favours vitamin D analogue -5 -2.5 0 2.5 5 Favours corticosteroid (potent)



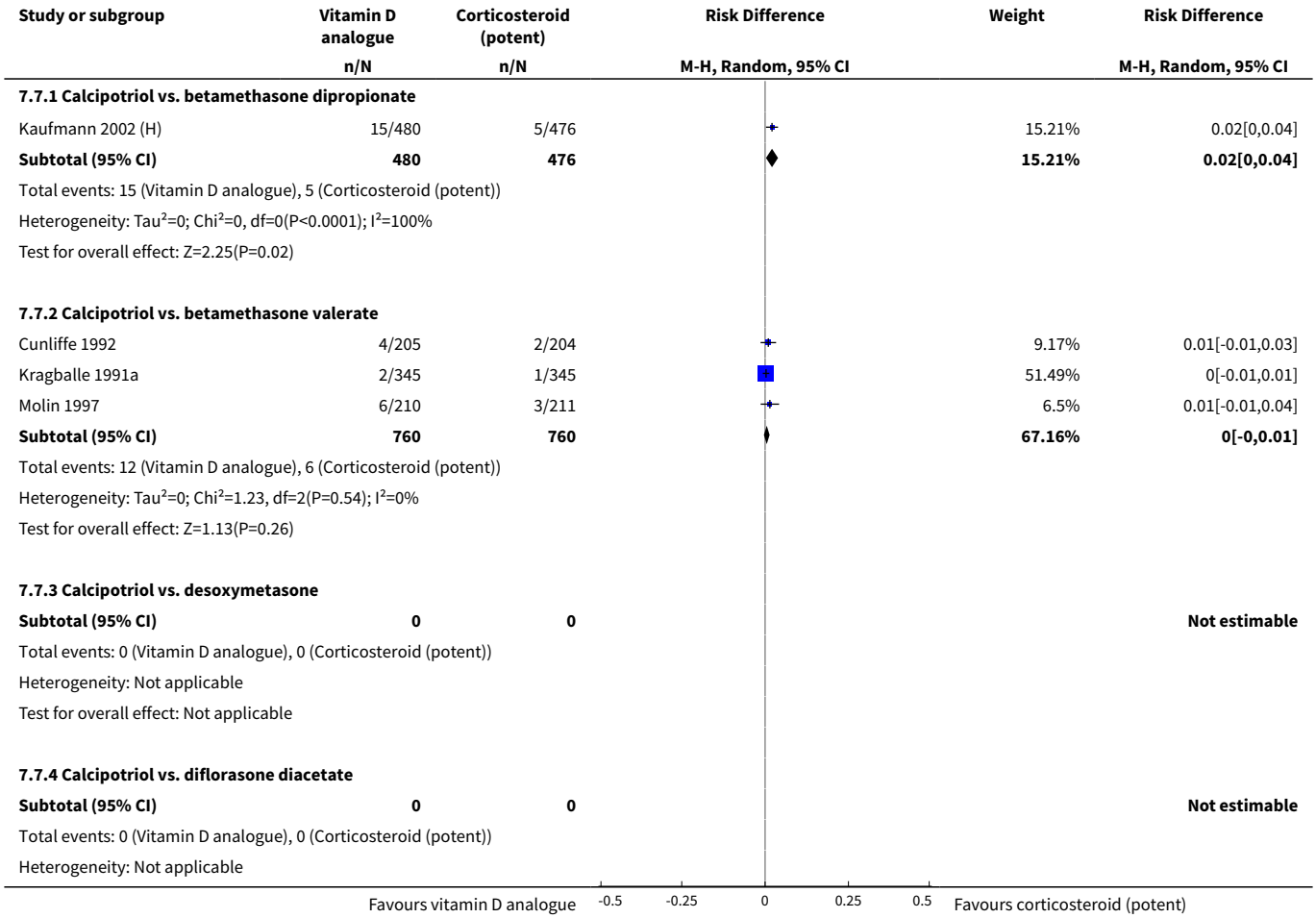
Analysis 7.6. Comparison 7 Vitamin D analogues versus corticosteroid (potent), Outcome 6 Total withdrawals.

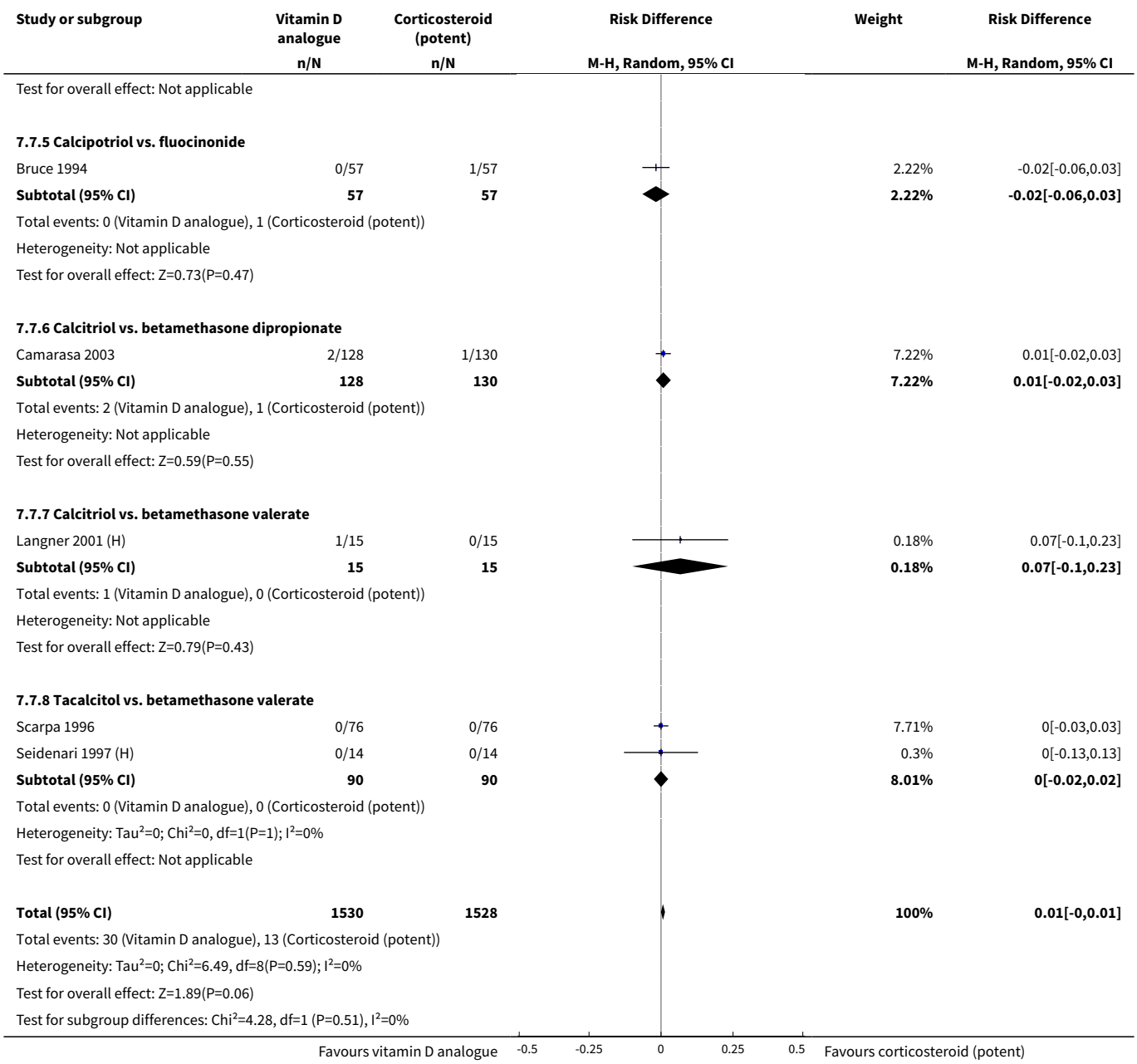
Study or subgroup	Vitamin D analogue n/N	Corticosteroid (potent) n/N	Risk Difference M-H, Random, 95% CI	Weight	Risk Difference M-H, Random, 95% CI
7.6.1 Calcipotriol vs. betamethasone dipropionate					
Fleming 2010 (H)	6/79	5/83		3.57%	0.02[-0.06,0.09]
Kaufmann 2002 (H)	39/480	22/476		22.62%	0.04[0,0.07]
Papp 2003 (H)	27/308	17/313		13.24%	0.03[-0.01,0.07]
Subtotal (95% CI)	**867**	**872**		**39.43%**	**0.03[0.01,0.06]**
Total events: 72 (Vitamin D analogue), 44 (Corticosteroid (potent))					
Heterogeneity: $Tau^2=0$; $Chi^2=0.21$, df=2(P=0.9); $I^2=0\%$					
Test for overall effect: Z=2.74(P=0.01)					
7.6.2 Calcipotriol vs. betamethasone valerate					
Cunliffe 1992	21/205	17/204		6.82%	0.02[-0.04,0.08]
Kragballe 1991a	15/345	15/345		23.28%	0[-0.03,0.03]
Molin 1997	14/210	7/211		12.52%	0.03[-0.01,0.07]
Subtotal (95% CI)	**760**	**760**		**42.61%**	**0.01[-0.01,0.04]**
Total events: 50 (Vitamin D analogue), 39 (Corticosteroid (potent))					
Heterogeneity: $Tau^2=0$; $Chi^2=1.7$, df=2(P=0.43); $I^2=0\%$					
Test for overall effect: Z=1.12(P=0.26)					
7.6.3 Calcipotriol vs. desoxymetasone					
Subtotal (95% CI)	**0**	**0**			**Not estimable**
Total events: 0 (Vitamin D analogue), 0 (Corticosteroid (potent))					
Heterogeneity: Not applicable					
Test for overall effect: Not applicable					
7.6.4 Calcipotriol vs. diflorasone diacetate					
Medansky 1996	6/134	6/134		8.79%	0[-0.05,0.05]
Subtotal (95% CI)	**134**	**134**		**8.79%**	**0[-0.05,0.05]**
Total events: 6 (Vitamin D analogue), 6 (Corticosteroid (potent))					
Heterogeneity: Not applicable					
Test for overall effect: Not applicable					
7.6.5 Calcipotriol vs. fluocinonide					
Subtotal (95% CI)	**0**	**0**			**Not estimable**
Total events: 0 (Vitamin D analogue), 0 (Corticosteroid (potent))					
Heterogeneity: Not applicable					
Test for overall effect: Not applicable					
7.6.6 Calcitriol vs. betamethasone dipropionate					
Camarasa 2003	6/128	9/130		6.64%	-0.02[-0.08,0.03]
Subtotal (95% CI)	**128**	**130**		**6.64%**	**-0.02[-0.08,0.03]**
Total events: 6 (Vitamin D analogue), 9 (Corticosteroid (potent))					
Heterogeneity: Not applicable					
Test for overall effect: Z=0.77(P=0.44)					
7.6.7 Calcitriol vs. betamethasone valerate					
Langner 2001 (H)	1/15	0/15		0.78%	0.07[-0.1,0.23]
Subtotal (95% CI)	**15**	**15**		**0.78%**	**0.07[-0.1,0.23]**
Total events: 1 (Vitamin D analogue), 0 (Corticosteroid (potent))					
Heterogeneity: Not applicable					



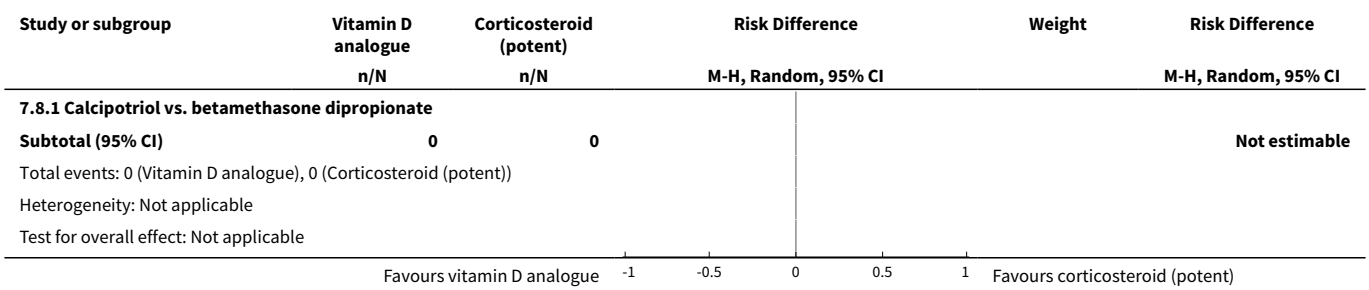


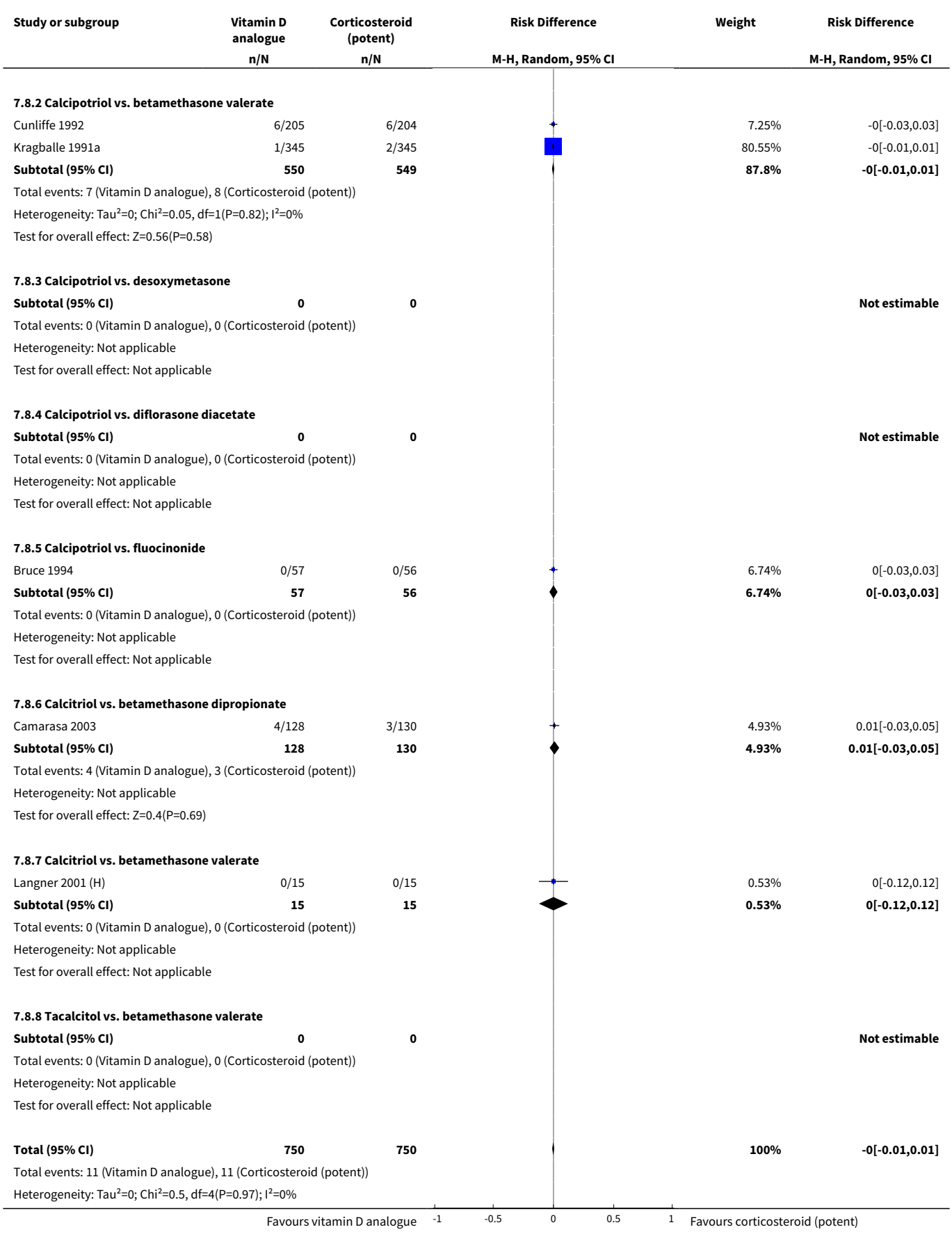
Analysis 7.7. Comparison 7 Vitamin D analogues versus corticosteroid (potent), Outcome 7 Withdrawals due to adverse events.





Analysis 7.8. Comparison 7 Vitamin D analogues versus corticosteroid (potent), Outcome 8 Withdrawals due to treatment failure.





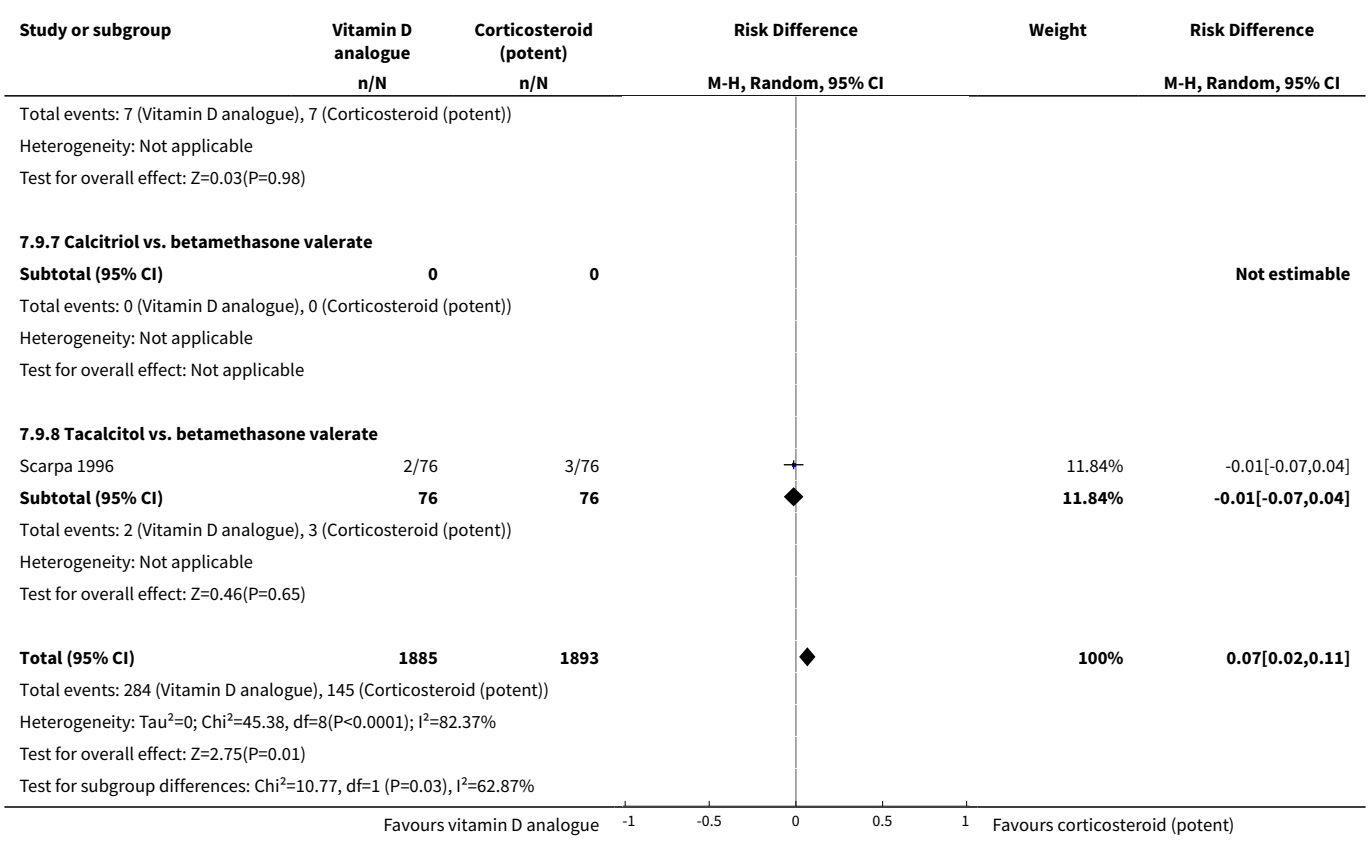
Study or subgroup	Vitamin D analogue n/N	Corticosteroid (potent) n/N	Risk Difference M-H, Random, 95% CI	Weight	Risk Difference M-H, Random, 95% CI
Test for overall effect: Z=0.43(P=0.67)					
Test for subgroup differences: Chi^2=0.29, df=1 (P=0.96), I^2=0%					

Favours vitamin D analogue -1 -0.5 0 0.5 1 Favours corticosteroid (potent)

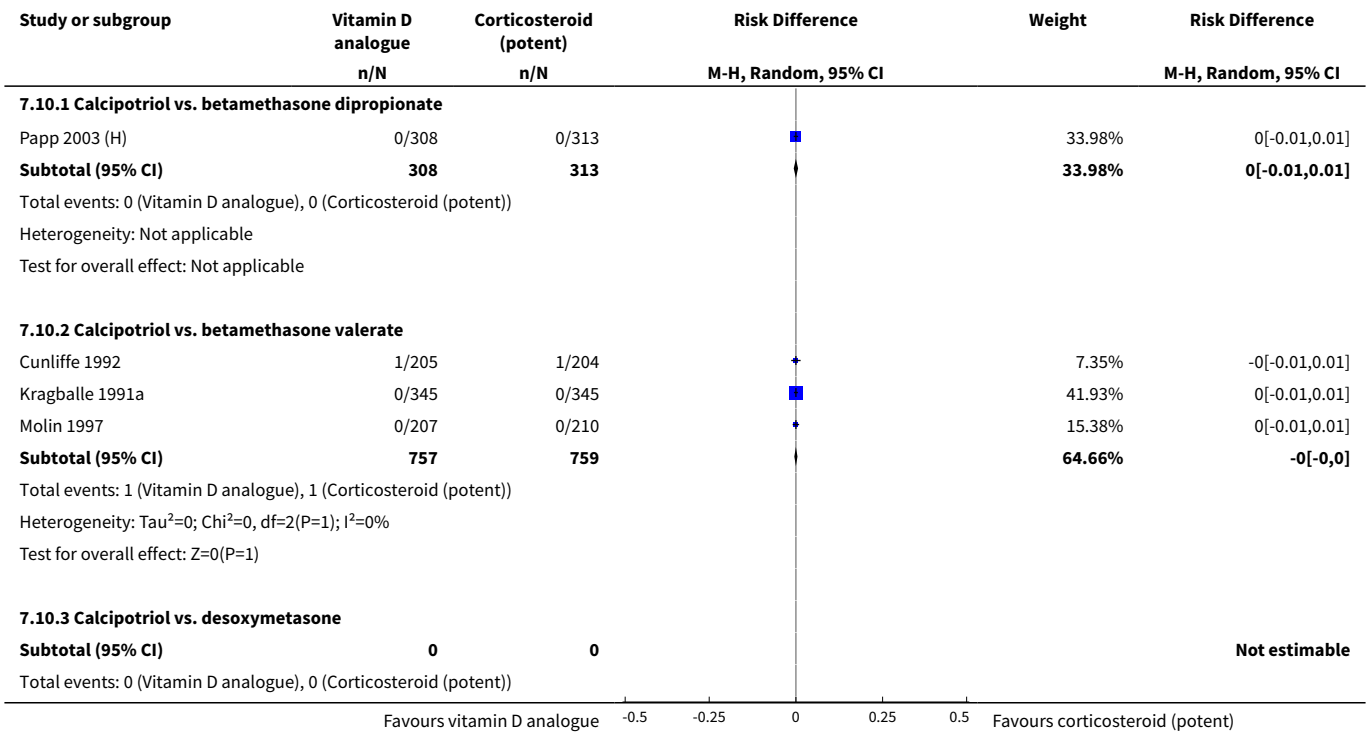
Analysis 7.9. Comparison 7 Vitamin D analogues versus corticosteroid (potent), Outcome 9 Adverse events (local).

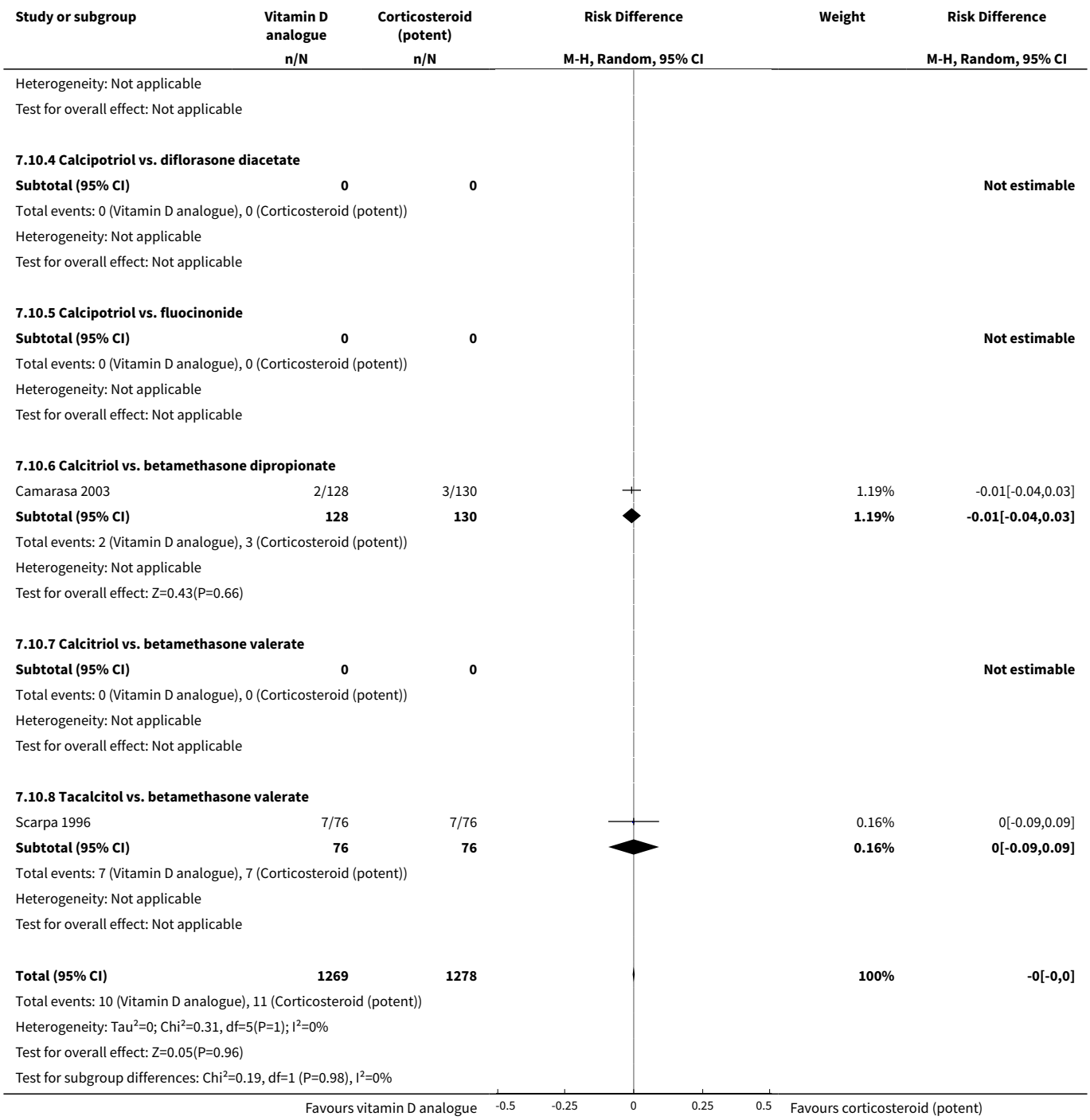
Study or subgroup	Vitamin D analogue n/N	Corticosteroid (potent) n/N	Risk Difference M-H, Random, 95% CI	Weight	Risk Difference M-H, Random, 95% CI
7.9.1 Calcipotriol vs. betamethasone dipropionate					
Fleming 2010 (H)	8/79	7/83		9.41%	0.02[-0.07,0.11]
Kaufmann 2002 (H)	54/480	23/476		13.31%	0.06[0.03,0.1]
Papp 2003 (H)	53/308	27/313		12.15%	0.09[0.03,0.14]
Subtotal (95% CI)	**867**	**872**		**34.87%**	**0.07[0.04,0.09]**
Total events: 115 (Vitamin D analogue), 57 (Corticosteroid (potent))					
Heterogeneity: Tau^2=0; Chi^2=1.73, df=2(P=0.42); I^2=0%					
Test for overall effect: Z=4.72(P<0.0001)					
7.9.2 Calcipotriol vs. betamethasone valerate					
Cunliffe 1992	64/205	18/204		10.52%	0.22[0.15,0.3]
Kragballe 1991a	37/345	35/345		12.61%	0.01[-0.04,0.05]
Molin 1997	49/207	21/210		10.8%	0.14[0.07,0.21]
Subtotal (95% CI)	**757**	**759**		**33.93%**	**0.12[-0.02,0.26]**
Total events: 150 (Vitamin D analogue), 74 (Corticosteroid (potent))					
Heterogeneity: Tau^2=0.01; Chi^2=28.15, df=2(P<0.0001); I^2=92.9%					
Test for overall effect: Z=1.72(P=0.08)					
7.9.3 Calcipotriol vs. desoxymetasone					
Subtotal (95% CI)	**0**	**0**			**Not estimable**
Total events: 0 (Vitamin D analogue), 0 (Corticosteroid (potent))					
Heterogeneity: Not applicable					
Test for overall effect: Not applicable					
7.9.4 Calcipotriol vs. diflorasone diacetate					
Subtotal (95% CI)	**0**	**0**			**Not estimable**
Total events: 0 (Vitamin D analogue), 0 (Corticosteroid (potent))					
Heterogeneity: Not applicable					
Test for overall effect: Not applicable					
7.9.5 Calcipotriol vs. fluocinonide					
Bruce 1994	10/57	4/56		7.41%	0.1[-0.02,0.22]
Subtotal (95% CI)	**57**	**56**		**7.41%**	**0.1[-0.02,0.22]**
Total events: 10 (Vitamin D analogue), 4 (Corticosteroid (potent))					
Heterogeneity: Not applicable					
Test for overall effect: Z=1.7(P=0.09)					
7.9.6 Calcitriol vs. betamethasone dipropionate					
Camarasa 2003	7/128	7/130		11.94%	0[-0.05,0.06]
Subtotal (95% CI)	**128**	**130**		**11.94%**	**0[-0.05,0.06]**

Favours vitamin D analogue -1 -0.5 0 0.5 1 Favours corticosteroid (potent)



Analysis 7.10. Comparison 7 Vitamin D analogues versus corticosteroid (potent), Outcome 10 Adverse events (systemic).





Comparison 8. Vitamin D analogues versus corticosteroid (very potent)

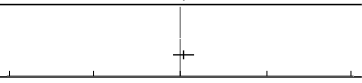
Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 IAGI	1		Std. Mean Difference (IV, Random, 95% CI)	Totals not selected

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1.1 Calcipotriol vs. Clobetasol propionate	1		Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
2 TSS	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
2.1 Calcipotriol vs. Clobetasol propionate	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
3 PASI	1		Std. Mean Difference (IV, Random, 95% CI)	Totals not selected
3.1 Calcipotriol vs. Clobetasol propionate	1		Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
4 PAGI	1		Std. Mean Difference (IV, Random, 95% CI)	Totals not selected
4.1 Calcipotriol vs. Clobetasol propionate	1		Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
5 Combined end point (IAGI/TSS/PASI/PAGI)	2	82	Std. Mean Difference (IV, Random, 95% CI)	-0.06 [-0.57, 0.44]
5.1 Calcipotriol vs. Clobetasol propionate	2	82	Std. Mean Difference (IV, Random, 95% CI)	-0.06 [-0.57, 0.44]
6 Total withdrawals	1		Risk Difference (M-H, Random, 95% CI)	Totals not selected
6.1 Calcipotriol vs. Clobetasol propionate	1		Risk Difference (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
7 Withdrawals due to adverse events	1		Risk Difference (M-H, Random, 95% CI)	Totals not selected
7.1 Calcipotriol vs. Clobetasol propionate	1		Risk Difference (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
8 Withdrawals due to treatment failure	1		Risk Difference (M-H, Random, 95% CI)	Totals not selected
8.1 Calcipotriol vs. Clobetasol propionate	1		Risk Difference (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
9 Adverse events (local)	1		Risk Difference (M-H, Random, 95% CI)	Totals not selected
9.1 Calcipotriol vs. Clobetasol propionate	1		Risk Difference (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
10 Adverse events (systemic)	1		Risk Difference (M-H, Random, 95% CI)	Totals not selected

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
10.1 Calcipotriol vs. Clobetasol propionate	1		Risk Difference (M-H, Random, 95% CI)	0.0 [0.0, 0.0]

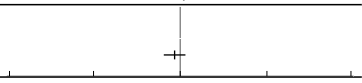
Analysis 8.1. Comparison 8 Vitamin D analogues versus corticosteroid (very potent), Outcome 1 IAGI.

Study or subgroup	Vitamin D analogue N	Vitamin D analogue Mean(SD)	Corticosteroid (v potent) N	Corticosteroid (v potent) Mean(SD)	Std. Mean Difference Random, 95% CI	Std. Mean Difference Random, 95% CI
8.1.1 Calcipotriol vs. Clobetasol propionate						
Koo 2006	21	3.2 (1.2)	21	2.9 (1.2)		0.19[-0.42,0.8]



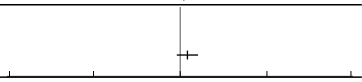
Analysis 8.3. Comparison 8 Vitamin D analogues versus corticosteroid (very potent), Outcome 3 PASI.

Study or subgroup	Vitamin D analogue N	Vitamin D analogue Mean(SD)	Corticosteroid (v potent) N	Corticosteroid (v potent) Mean(SD)	Std. Mean Difference Random, 95% CI	Std. Mean Difference Random, 95% CI
8.3.1 Calcipotriol vs. Clobetasol propionate						
Landi 1993	20	1.3 (1.4)	20	2 (2.6)		-0.32[-0.95,0.3]



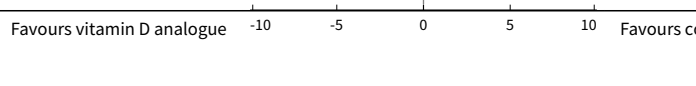
Analysis 8.4. Comparison 8 Vitamin D analogues versus corticosteroid (very potent), Outcome 4 PAGI.

Study or subgroup	Vitamin D analogue N	Vitamin D analogue Mean(SD)	Corticosteroid (v potent) N	Corticosteroid (v potent) Mean(SD)	Std. Mean Difference Random, 95% CI	Std. Mean Difference Random, 95% CI
8.4.1 Calcipotriol vs. Clobetasol propionate						
Koo 2006	21	3.3 (1.3)	21	2.7 (1.3)		0.42[-0.2,1.03]

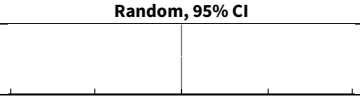


Analysis 8.5. Comparison 8 Vitamin D analogues versus corticosteroid (very potent), Outcome 5 Combined end point (IAGI/TSS/PASI/PAGI).

Study or subgroup	Vitamin D analogue N	Vitamin D analogue Mean(SD)	Corticosteroid (v potent) N	Corticosteroid (v potent) Mean(SD)	Std. Mean Difference Random, 95% CI	Weight	Std. Mean Difference Random, 95% CI
8.5.1 Calcipotriol vs. Clobetasol propionate							
Koo 2006	21	3.2 (1.2)	21	2.9 (1.2)		51.08%	0.19[-0.42,0.8]
Landi 1993	20	1.3 (1.4)	20	2 (2.6)		48.92%	-0.32[-0.95,0.3]
Subtotal ***	**41**		**41**			**100%**	**-0.06[-0.57,0.44]**
Heterogeneity: Tau²=0.03; Chi²=1.35, df=1(P=0.25); I²=25.69%							
Test for overall effect: Z=0.24(P=0.81)							
Total ***	**41**		**41**			**100%**	**-0.06[-0.57,0.44]**

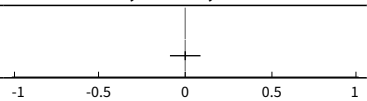


Study or subgroup	Vitamin D analogue		Corticosteroid (v potent)		Std. Mean Difference	Weight	Std. Mean Difference
	N	Mean(SD)	N	Mean(SD)	Random, 95% CI		Random, 95% CI
Heterogeneity: Tau²=0.03; Chi²=1.35, df=1(P=0.25); I²=25.69%							
Test for overall effect: Z=0.24(P=0.81)							



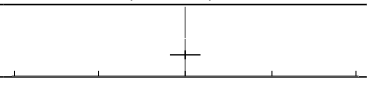
Analysis 8.6. Comparison 8 Vitamin D analogues versus corticosteroid (very potent), Outcome 6 Total withdrawals.

Study or subgroup	Vitamin D analogue n/N	Corticosteroid (v potent) n/N	Risk Difference M-H, Random, 95% CI	Risk Difference M-H, Random, 95% CI
8.6.1 Calcipotriol vs. Clobetasol propionate				
Koo 2006	0/21	0/21		0[-0.09,0.09]



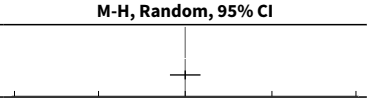
Analysis 8.7. Comparison 8 Vitamin D analogues versus corticosteroid (very potent), Outcome 7 Withdrawals due to adverse events.

Study or subgroup	Vitamin D analogue n/N	Corticosteroid (v potent) n/N	Risk Difference M-H, Random, 95% CI	Risk Difference M-H, Random, 95% CI
8.7.1 Calcipotriol vs. Clobetasol propionate				
Koo 2006	0/21	0/21		0[-0.09,0.09]



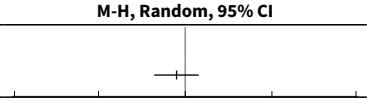
Analysis 8.8. Comparison 8 Vitamin D analogues versus corticosteroid (very potent), Outcome 8 Withdrawals due to treatment failure.

Study or subgroup	Vitamin D analogue n/N	Corticosteroid (v potent) n/N	Risk Difference M-H, Random, 95% CI	Risk Difference M-H, Random, 95% CI
8.8.1 Calcipotriol vs. Clobetasol propionate				
Koo 2006	0/21	0/21		0[-0.09,0.09]



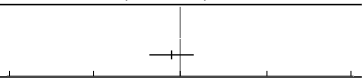
Analysis 8.9. Comparison 8 Vitamin D analogues versus corticosteroid (very potent), Outcome 9 Adverse events (local).

Study or subgroup	Vitamin D analogue n/N	Corticosteroid (v potent) n/N	Risk Difference M-H, Random, 95% CI	Risk Difference M-H, Random, 95% CI
8.9.1 Calcipotriol vs. Clobetasol propionate				
Landi 1993	0/20	1/20		-0.05[-0.18,0.08]



Analysis 8.10. Comparison 8 Vitamin D analogues versus corticosteroid (very potent), Outcome 10 Adverse events (systemic).

Study or subgroup	Vitamin D analogue n/N	Corticosteroid (v potent) n/N	Risk Difference M-H, Random, 95% CI	Risk Difference M-H, Random, 95% CI
8.10.1 Calcipotriol vs. Clobetasol propionate				
Landi 1993	0/20	1/20		-0.05[-0.18,0.08]



Comparison 9. Vitamin D combined with corticosteroid versus corticosteroid

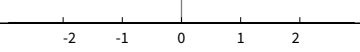
Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 IAGI	4		Std. Mean Difference (IV, Random, 95% CI)	Subtotals only
1.1 Calcipotriol + betamethasone dipropionate vs. betamethasone dipropionate	3	1926	Std. Mean Difference (IV, Random, 95% CI)	-0.40 [-0.52, -0.27]
1.2 Calcipotriol + betamethasone dipropionate vs. clobetasol propionate	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
1.3 Calcipotriol + clobetasol propionate vs. clobetasol propionate	1	65	Std. Mean Difference (IV, Random, 95% CI)	-0.69 [-1.22, -0.15]
2 TSS	1		Std. Mean Difference (IV, Random, 95% CI)	Totals not selected
2.1 Calcipotriol + betamethasone dipropionate vs. betamethasone dipropionate	0		Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
2.2 Calcipotriol + betamethasone dipropionate vs. clobetasol propionate	1		Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
2.3 Calcipotriol + clobetasol propionate vs. clobetasol propionate	0		Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
3 PASI	3	1876	Std. Mean Difference (IV, Random, 95% CI)	-0.44 [-0.55, -0.33]
3.1 Calcipotriol + betamethasone dipropionate vs. betamethasone dipropionate	3	1876	Std. Mean Difference (IV, Random, 95% CI)	-0.44 [-0.55, -0.33]
3.2 Calcipotriol + betamethasone dipropionate vs. clobetasol propionate	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
3.3 Calcipotriol + clobetasol propionate vs. clobetasol propionate	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
4 PAGI	1		Std. Mean Difference (IV, Random, 95% CI)	Totals not selected

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
4.1 Calcipotriol + betamethasone dipropionate vs. betamethasone dipropionate	0		Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
4.2 Calcipotriol + betamethasone dipropionate vs. clobetasol propionate	0		Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
4.3 Calcipotriol + clobetasol propionate vs. clobetasol propionate	1		Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
5 Combined end point (IAGI/TSS/PASI/PAGI)	5		Std. Mean Difference (IV, Random, 95% CI)	Subtotals only
5.1 Calcipotriol + betamethasone dipropionate vs. betamethasone dipropionate	3	1926	Std. Mean Difference (IV, Random, 95% CI)	-0.40 [-0.52, -0.27]
5.2 Calcipotriol + betamethasone dipropionate vs. clobetasol propionate	1	122	Std. Mean Difference (IV, Random, 95% CI)	0.45 [0.09, 0.81]
5.3 Calcipotriol + clobetasol propionate vs. clobetasol propionate	1	65	Std. Mean Difference (IV, Random, 95% CI)	-0.69 [-1.22, -0.15]
6 Total withdrawals	5	2135	Risk Difference (M-H, Random, 95% CI)	-0.00 [-0.02, 0.01]
6.1 Calcipotriol + betamethasone dipropionate vs. betamethasone dipropionate	3	1948	Risk Difference (M-H, Random, 95% CI)	-0.00 [-0.03, 0.03]
6.2 Calcipotriol + betamethasone dipropionate vs. clobetasol propionate	1	122	Risk Difference (M-H, Random, 95% CI)	0.0 [-0.03, 0.03]
6.3 Calcipotriol + clobetasol propionate vs. clobetasol propionate	1	65	Risk Difference (M-H, Random, 95% CI)	0.0 [-0.07, 0.07]
7 Withdrawals due to adverse events	3		Risk Difference (M-H, Random, 95% CI)	Totals not selected
7.1 Calcipotriol + betamethasone dipropionate vs. betamethasone dipropionate	1		Risk Difference (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
7.2 Calcipotriol + betamethasone dipropionate vs. clobetasol propionate	1		Risk Difference (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
7.3 Calcipotriol + clobetasol propionate vs. clobetasol propionate	1		Risk Difference (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
8 Withdrawals due to treatment failure	2		Risk Difference (M-H, Random, 95% CI)	Totals not selected
8.1 Calcipotriol + betamethasone dipropionate vs. betamethasone dipropionate	0		Risk Difference (M-H, Random, 95% CI)	0.0 [0.0, 0.0]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
8.2 Calcipotriol + betamethasone dipropionate vs. clobetasol propionate	1		Risk Difference (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
8.3 Calcipotriol + clobetasol propionate vs. clobetasol propionate	1		Risk Difference (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
9 Adverse events (local)	4		Risk Difference (M-H, Random, 95% CI)	Subtotals only
9.1 Calcipotriol + betamethasone dipropionate vs. betamethasone dipropionate	3	1946	Risk Difference (M-H, Random, 95% CI)	0.02 [-0.00, 0.04]
9.2 Calcipotriol + betamethasone dipropionate vs. clobetasol propionate	1	122	Risk Difference (M-H, Random, 95% CI)	-0.04 [-0.13, 0.06]
9.3 Calcipotriol + clobetasol propionate vs. clobetasol propionate	0	0	Risk Difference (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
10 Adverse events (systemic)	1		Risk Difference (M-H, Random, 95% CI)	Totals not selected
10.1 Calcipotriol + betamethasone dipropionate vs. betamethasone dipropionate	1		Risk Difference (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
10.2 Calcipotriol + betamethasone dipropionate vs. clobetasol propionate	0		Risk Difference (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
10.3 Calcipotriol + clobetasol propionate vs. clobetasol propionate	0		Risk Difference (M-H, Random, 95% CI)	0.0 [0.0, 0.0]

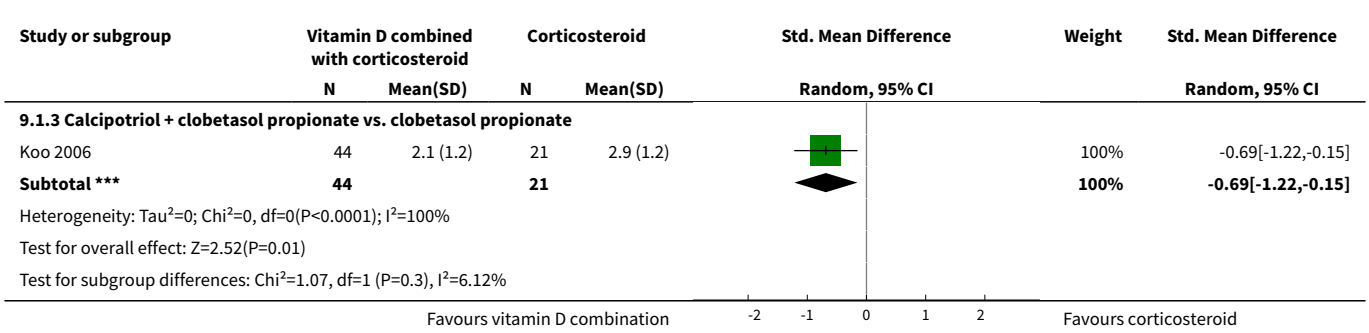
Analysis 9.1. Comparison 9 Vitamin D combined with corticosteroid versus corticosteroid, Outcome 1 IAGI.

Study or subgroup	Vitamin D combined with corticosteroid N	Mean(SD)	Corticosteroid N	Mean(SD)	Std. Mean Difference Random, 95% CI	Weight	Std. Mean Difference Random, 95% CI
9.1.1 Calcipotriol + betamethasone dipropionate vs. betamethasone dipropionate							
Douglas 2002	369	-3.7 (1)	363	-3.2 (1.1)		38.73%	-0.46[-0.6,-0.31]
Fleming 2010 (H)	150	1.9 (1.1)	78	2 (1.1)		16.98%	-0.17[-0.44,0.1]
Kaufmann 2002 (H)	490	1.5 (0.9)	476	1.9 (0.9)		44.29%	-0.43[-0.56,-0.31]
Subtotal ***	**1009**		**917**			**100%**	**-0.4[-0.52,-0.27]**
Heterogeneity: Tau^2=0.01; Chi^2=3.44, df=2(P=0.18); I^2=41.8%							
Test for overall effect: Z=6.12(P<0.0001)							
9.1.2 Calcipotriol + betamethasone dipropionate vs. clobetasol propionate							
Subtotal ***	**0**		**0**				**Not estimable**
Heterogeneity: Not applicable							
Test for overall effect: Not applicable							

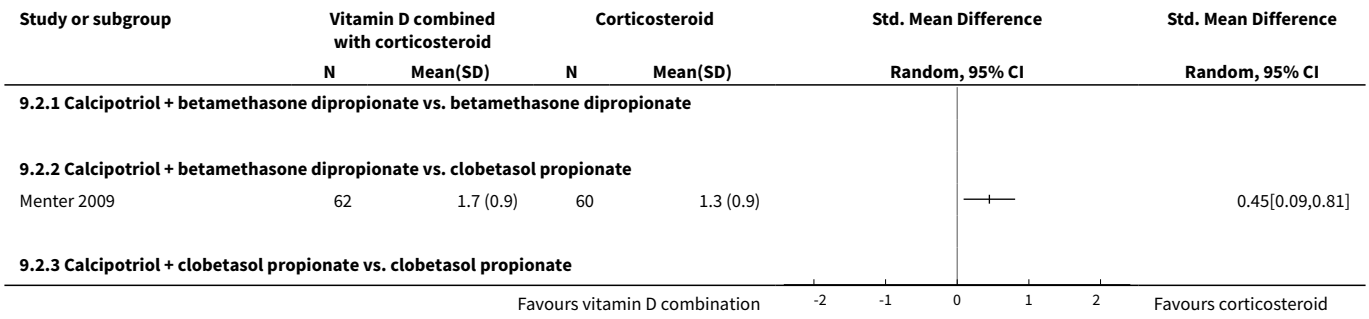


Favours vitamin D combination

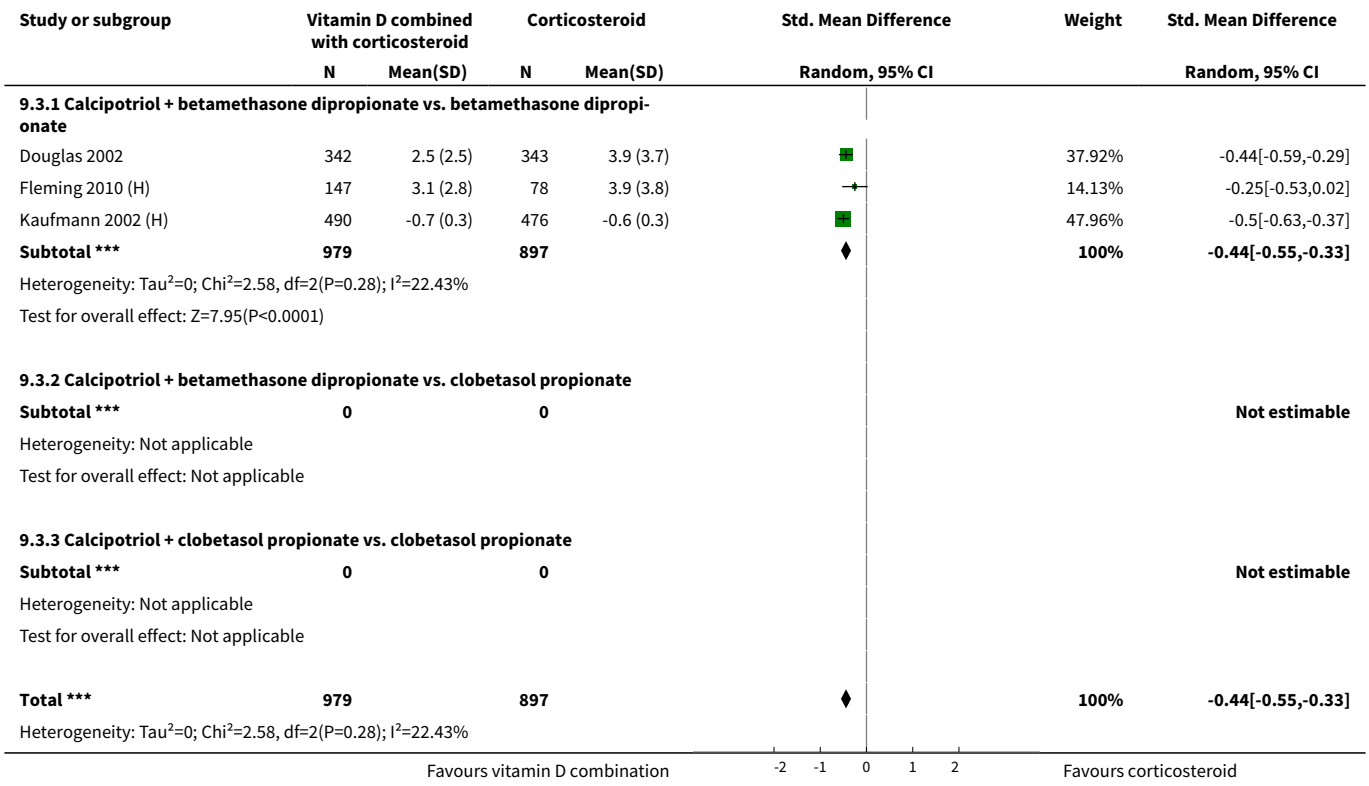
Favours corticosteroid



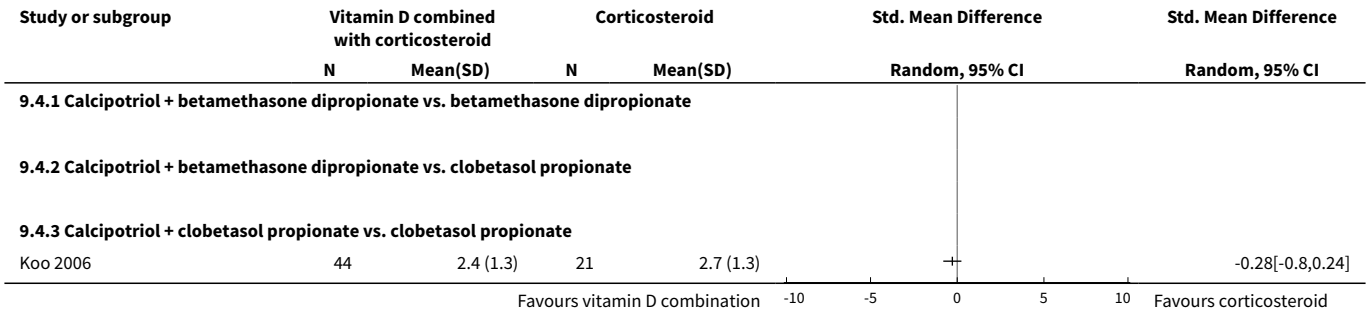
Analysis 9.2. Comparison 9 Vitamin D combined with corticosteroid versus corticosteroid, Outcome 2 TSS.



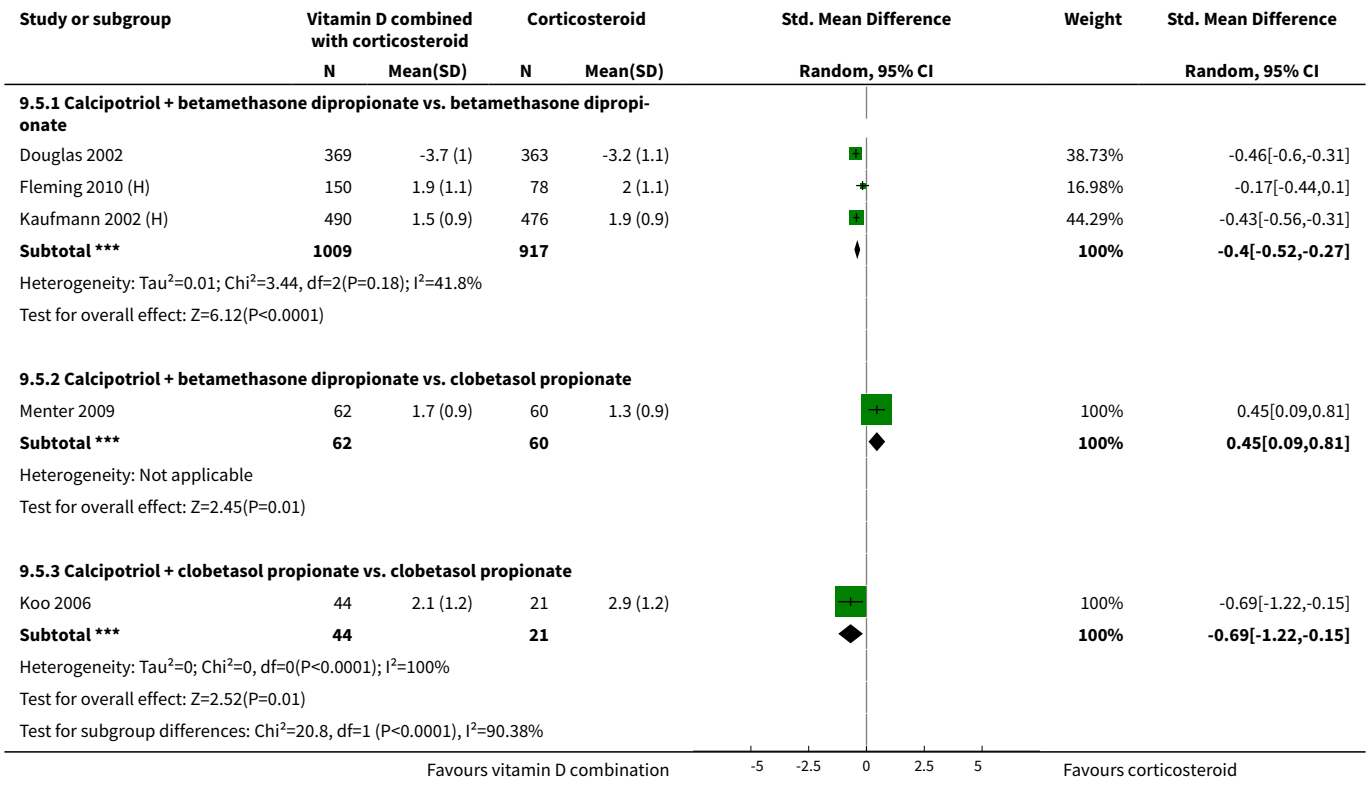
Analysis 9.3. Comparison 9 Vitamin D combined with corticosteroid versus corticosteroid, Outcome 3 PASI.



Analysis 9.4. Comparison 9 Vitamin D combined with corticosteroid versus corticosteroid, Outcome 4 PAGI.

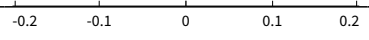


Analysis 9.5. Comparison 9 Vitamin D combined with corticosteroid versus corticosteroid, Outcome 5 Combined end point (IAGI/TSS/PASI/PAGI).



Analysis 9.6. Comparison 9 Vitamin D combined with corticosteroid versus corticosteroid, Outcome 6 Total withdrawals.

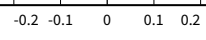
Study or subgroup	Vitamin D combined with corticosteroid n/N	Corticosteroid n/N	Risk Difference M-H, Random, 95% CI	Weight	Risk Difference M-H, Random, 95% CI
9.6.1 Calcipotriol + betamethasone dipropionate vs. betamethasone dipropionate					
Douglas 2002	28/372	21/365		19.33%	0.02[-0.02,0.05]
Fleming 2010 (H)	13/162	5/83		5.7%	0.02[-0.05,0.09]
Kaufmann 2002 (H)	13/490	22/476		44.66%	-0.02[-0.04,0]
Subtotal (95% CI)	**1024**	**924**		**69.69%**	**-0[-0.03,0.03]**
Total events: 54 (Vitamin D combined with corticosteroid), 48 (Corticosteroid)					
Heterogeneity: Tau^2=0; Chi^2=3.86, df=2(P=0.15); I^2=48.16%					
Test for overall effect: Z=0.01(P=0.99)					
9.6.2 Calcipotriol + betamethasone dipropionate vs. clobetasol propionate					
Menter 2009	0/62	0/60		25.13%	0[-0.03,0.03]
Subtotal (95% CI)	**62**	**60**		**25.13%**	**0[-0.03,0.03]**
Total events: 0 (Vitamin D combined with corticosteroid), 0 (Corticosteroid)					
Heterogeneity: Not applicable					
Test for overall effect: Not applicable					
9.6.3 Calcipotriol + clobetasol propionate vs. clobetasol propionate					
Koo 2006	0/44	0/21		5.18%	0[-0.07,0.07]
Subtotal (95% CI)	**44**	**21**		**5.18%**	**0[-0.07,0.07]**
Total events: 0 (Vitamin D combined with corticosteroid), 0 (Corticosteroid)					
Heterogeneity: Not applicable					
Test for overall effect: Not applicable					
Total (95% CI)	**1130**	**1005**		**100%**	**-0[-0.02,0.01]**
Total events: 54 (Vitamin D combined with corticosteroid), 48 (Corticosteroid)					
Heterogeneity: Tau^2=0; Chi^2=3.87, df=4(P=0.42); I^2=0%					
Test for overall effect: Z=0.52(P=0.6)					
Test for subgroup differences: Chi^2=0, df=1 (P=1), I^2=0%					



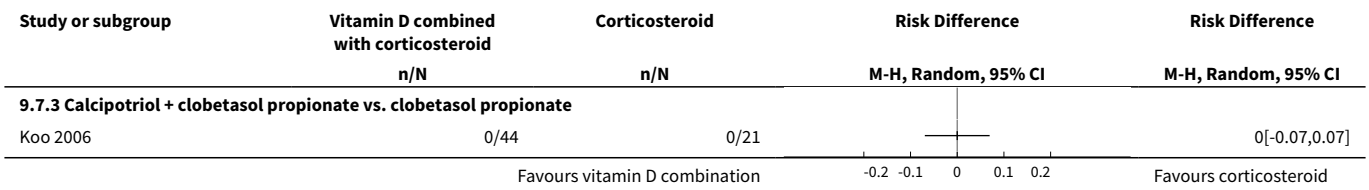
Favours vitamin D combination | Favours corticosteroid

Analysis 9.7. Comparison 9 Vitamin D combined with corticosteroid versus corticosteroid, Outcome 7 Withdrawals due to adverse events.

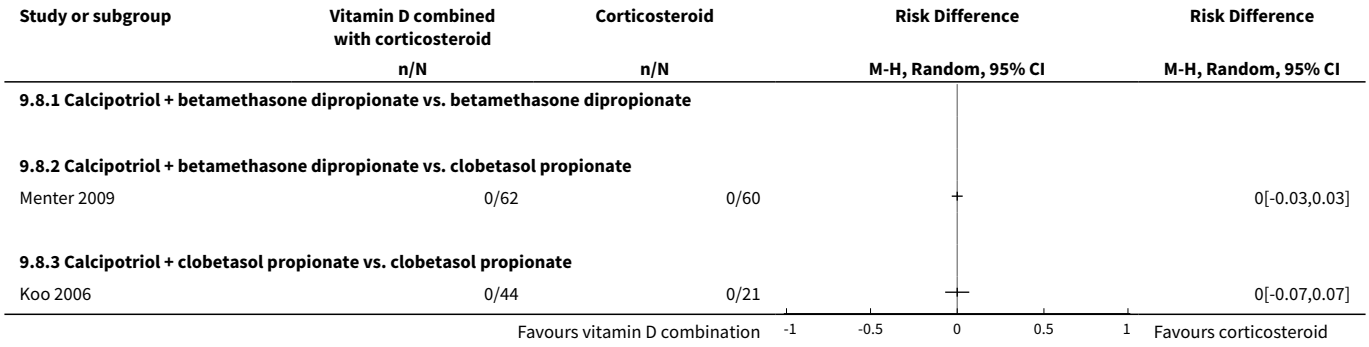
Study or subgroup	Vitamin D combined with corticosteroid n/N	Corticosteroid n/N	Risk Difference M-H, Random, 95% CI	Risk Difference M-H, Random, 95% CI
9.7.1 Calcipotriol + betamethasone dipropionate vs. betamethasone dipropionate				
Kaufmann 2002 (H)	3/490	5/476		-0[-0.02,0.01]
9.7.2 Calcipotriol + betamethasone dipropionate vs. clobetasol propionate				
Menter 2009	0/62	0/60		0[-0.03,0.03]



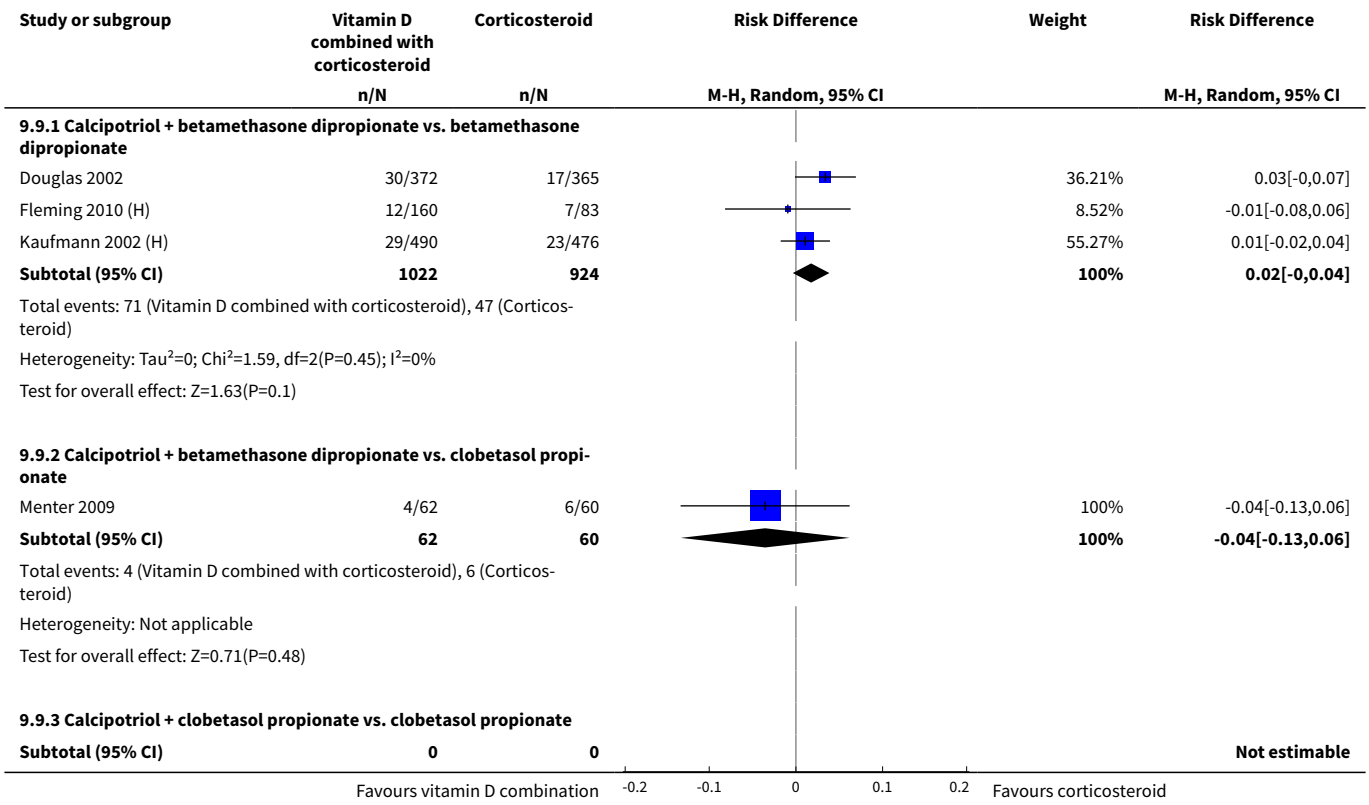
Favours vitamin D combination | Favours corticosteroid

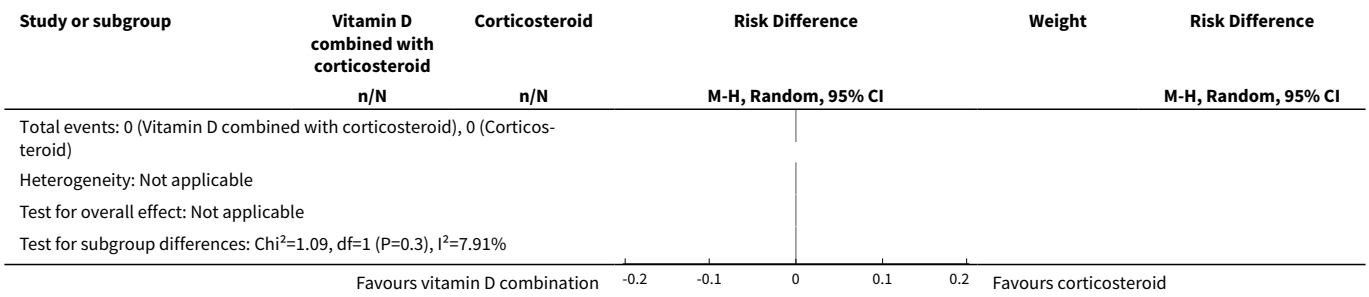


Analysis 9.8. Comparison 9 Vitamin D combined with corticosteroid versus corticosteroid, Outcome 8 Withdrawals due to treatment failure.

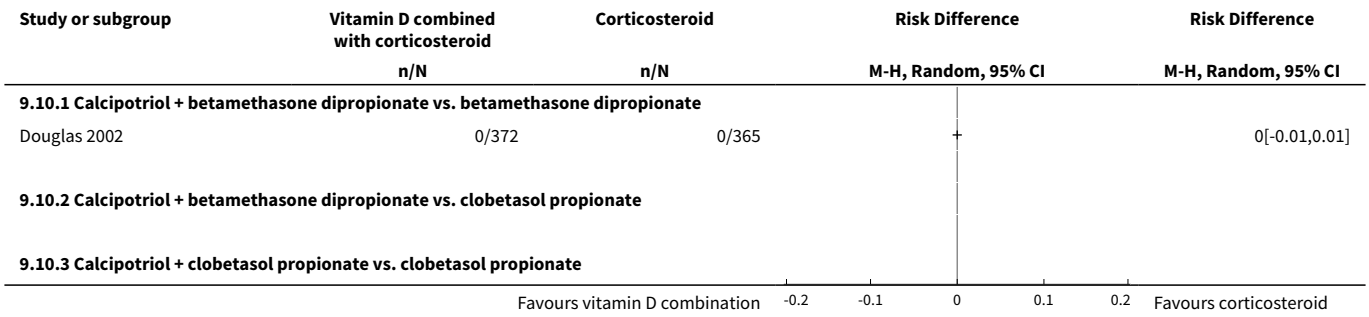


Analysis 9.9. Comparison 9 Vitamin D combined with corticosteroid versus corticosteroid, Outcome 9 Adverse events (local).





Analysis 9.10. Comparison 9 Vitamin D combined with corticosteroid versus corticosteroid, Outcome 10 Adverse events (systemic).



Comparison 10. Vitamin D alone or in combination versus dithranol

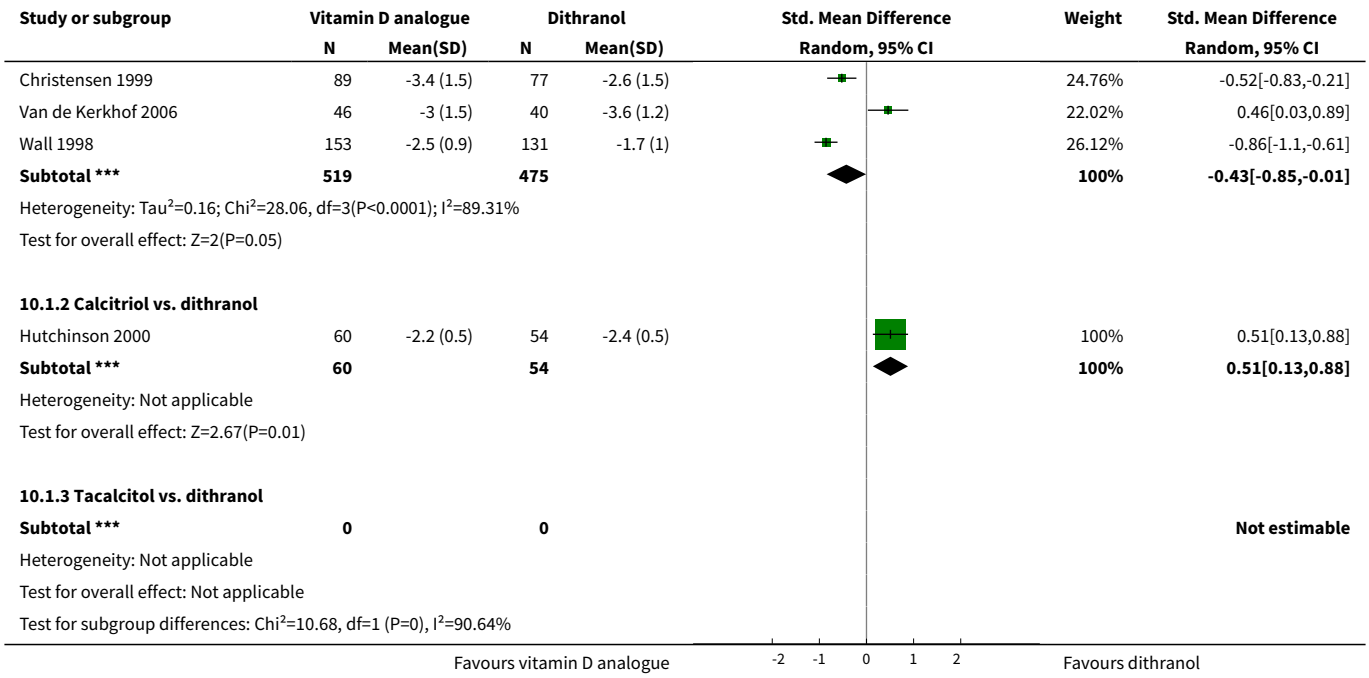
Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 IAGI	5		Std. Mean Difference (IV, Random, 95% CI)	Subtotals only
1.1 Calcipotriol vs. dithranol	4	994	Std. Mean Difference (IV, Random, 95% CI)	-0.43 [-0.85, -0.01]
1.2 Calcitriol vs. dithranol	1	114	Std. Mean Difference (IV, Random, 95% CI)	0.51 [0.13, 0.88]
1.3 Tacalcitol vs. dithranol	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
2 TSS	4		Std. Mean Difference (IV, Random, 95% CI)	Subtotals only
2.1 Calcipotriol vs. dithranol	2	210	Std. Mean Difference (IV, Random, 95% CI)	-0.54 [-1.16, 0.08]
2.2 Calcitriol vs. dithranol	1	114	Std. Mean Difference (IV, Random, 95% CI)	0.13 [-0.24, 0.50]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
2.3 Tacalcitol vs. dithranol	1	84	Std. Mean Difference (IV, Random, 95% CI)	-0.18 [-0.60, 0.25]
3 PASI	5		Std. Mean Difference (IV, Random, 95% CI)	Totals not selected
3.1 Calcipotriol vs. dithranol	3		Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
3.2 Calcitriol vs. dithranol	1		Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
3.3 Tacalcitol vs. dithranol	1		Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
4 PAGI	2		Std. Mean Difference (IV, Random, 95% CI)	Subtotals only
4.1 Calcipotriol vs. dithranol	2	544	Std. Mean Difference (IV, Random, 95% CI)	-0.05 [-0.90, 0.80]
4.2 Calcitriol vs. dithranol	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
4.3 Tacalcitol vs. dithranol	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
5 Combined end point (IAGI/TSS/PASI/PAGI)	8		Std. Mean Difference (IV, Random, 95% CI)	Totals not selected
5.1 Calcipotriol vs. dithranol	6		Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
5.2 Calcitriol vs. dithranol	1		Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
5.3 Tacalcitol vs. dithranol	1		Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
6 Total withdrawals	7	615	Risk Difference (M-H, Random, 95% CI)	-0.02 [-0.06, 0.01]
6.1 Calcipotriol vs. dithranol	5	417	Risk Difference (M-H, Random, 95% CI)	-0.01 [-0.07, 0.04]
6.2 Calcitriol vs. dithranol	1	114	Risk Difference (M-H, Random, 95% CI)	-0.10 [-0.25, 0.06]
6.3 Tacalcitol vs. dithranol	1	84	Risk Difference (M-H, Random, 95% CI)	-0.02 [-0.16, 0.11]
7 Withdrawals due to adverse events	7	1265	Risk Difference (M-H, Random, 95% CI)	-0.03 [-0.06, -0.00]

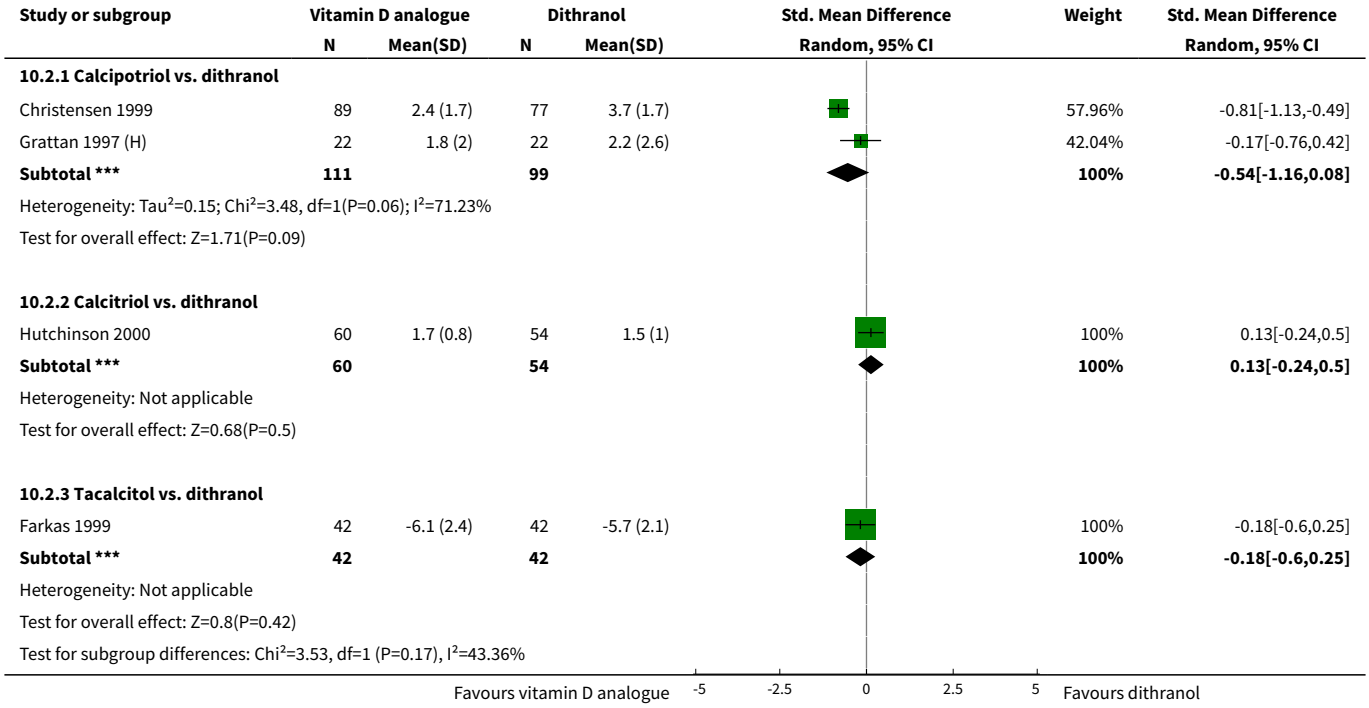
Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
7.1 Calcipotriol vs. dithranol	6	1151	Risk Difference (M-H, Random, 95% CI)	-0.03 [-0.06, 0.00]
7.2 Calcitriol vs. dithranol	1	114	Risk Difference (M-H, Random, 95% CI)	-0.06 [-0.13, 0.02]
7.3 Tacalcitol vs. dithranol	0	0	Risk Difference (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
8 Withdrawals due to treatment failure	5	788	Risk Difference (M-H, Random, 95% CI)	-0.00 [-0.02, 0.02]
8.1 Calcipotriol vs. dithranol	4	674	Risk Difference (M-H, Random, 95% CI)	0.00 [-0.02, 0.02]
8.2 Calcitriol vs. dithranol	1	114	Risk Difference (M-H, Random, 95% CI)	-0.02 [-0.08, 0.04]
8.3 Tacalcitol vs. dithranol	0	0	Risk Difference (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
9 Adverse events (local)	9	1543	Risk Difference (M-H, Random, 95% CI)	-0.32 [-0.43, -0.20]
9.1 Calcipotriol vs. dithranol	7	1345	Risk Difference (M-H, Random, 95% CI)	-0.25 [-0.32, -0.17]
9.2 Calcitriol vs. dithranol	1	114	Risk Difference (M-H, Random, 95% CI)	-0.67 [-0.80, -0.54]
9.3 Tacalcitol vs. dithranol	1	84	Risk Difference (M-H, Random, 95% CI)	-0.36 [-0.52, -0.20]
10 Adverse events (systemic)	4	746	Risk Difference (M-H, Random, 95% CI)	-0.00 [-0.01, 0.01]
10.1 Calcipotriol vs. dithranol	2	548	Risk Difference (M-H, Random, 95% CI)	-0.00 [-0.02, 0.01]
10.2 Calcitriol vs. dithranol	1	114	Risk Difference (M-H, Random, 95% CI)	0.0 [-0.03, 0.03]
10.3 Tacalcitol vs. dithranol	1	84	Risk Difference (M-H, Random, 95% CI)	0.0 [-0.05, 0.05]

Analysis 10.1. Comparison 10 Vitamin D alone or in combination versus dithranol, Outcome 1 IAGI.

Study or subgroup	Vitamin D analogue N	Vitamin D analogue Mean(SD)	Dithranol N	Dithranol Mean(SD)	Std. Mean Difference Random, 95% CI	Weight	Std. Mean Difference Random, 95% CI
10.1.1 Calcipotriol vs. dithranol							
Berth Jones 1992b	231	-2.8 (0.6)	227	-2.3 (1)		27.09%	-0.64[-0.83,-0.46]
					Favours vitamin D analogue -2 -1 0 1 2 Favours dithranol		

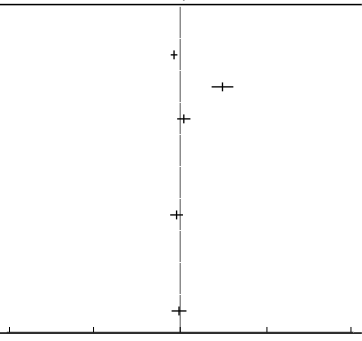


Analysis 10.2. Comparison 10 Vitamin D alone or in combination versus dithranol, Outcome 2 TSS.



Analysis 10.3. Comparison 10 Vitamin D alone or in combination versus dithranol, Outcome 3 PASI.

Study or subgroup	Vitamin D analogue N	Vitamin D analogue Mean(SD)	Dithranol N	Dithranol Mean(SD)	Std. Mean Difference Random, 95% CI	Std. Mean Difference Random, 95% CI
10.3.1 Calcipotriol vs. dithranol						
Berth Jones 1992b	214	3.4 (2.7)	208	4.7 (4.4)		-0.36[-0.55,-0.16]
Monastirli 2000	35	2.6 (1.2)	35	0.3 (0.5)		2.44[1.81,3.06]
Van de Kerkhof 2006	54	-0.6 (0.4)	52	-0.6 (0.3)		0.21[-0.18,0.59]
10.3.2 Calcitriol vs. dithranol						
Hutchinson 2000	60	4.2 (3.9)	54	5.2 (5.5)		-0.21[-0.58,0.16]
10.3.3 Tacalcitol vs. dithranol						
Farkas 1999	42	4.2 (3.2)	42	4.4 (3.1)		-0.07[-0.5,0.36]

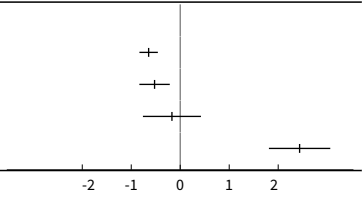


Analysis 10.4. Comparison 10 Vitamin D alone or in combination versus dithranol, Outcome 4 PAGI.

Study or subgroup	Vitamin D analogue N	Vitamin D analogue Mean(SD)	Dithranol N	Dithranol Mean(SD)	Std. Mean Difference Random, 95% CI	Weight	Std. Mean Difference Random, 95% CI
10.4.1 Calcipotriol vs. dithranol							
Berth Jones 1992b	231	-2.7 (0.7)	227	-2.3 (1)		52.56%	-0.47[-0.65,-0.28]
Van de Kerkhof 2006	46	-2.9 (1.7)	40	-3.5 (1.4)		47.44%	0.4[-0.02,0.83]
Subtotal ***	**277**		**267**			**100%**	**-0.05[-0.9,0.8]**
Heterogeneity: Tau^2=0.35; Chi^2=13.35, df=1(P=0); I^2=92.51%							
Test for overall effect: Z=0.12(P=0.9)							
10.4.2 Calcitriol vs. dithranol							
Subtotal ***	**0**		**0**				**Not estimable**
Heterogeneity: Not applicable							
Test for overall effect: Not applicable							
10.4.3 Tacalcitol vs. dithranol							
Subtotal ***	**0**		**0**				**Not estimable**
Heterogeneity: Not applicable							
Test for overall effect: Not applicable							
Test for subgroup differences: Not applicable							

Analysis 10.5. Comparison 10 Vitamin D alone or in combination versus dithranol, Outcome 5 Combined end point (IAGI/TSS/PASI/PAGI).

Study or subgroup	Vitamin D analogue N	Vitamin D analogue Mean(SD)	Dithranol N	Dithranol Mean(SD)	Std. Mean Difference Random, 95% CI	Std. Mean Difference Random, 95% CI
10.5.1 Calcipotriol vs. dithranol						
Berth Jones 1992b	231	-2.8 (0.6)	227	-2.3 (1)		-0.64[-0.83,-0.46]
Christensen 1999	89	-3.4 (1.5)	77	-2.6 (1.5)		-0.52[-0.83,-0.21]
Grattan 1997 (H)	22	1.8 (2)	22	2.2 (2.6)		-0.17[-0.76,0.42]
Monastirli 2000	35	2.6 (1.2)	35	0.3 (0.5)		2.44[1.81,3.06]



Study or subgroup	Vitamin D analogue N	Vitamin D analogue Mean(SD)	Dithranol N	Dithranol Mean(SD)	Std. Mean Difference Random, 95% CI	Std. Mean Difference Random, 95% CI
Van de Kerkhof 2006	46	-3 (1.5)	40	-3.6 (1.2)		0.46[0.03,0.89]
Wall 1998	153	-2.5 (0.9)	131	-1.7 (1)		-0.86[-1.1,-0.61]
10.5.2 Calcitriol vs. dithranol						
Hutchinson 2000	60	-2.2 (0.5)	54	-2.4 (0.5)		0.51[0.13,0.88]
10.5.3 Tacalcitol vs. dithranol						
Farkas 1999	42	-6.1 (2.4)	42	-5.7 (2.1)		-0.18[-0.6,0.25]

Favours vitamin D analogue — Favours dithranol

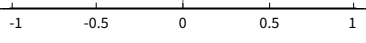
Analysis 10.6. Comparison 10 Vitamin D alone or in combination versus dithranol, Outcome 6 Total withdrawals.

Study or subgroup	Vitamin D analogue n/N	Dithranol n/N	Risk Difference M-H, Random, 95% CI	Weight	Risk Difference M-H, Random, 95% CI
10.6.1 Calcipotriol vs. dithranol					
Christensen 1999	0/89	5/82		37.44%	-0.06[-0.12,-0.01]
Grattan 1997 (H)	3/25	3/25		3.58%	0[-0.18,0.18]
Monastirli 2000	0/35	0/35		39.7%	0[-0.05,0.05]
Van de Kerkhof 2006	17/54	11/52		4.19%	0.1[-0.06,0.27]
Van der Vleuten 1995	0/10	0/10		3.83%	0[-0.17,0.17]
Subtotal (95% CI)	**213**	**204**		**88.73%**	**-0.01[-0.07,0.04]**
Total events: 20 (Vitamin D analogue), 19 (Dithranol)					
Heterogeneity: Tau^2=0; Chi^2=6.25, df=4(P=0.18); I^2=36.01%					
Test for overall effect: Z=0.48(P=0.63)					
10.6.2 Calcitriol vs. dithranol					
Hutchinson 2000	12/60	16/54		4.63%	-0.1[-0.25,0.06]
Subtotal (95% CI)	**60**	**54**		**4.63%**	**-0.1[-0.25,0.06]**
Total events: 12 (Vitamin D analogue), 16 (Dithranol)					
Heterogeneity: Not applicable					
Test for overall effect: Z=1.19(P=0.23)					
10.6.3 Tacalcitol vs. dithranol					
Farkas 1999	4/42	5/42		6.64%	-0.02[-0.16,0.11]
Subtotal (95% CI)	**42**	**42**		**6.64%**	**-0.02[-0.16,0.11]**
Total events: 4 (Vitamin D analogue), 5 (Dithranol)					
Heterogeneity: Not applicable					
Test for overall effect: Z=0.35(P=0.72)					
Total (95% CI)	**315**	**300**		**100%**	**-0.02[-0.06,0.01]**
Total events: 36 (Vitamin D analogue), 40 (Dithranol)					
Heterogeneity: Tau^2=0; Chi^2=5.7, df=6(P=0.46); I^2=0%					
Test for overall effect: Z=1.41(P=0.16)					
Test for subgroup differences: Chi^2=0.95, df=1 (P=0.62), I^2=0%					

Favours vitamin D analogue — Favours dithranol

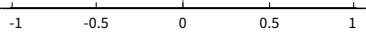
Analysis 10.7. Comparison 10 Vitamin D alone or in combination versus dithranol, Outcome 7 Withdrawals due to adverse events.

Study or subgroup	Vitamin D analogue n/N	Dithranol n/N	Risk Difference M-H, Random, 95% CI	Weight	Risk Difference M-H, Random, 95% CI
10.7.1 Calcipotriol vs. dithranol					
Berth Jones 1992b	4/239	12/239		33%	-0.03[-0.07,-0]
Lister 1997	2/89	6/82		14.66%	-0.05[-0.11,0.01]
Monastirli 2000	0/35	0/35		18.7%	0[-0.05,0.05]
Van de Kerkhof 2006	7/54	3/52		6.05%	0.07[-0.04,0.18]
Van der Vleuten 1995	0/10	0/10		2.57%	0[-0.17,0.17]
Wall 1998	9/161	20/145		13.95%	-0.08[-0.15,-0.02]
Subtotal (95% CI)	**588**	**563**		**88.93%**	**-0.03[-0.06,0]**
Total events: 22 (Vitamin D analogue), 41 (Dithranol)					
Heterogeneity: Tau^2=0; Chi^2=7.71, df=5(P=0.17); I^2=35.12%					
Test for overall effect: Z=1.69(P=0.09)					
10.7.2 Calcitriol vs. dithranol					
Hutchinson 2000	1/60	4/54		11.07%	-0.06[-0.13,0.02]
Subtotal (95% CI)	**60**	**54**		**11.07%**	**-0.06[-0.13,0.02]**
Total events: 1 (Vitamin D analogue), 4 (Dithranol)					
Heterogeneity: Not applicable					
Test for overall effect: Z=1.46(P=0.14)					
10.7.3 Tacalcitol vs. dithranol					
Subtotal (95% CI)	**0**	**0**			**Not estimable**
Total events: 0 (Vitamin D analogue), 0 (Dithranol)					
Heterogeneity: Not applicable					
Test for overall effect: Not applicable					
Total (95% CI)	**648**	**617**		**100%**	**-0.03[-0.06,-0]**
Total events: 23 (Vitamin D analogue), 45 (Dithranol)					
Heterogeneity: Tau^2=0; Chi^2=8.14, df=6(P=0.23); I^2=26.27%					
Test for overall effect: Z=2.19(P=0.03)					
Test for subgroup differences: Chi^2=0.47, df=1 (P=0.49), I^2=0%					



Analysis 10.8. Comparison 10 Vitamin D alone or in combination versus dithranol, Outcome 8 Withdrawals due to treatment failure.

Study or subgroup	Vitamin D analogue n/N	Dithranol n/N	Risk Difference M-H, Random, 95% CI	Weight	Risk Difference M-H, Random, 95% CI
10.8.1 Calcipotriol vs. dithranol					
Berth Jones 1992b	3/239	3/239		77.48%	0[-0.02,0.02]
Monastirli 2000	0/35	0/35		10.56%	0[-0.05,0.05]
Van de Kerkhof 2006	7/54	4/52		2.33%	0.05[-0.06,0.17]
Van der Vleuten 1995	0/10	0/10		1.02%	0[-0.17,0.17]
Subtotal (95% CI)	**338**	**336**		**91.39%**	**0[-0.02,0.02]**
Total events: 10 (Vitamin D analogue), 7 (Dithranol)					
Heterogeneity: Tau^2=0; Chi^2=1.33, df=3(P=0.72); I^2=0%					

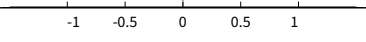


Study or subgroup	Vitamin D analogue n/N	Dithranol n/N	Risk Difference M-H, Random, 95% CI	Weight	Risk Difference M-H, Random, 95% CI
Test for overall effect: Z=0.14(P=0.89)					
10.8.2 Calcitriol vs. dithranol					
Hutchinson 2000	1/60	2/54		8.61%	-0.02[-0.08,0.04]
Subtotal (95% CI)	**60**	**54**		**8.61%**	**-0.02[-0.08,0.04]**
Total events: 1 (Vitamin D analogue), 2 (Dithranol)					
Heterogeneity: Not applicable					
Test for overall effect: Z=0.67(P=0.5)					
10.8.3 Tacalcitol vs. dithranol					
Subtotal (95% CI)	**0**	**0**			**Not estimable**
Total events: 0 (Vitamin D analogue), 0 (Dithranol)					
Heterogeneity: Not applicable					
Test for overall effect: Not applicable					
Total (95% CI)	**398**	**390**		**100%**	**-0[-0.02,0.02]**
Total events: 11 (Vitamin D analogue), 9 (Dithranol)					
Heterogeneity: Tau^2=0; Chi^2=1.52, df=4(P=0.82); I^2=0%					
Test for overall effect: Z=0.06(P=0.95)					
Test for subgroup differences: Chi^2=0.46, df=1 (P=0.5), I^2=0%					

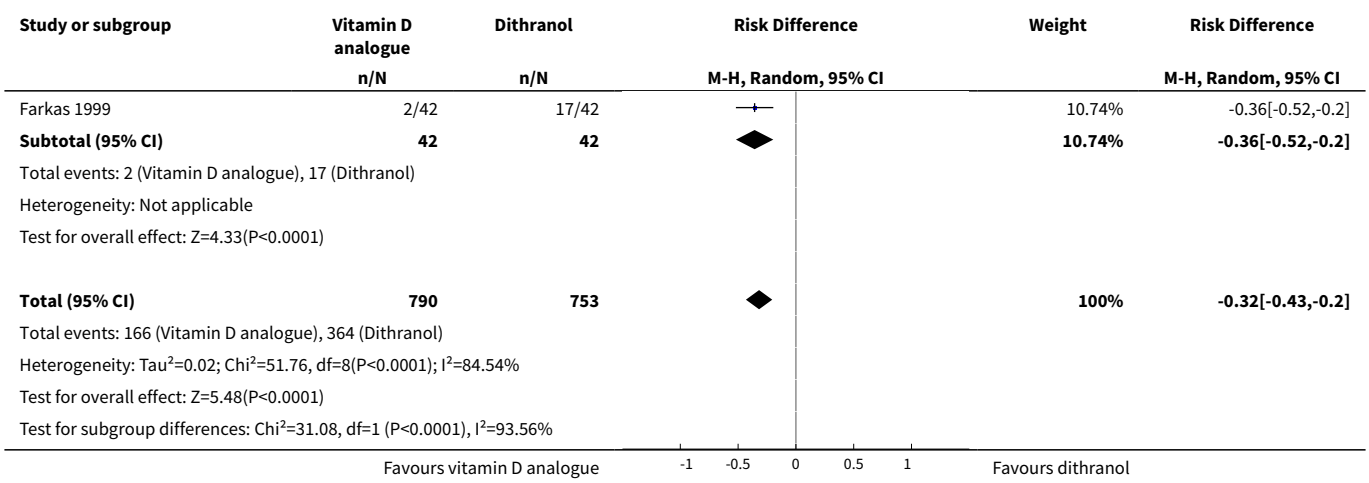
Favours vitamin D analogue — Favours dithranol

Analysis 10.9. Comparison 10 Vitamin D alone or in combination versus dithranol, Outcome 9 Adverse events (local).

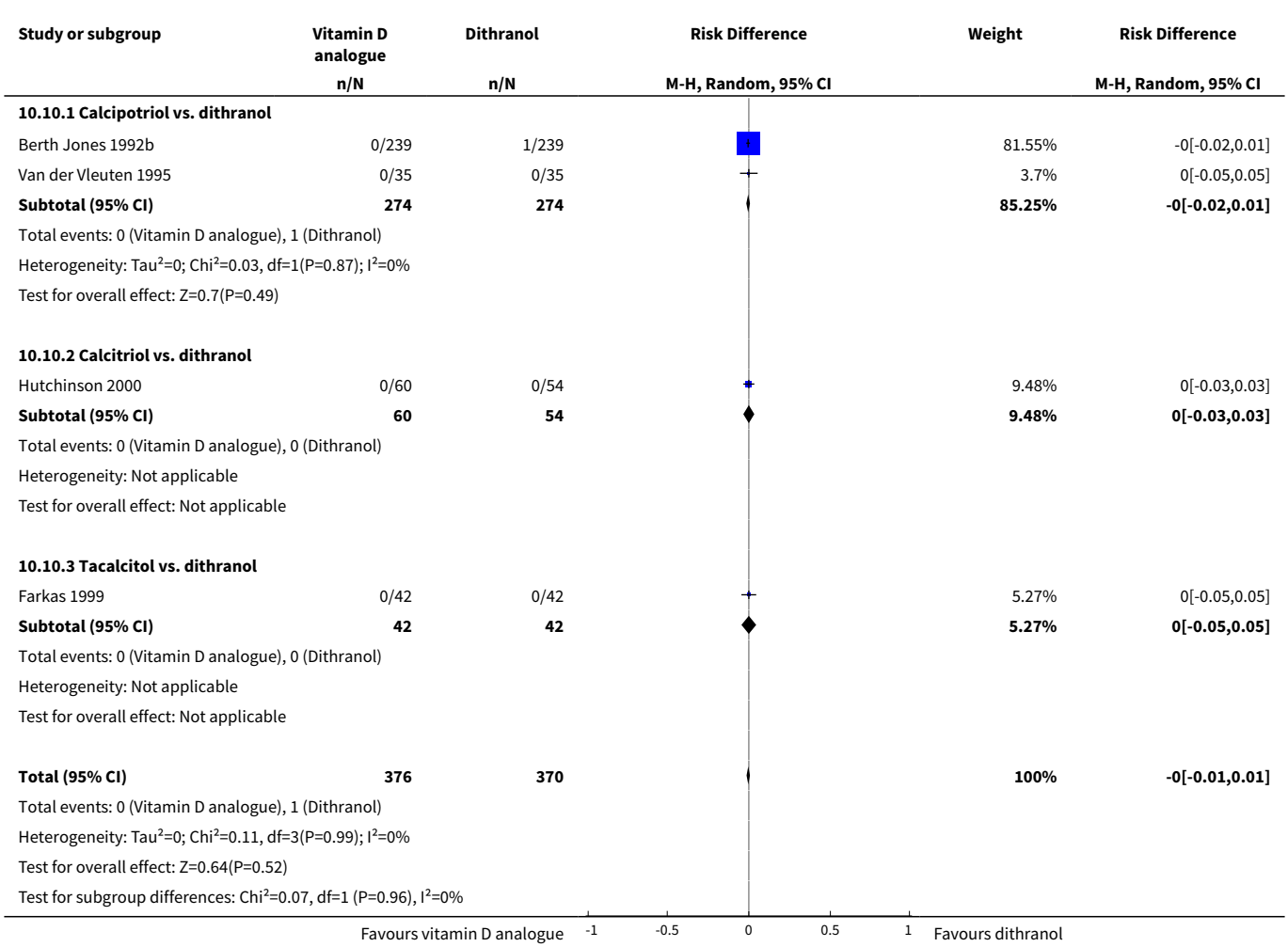
Study or subgroup	Vitamin D analogue n/N	Dithranol n/N	Risk Difference M-H, Random, 95% CI	Weight	Risk Difference M-H, Random, 95% CI
10.9.1 Calcipotriol vs. dithranol					
Berth Jones 1992b	84/239	127/239		12.69%	-0.18[-0.27,-0.09]
Christensen 1999	11/89	23/82		11.93%	-0.16[-0.28,-0.04]
Grattan 1997 (H)	1/22	11/22		8.9%	-0.45[-0.68,-0.23]
Lister 1997	11/89	23/82		11.93%	-0.16[-0.28,-0.04]
Monastirli 2000	5/35	16/35		9.59%	-0.31[-0.52,-0.11]
Van de Kerkhof 2006	21/53	37/52		10.21%	-0.32[-0.5,-0.14]
Wall 1998	28/161	71/145		12.4%	-0.32[-0.42,-0.22]
Subtotal (95% CI)	**688**	**657**		**77.66%**	**-0.25[-0.32,-0.17]**
Total events: 161 (Vitamin D analogue), 308 (Dithranol)					
Heterogeneity: Tau^2=0; Chi^2=12.28, df=6(P=0.06); I^2=51.14%					
Test for overall effect: Z=6.65(P<0.0001)					
10.9.2 Calcitriol vs. dithranol					
Hutchinson 2000	3/60	39/54		11.6%	-0.67[-0.8,-0.54]
Subtotal (95% CI)	**60**	**54**		**11.6%**	**-0.67[-0.8,-0.54]**
Total events: 3 (Vitamin D analogue), 39 (Dithranol)					
Heterogeneity: Not applicable					
Test for overall effect: Z=10.01(P<0.0001)					
10.9.3 Tacalcitol vs. dithranol					



Favours vitamin D analogue — Favours dithranol



Analysis 10.10. Comparison 10 Vitamin D alone or in combination versus dithranol, Outcome 10 Adverse events (systemic).



Comparison 11. Vitamin D alone or in combination versus other vitamin D analogue

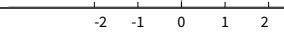
Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 IAGI	3		Std. Mean Difference (IV, Random, 95% CI)	Subtotals only
1.1 Calcipotriol vs. calcitriol	1	246	Std. Mean Difference (IV, Random, 95% CI)	0.0 [-0.25, 0.25]
1.2 Calcipotriol vs. tacalcitol	1	226	Std. Mean Difference (IV, Random, 95% CI)	-0.47 [-0.73, -0.21]
1.3 Calcipotriol vs. maxacalcitol	1	52	Std. Mean Difference (IV, Random, 95% CI)	0.43 [-0.12, 0.98]
2 TSS	3	589	Std. Mean Difference (IV, Random, 95% CI)	-0.31 [-0.55, -0.06]
2.1 Calcipotriol vs. calcitriol	1	250	Std. Mean Difference (IV, Random, 95% CI)	-0.32 [-0.57, -0.07]
2.2 Calcipotriol vs. tacalcitol	1	287	Std. Mean Difference (IV, Random, 95% CI)	-0.45 [-0.68, -0.22]
2.3 Calcipotriol vs. maxacalcitol	1	52	Std. Mean Difference (IV, Random, 95% CI)	0.13 [-0.41, 0.68]
3 PASI	1		Std. Mean Difference (IV, Random, 95% CI)	Totals not selected
3.1 Calcipotriol vs. calcitriol	1		Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
3.2 Calcipotriol vs. tacalcitol	0		Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
3.3 Calcipotriol vs. maxacalcitol	0		Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
4 PAGI	1		Std. Mean Difference (IV, Random, 95% CI)	Totals not selected
4.1 Calcipotriol vs. calcitriol	1		Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
4.2 Calcipotriol vs. tacalcitol	0		Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
4.3 Calcipotriol vs. maxacalcitol	0		Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
5 Combined end point (IAGI/TSS/PASI/PAGI)	4	539	Std. Mean Difference (IV, Random, 95% CI)	-0.17 [-0.62, 0.27]
5.1 Calcipotriol vs. calcitriol	2	261	Std. Mean Difference (IV, Random, 95% CI)	-0.41 [-1.46, 0.64]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
5.2 Calcipotriol vs. tacalcitol	1	226	Std. Mean Difference (IV, Random, 95% CI)	-0.47 [-0.73, -0.21]
5.3 Calcipotriol vs. maxacalcitol	1	52	Std. Mean Difference (IV, Random, 95% CI)	0.43 [-0.12, 0.98]
6 Total withdrawals	3	334	Risk Difference (M-H, Random, 95% CI)	0.02 [-0.04, 0.08]
6.1 Calcipotriol vs. calcitriol	2	274	Risk Difference (M-H, Random, 95% CI)	0.02 [-0.04, 0.09]
6.2 Calcipotriol vs. tacalcitol	0	0	Risk Difference (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
6.3 Calcipotriol vs. maxacalcitol	1	60	Risk Difference (M-H, Random, 95% CI)	0.0 [-0.17, 0.17]
7 Withdrawals due to adverse events	3	334	Risk Difference (M-H, Random, 95% CI)	0.02 [-0.01, 0.06]
7.1 Calcipotriol vs. calcitriol	2	274	Risk Difference (M-H, Random, 95% CI)	0.03 [-0.01, 0.07]
7.2 Calcipotriol vs. tacalcitol	0	0	Risk Difference (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
7.3 Calcipotriol vs. maxacalcitol	1	60	Risk Difference (M-H, Random, 95% CI)	0.0 [-0.06, 0.06]
8 Withdrawals due to treatment failure	3	334	Risk Difference (M-H, Random, 95% CI)	-0.00 [-0.02, 0.01]
8.1 Calcipotriol vs. calcitriol	2	274	Risk Difference (M-H, Random, 95% CI)	-0.01 [-0.08, 0.07]
8.2 Calcipotriol vs. tacalcitol	0	0	Risk Difference (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
8.3 Calcipotriol vs. maxacalcitol	1	60	Risk Difference (M-H, Random, 95% CI)	0.0 [-0.06, 0.06]
9 Adverse events (local)	2	537	Risk Difference (M-H, Random, 95% CI)	0.03 [-0.05, 0.12]
9.1 Calcipotriol vs. calcitriol	1	250	Risk Difference (M-H, Random, 95% CI)	0.07 [0.01, 0.14]
9.2 Calcipotriol vs. tacalcitol	1	287	Risk Difference (M-H, Random, 95% CI)	-0.01 [-0.09, 0.07]
9.3 Calcipotriol vs. maxacalcitol	0	0	Risk Difference (M-H, Random, 95% CI)	0.0 [0.0, 0.0]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
10 Adverse events (systemic)	3	597	Risk Difference (M-H, Random, 95% CI)	0.0 [-0.01, 0.01]
10.1 Calcipotriol vs. calcitriol	1	250	Risk Difference (M-H, Random, 95% CI)	0.0 [-0.02, 0.02]
10.2 Calcipotriol vs. tacalcitol	1	287	Risk Difference (M-H, Random, 95% CI)	0.0 [-0.01, 0.01]
10.3 Calcipotriol vs. maxacalcitol	1	60	Risk Difference (M-H, Random, 95% CI)	0.0 [-0.06, 0.06]

Analysis 11.1. Comparison 11 Vitamin D alone or in combination versus other vitamin D analogue, Outcome 1 IAGI.

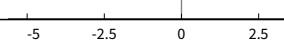
Study or subgroup	Vitamin D alone or in combination N	Mean(SD)	Other vitamin D analogue N	Mean(SD)	Std. Mean Difference Random, 95% CI	Weight	Std. Mean Difference Random, 95% CI
11.1.1 Calcipotriol vs. calcitriol							
Ji 2008	122	-2.1 (0.8)	124	-2.1 (0.7)		100%	0[-0.25,0.25]
Subtotal ***	**122**		**124**			**100%**	**0[-0.25,0.25]**
Heterogeneity: Not applicable							
Test for overall effect: Not applicable							
11.1.2 Calcipotriol vs. tacalcitol							
Veien 1997	113	-3.8 (0.9)	113	-3.3 (1.2)		100%	-0.47[-0.73,-0.21]
Subtotal ***	**113**		**113**			**100%**	**-0.47[-0.73,-0.21]**
Heterogeneity: Not applicable							
Test for overall effect: Z=3.48(P=0)							
11.1.3 Calcipotriol vs. maxacalcitol							
Barker 1999 (H)	26	-3.2 (1.3)	26	-3.7 (1.2)		100%	0.43[-0.12,0.98]
Subtotal ***	**26**		**26**			**100%**	**0.43[-0.12,0.98]**
Heterogeneity: Not applicable							
Test for overall effect: Z=1.52(P=0.13)							
Test for subgroup differences: Chi^2=11.22, df=1 (P=0), I^2=82.18%							



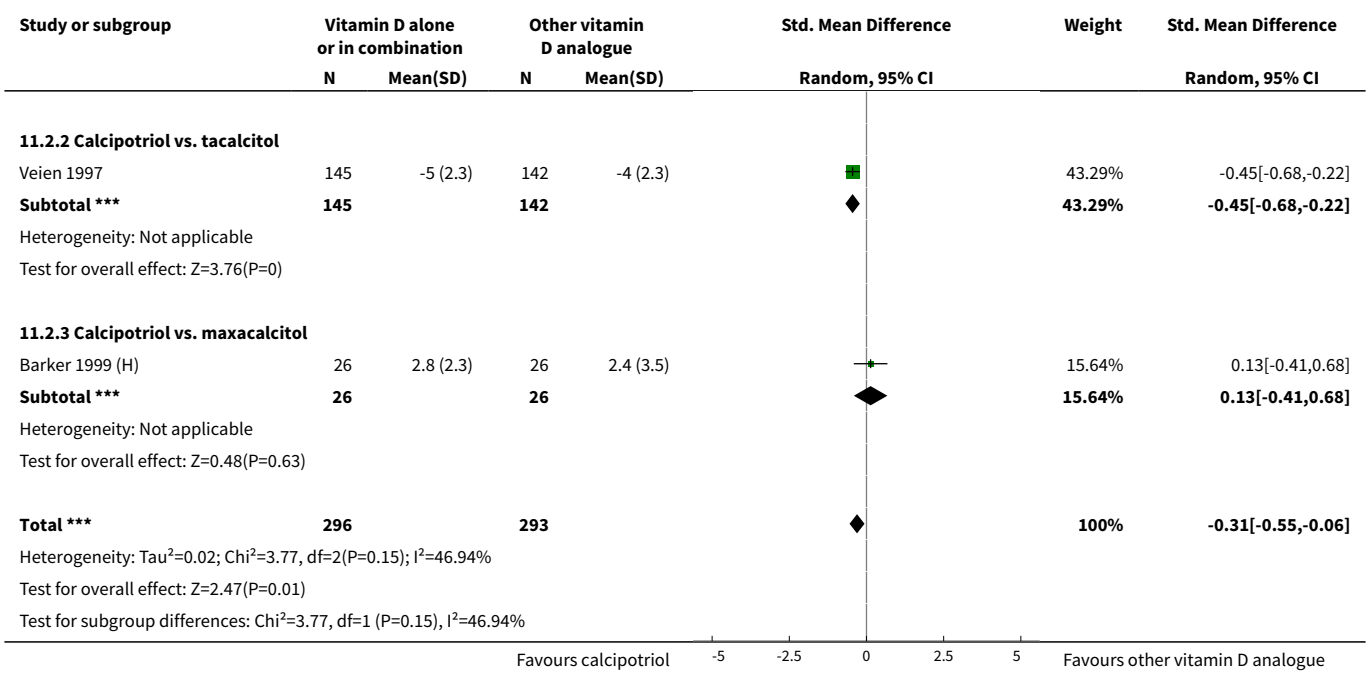
Favours calcipotriol — Favours other vitamin D analogue

Analysis 11.2. Comparison 11 Vitamin D alone or in combination versus other vitamin D analogue, Outcome 2 TSS.

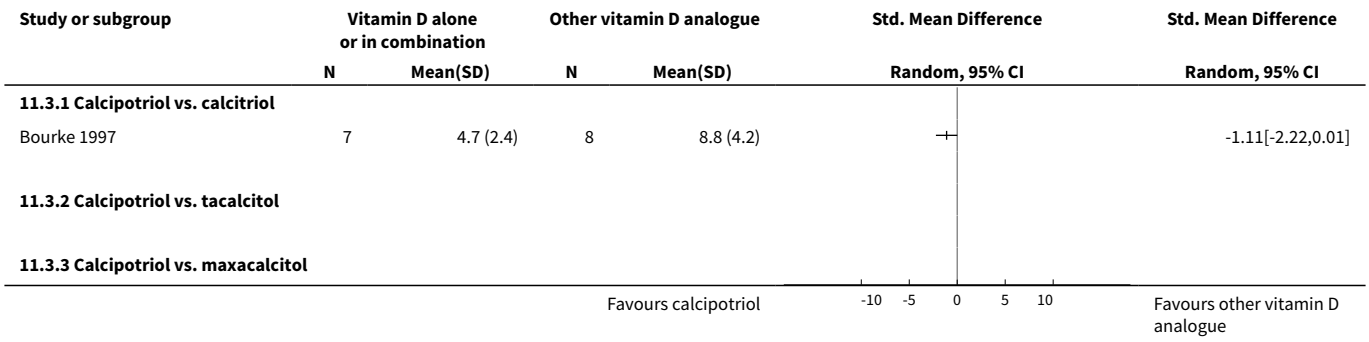
Study or subgroup	Vitamin D alone or in combination N	Mean(SD)	Other vitamin D analogue N	Mean(SD)	Std. Mean Difference Random, 95% CI	Weight	Std. Mean Difference Random, 95% CI
11.2.1 Calcipotriol vs. calcitriol							
Ji 2008	125	1.9 (2.1)	125	2.5 (2.1)		41.07%	-0.32[-0.57,-0.07]
Subtotal ***	**125**		**125**			**41.07%**	**-0.32[-0.57,-0.07]**
Heterogeneity: Not applicable							
Test for overall effect: Z=2.53(P=0.01)							



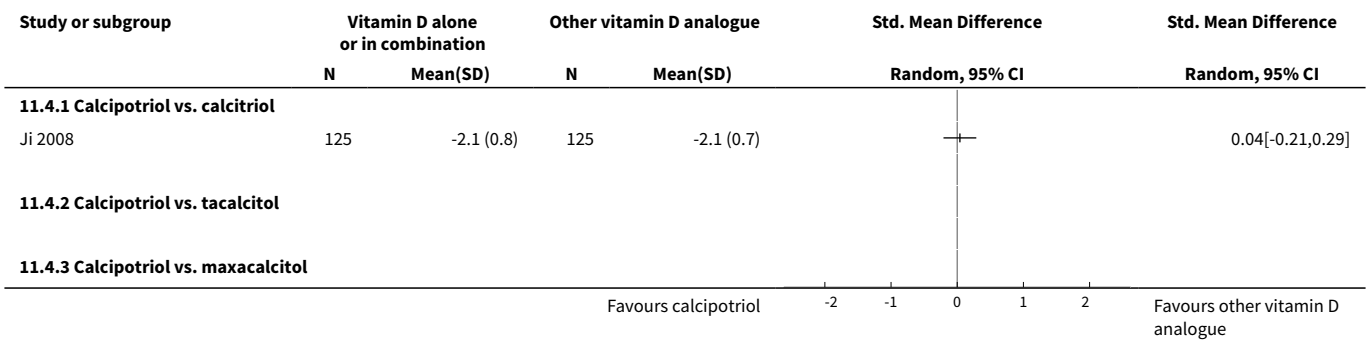
Favours calcipotriol — Favours other vitamin D analogue



Analysis 11.3. Comparison 11 Vitamin D alone or in combination versus other vitamin D analogue, Outcome 3 PASI.

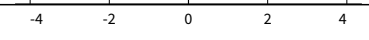


Analysis 11.4. Comparison 11 Vitamin D alone or in combination versus other vitamin D analogue, Outcome 4 PAGI.



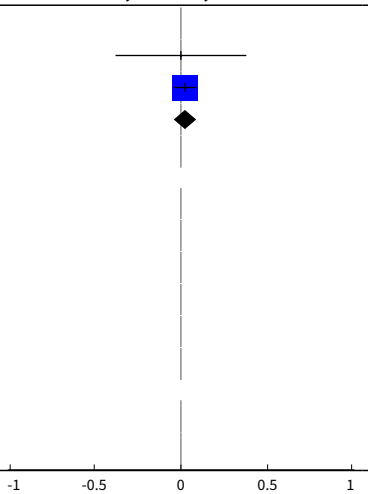
Analysis 11.5. Comparison 11 Vitamin D alone or in combination versus other vitamin D analogue, Outcome 5 Combined end point (IAGI/TSS/PASI/PAGI).

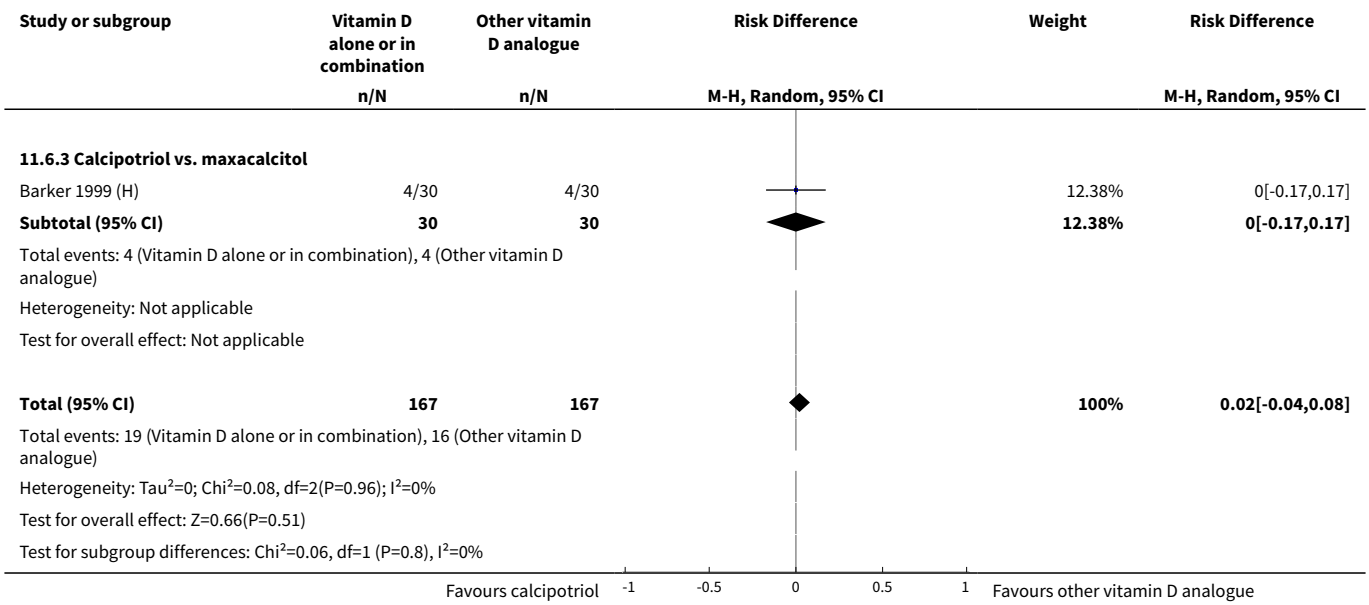
Study or subgroup	Vitamin D alone or in combination N	Mean(SD)	Other vitamin D analogue N	Mean(SD)	Std. Mean Difference Random, 95% CI	Weight	Std. Mean Difference Random, 95% CI
11.5.1 Calcipotriol vs. calcitriol							
Bourke 1997	7	4.7 (2.4)	8	8.8 (4.2)		11.01%	-1.11[-2.22,0.01]
Ji 2008	122	-2.1 (0.8)	124	-2.1 (0.7)		32.98%	0[-0.25,0.25]
Subtotal ***	**129**		**132**			**43.99%**	**-0.41[-1.46,0.64]**
Heterogeneity: Tau^2=0.44; Chi^2=3.61, df=1(P=0.06); I^2=72.28%							
Test for overall effect: Z=0.77(P=0.44)							
11.5.2 Calcipotriol vs. tacalcitol							
Veien 1997	113	-3.8 (0.9)	113	-3.3 (1.2)		32.57%	-0.47[-0.73,-0.21]
Subtotal ***	**113**		**113**			**32.57%**	**-0.47[-0.73,-0.21]**
Heterogeneity: Not applicable							
Test for overall effect: Z=3.48(P=0)							
11.5.3 Calcipotriol vs. maxacalcitol							
Barker 1999 (H)	26	-3.2 (1.3)	26	-3.7 (1.2)		23.45%	0.43[-0.12,0.98]
Subtotal ***	**26**		**26**			**23.45%**	**0.43[-0.12,0.98]**
Heterogeneity: Not applicable							
Test for overall effect: Z=1.52(P=0.13)							
Total ***	**268**		**271**			**100%**	**-0.17[-0.62,0.27]**
Heterogeneity: Tau^2=0.14; Chi^2=13.94, df=3(P=0); I^2=78.48%							
Test for overall effect: Z=0.78(P=0.44)							
Test for subgroup differences: Chi^2=8.33, df=1 (P=0.02), I^2=76%							



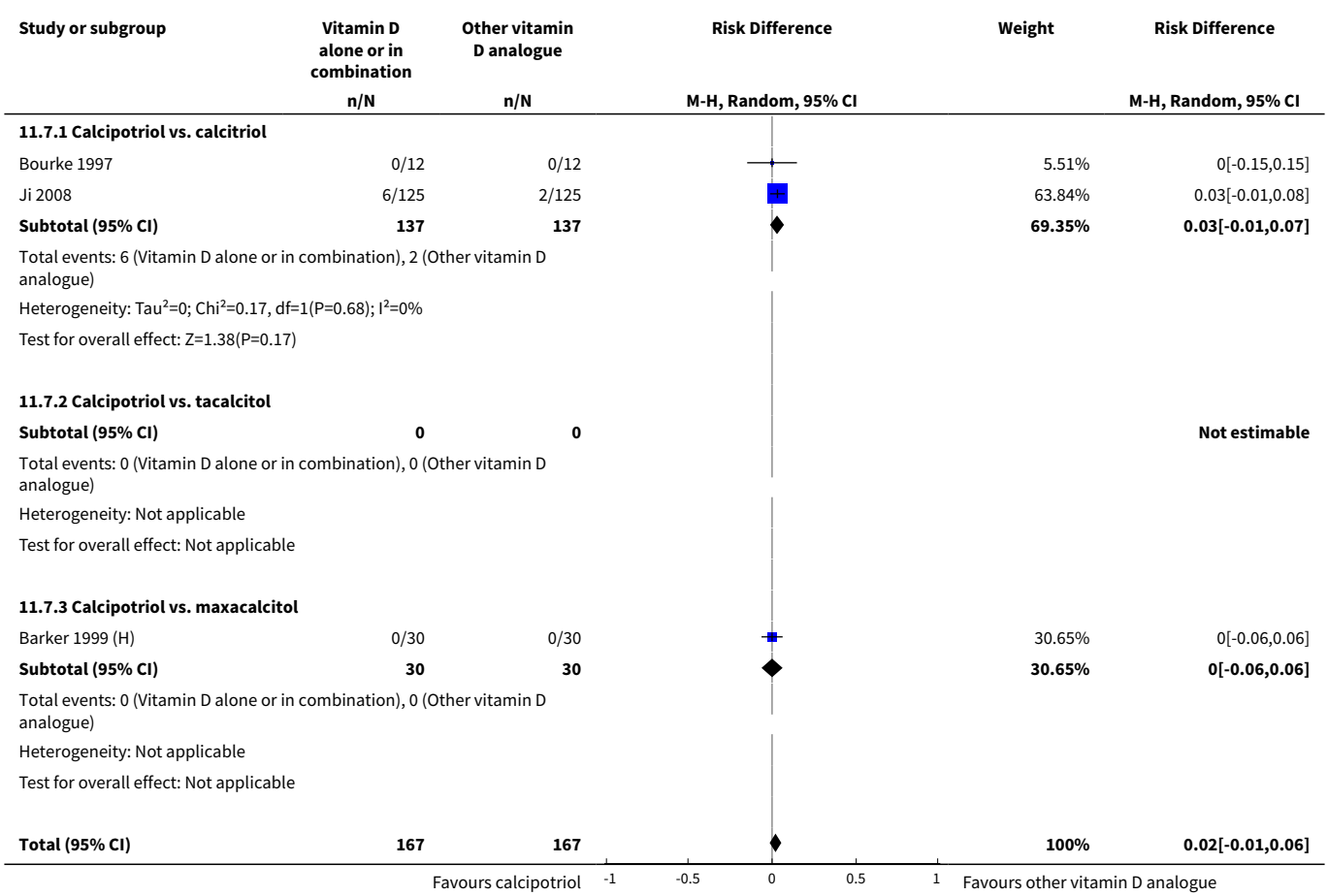
Analysis 11.6. Comparison 11 Vitamin D alone or in combination versus other vitamin D analogue, Outcome 6 Total withdrawals.

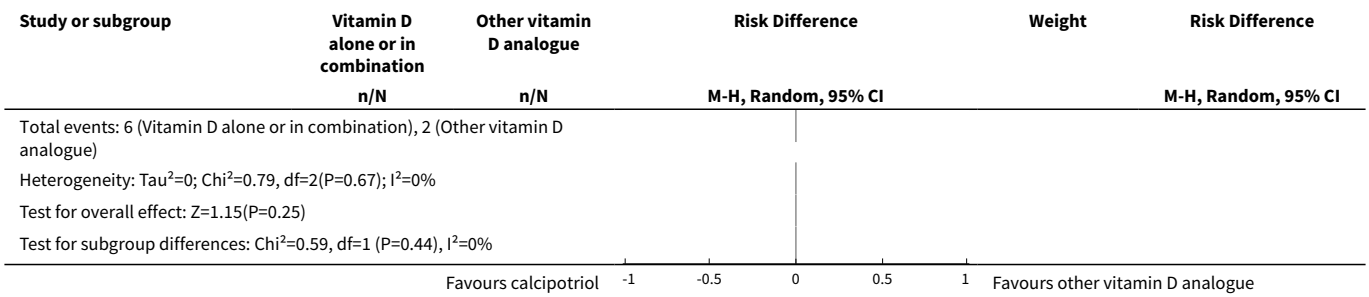
Study or subgroup	Vitamin D alone or in combination n/N	Other vitamin D analogue n/N	Risk Difference M-H, Random, 95% CI	Weight	Risk Difference M-H, Random, 95% CI
11.6.1 Calcipotriol vs. calcitriol					
Bourke 1997	4/12	4/12		2.57%	0[-0.38,0.38]
Ji 2008	11/125	8/125		85.05%	0.02[-0.04,0.09]
Subtotal (95% CI)	**137**	**137**		**87.62%**	**0.02[-0.04,0.09]**
Total events: 15 (Vitamin D alone or in combination), 12 (Other vitamin D analogue)					
Heterogeneity: Tau^2=0; Chi^2=0.02, df=1(P=0.9); I^2=0%					
Test for overall effect: Z=0.71(P=0.48)					
11.6.2 Calcipotriol vs. tacalcitol					
Subtotal (95% CI)	**0**	**0**			**Not estimable**
Total events: 0 (Vitamin D alone or in combination), 0 (Other vitamin D analogue)					
Heterogeneity: Not applicable					
Test for overall effect: Not applicable					



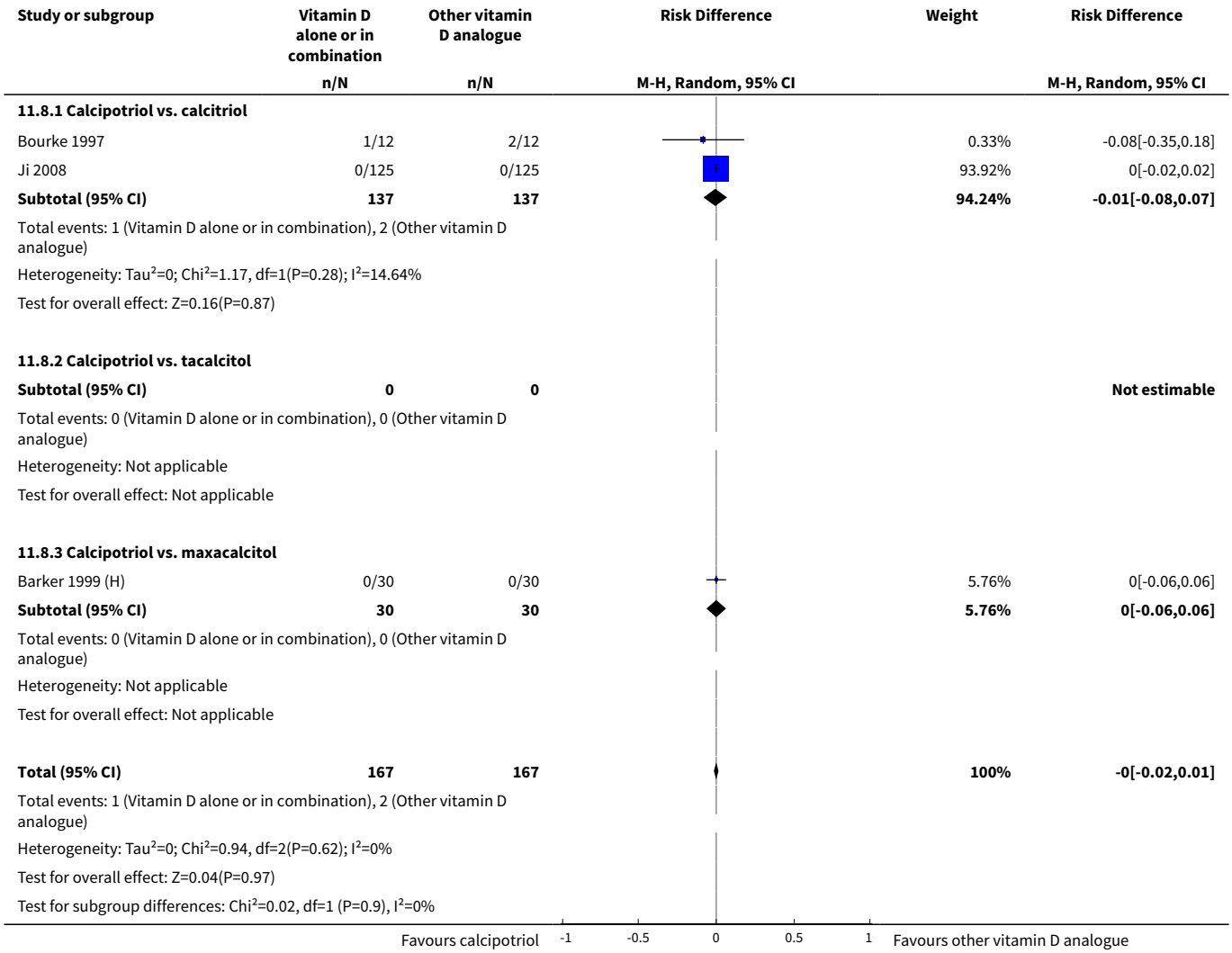


Analysis 11.7. Comparison 11 Vitamin D alone or in combination versus other vitamin D analogue, Outcome 7 Withdrawals due to adverse events.



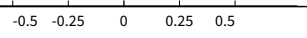


Analysis 11.8. Comparison 11 Vitamin D alone or in combination versus other vitamin D analogue, Outcome 8 Withdrawals due to treatment failure.



Analysis 11.9. Comparison 11 Vitamin D alone or in combination versus other vitamin D analogue, Outcome 9 Adverse events (local).

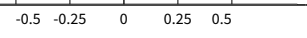
Study or subgroup	Vitamin D alone or in combination n/N	Other vitamin D analogue n/N	Risk Difference M-H, Random, 95% CI	Weight	Risk Difference M-H, Random, 95% CI
11.9.1 Calcipotriol vs. calcitriol					
Ji 2008	14/125	5/125		52.8%	0.07[0.01,0.14]
Subtotal (95% CI)	**125**	**125**		**52.8%**	**0.07[0.01,0.14]**
Total events: 14 (Vitamin D alone or in combination), 5 (Other vitamin D analogue)					
Heterogeneity: Not applicable					
Test for overall effect: Z=2.17(P=0.03)					
11.9.2 Calcipotriol vs. tacalcitol					
Veien 1997	17/145	18/142		47.2%	-0.01[-0.09,0.07]
Subtotal (95% CI)	**145**	**142**		**47.2%**	**-0.01[-0.09,0.07]**
Total events: 17 (Vitamin D alone or in combination), 18 (Other vitamin D analogue)					
Heterogeneity: Not applicable					
Test for overall effect: Z=0.25(P=0.81)					
11.9.3 Calcipotriol vs. maxacalcitol					
Subtotal (95% CI)	**0**	**0**			**Not estimable**
Total events: 0 (Vitamin D alone or in combination), 0 (Other vitamin D analogue)					
Heterogeneity: Not applicable					
Test for overall effect: Not applicable					
Total (95% CI)	**270**	**267**		**100%**	**0.03[-0.05,0.12]**
Total events: 31 (Vitamin D alone or in combination), 23 (Other vitamin D analogue)					
Heterogeneity: $Tau^2=0$; $Chi^2=2.69$, df=1(P=0.1); $I^2=62.76\%$					
Test for overall effect: Z=0.8(P=0.42)					
Test for subgroup differences: $Chi^2=2.56$, df=1 (P=0.11), $I^2=60.93\%$					



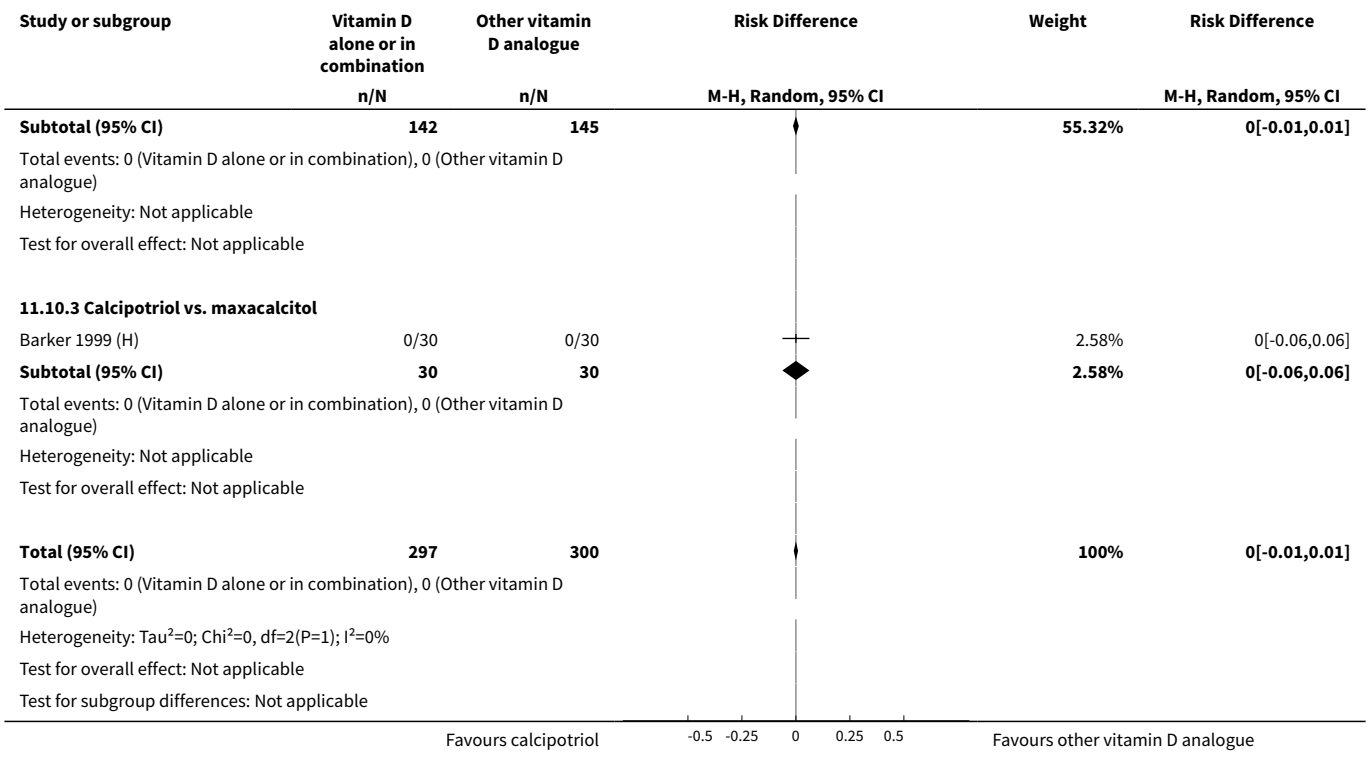
Favours calcipotriol — Favours other vitamin D analogue

Analysis 11.10. Comparison 11 Vitamin D alone or in combination versus other vitamin D analogue, Outcome 10 Adverse events (systemic).

Study or subgroup	Vitamin D alone or in combination n/N	Other vitamin D analogue n/N	Risk Difference M-H, Random, 95% CI	Weight	Risk Difference M-H, Random, 95% CI
11.10.1 Calcipotriol vs. calcitriol					
Ji 2008	0/125	0/125		42.1%	0[-0.02,0.02]
Subtotal (95% CI)	**125**	**125**		**42.1%**	**0[-0.02,0.02]**
Total events: 0 (Vitamin D alone or in combination), 0 (Other vitamin D analogue)					
Heterogeneity: Not applicable					
Test for overall effect: Not applicable					
11.10.2 Calcipotriol vs. tacalcitol					
Veien 1997	0/142	0/145		55.32%	0[-0.01,0.01]



Favours calcipotriol — Favours other vitamin D analogue



Comparison 12. Vitamin D alone or in combination versus vitamin D + corticosteroid

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 IAGI	11		Std. Mean Difference (IV, Random, 95% CI)	Subtotals only
1.1 Calcipotriol twice daily vs. calcipotriol OM, BMD ON	1	154	Std. Mean Difference (IV, Random, 95% CI)	0.56 [0.23, 0.88]
1.2 Calcipotriol OD vs. combined calcipotriol + BMD OD	2	1194	Std. Mean Difference (IV, Random, 95% CI)	0.66 [0.31, 1.02]
1.3 Calcipotriol twice daily vs. combined calcipotriol + BMD OD	1	377	Std. Mean Difference (IV, Random, 95% CI)	0.27 [0.06, 0.48]
1.4 Calcipotriol twice daily vs. combined calcipotriol + BMD twice daily	3	1804	Std. Mean Difference (IV, Random, 95% CI)	0.66 [0.40, 0.93]
1.5 Calcipotriol twice daily vs. calcipotriol OM, BMV ON	2	510	Std. Mean Difference (IV, Random, 95% CI)	0.27 [-0.19, 0.74]
1.6 Calcipotriol twice daily vs. calcipotriol OM, clobetasone butyrate ON	1	344	Std. Mean Difference (IV, Random, 95% CI)	0.27 [0.05, 0.48]
1.7 Calcipotriol twice daily vs. calcipotriol twice daily + clobetasol propionate twice daily	1	65	Std. Mean Difference (IV, Random, 95% CI)	0.88 [0.34, 1.42]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1.8 Calcipotriol twice daily vs. calcipotriol OM, diflucortolone valerate ON	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
1.9 Calcipotriol OD vs. calcipotriol OM, fluocinonide acetonide ON	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
1.10 Calcipotriol OD vs. combined calcipotriol + hydrocortisone OD	1	408	Std. Mean Difference (IV, Random, 95% CI)	0.14 [-0.06, 0.33]
1.11 Calcitriol twice daily vs. diflucortolone valerate OM, calcitriol ON	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
1.12 Tacalcitol OD vs. combined calcipotriol + BMD OD	1	334	Std. Mean Difference (IV, Random, 95% CI)	0.48 [0.26, 0.70]
2 TSS	1		Std. Mean Difference (IV, Random, 95% CI)	Totals not selected
2.1 Calcipotriol twice daily vs. calcipotriol OM, BMD ON	0		Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
2.2 Calcipotriol OD vs. combined calcipotriol + BMD OD	0		Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
2.3 Calcipotriol twice daily vs. combined calcipotriol + BMD OD	1		Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
2.4 Calcipotriol twice daily vs. combined calcipotriol + BMD twice daily	0		Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
2.5 Calcipotriol twice daily vs. calcipotriol OM, BMV ON	0		Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
2.6 Calcipotriol twice daily vs. calcipotriol OM, clobetasone butyrate ON	0		Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
2.7 Calcipotriol twice daily vs. calcipotriol twice daily + clobetasol propionate twice daily	0		Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
2.8 Calcipotriol twice daily vs. calcipotriol OM, diflucortolone valerate ON	0		Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
2.9 Calcipotriol OD vs. calcipotriol OM, fluocinonide acetonide ON	0		Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
2.10 Calcipotriol OD vs. combined calcipotriol + hydrocortisone OD	0		Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
2.11 Calcitriol twice daily vs. diflucortolone valerate OM, calcitriol ON	0		Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
2.12 Tacalcitol OD vs. combined calcipotriol + BMD OD	0		Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
3 PASI	16		Std. Mean Difference (IV, Random, 95% CI)	Subtotals only
3.1 Calcipotriol twice daily vs. calcipotriol OM, BMD ON	1	124	Std. Mean Difference (IV, Random, 95% CI)	0.46 [0.10, 0.82]
3.2 Calcipotriol OD vs. combined calcipotriol + BMD OD	2	1191	Std. Mean Difference (IV, Random, 95% CI)	0.67 [0.23, 1.11]
3.3 Calcipotriol twice daily vs. combined calcipotriol + BMD OD	4	1204	Std. Mean Difference (IV, Random, 95% CI)	0.52 [0.38, 0.67]
3.4 Calcipotriol twice daily vs. combined calcipotriol + BMD twice daily	3	1744	Std. Mean Difference (IV, Random, 95% CI)	0.64 [0.46, 0.83]
3.5 Calcipotriol twice daily vs. calcipotriol OM, BMV ON	2	515	Std. Mean Difference (IV, Random, 95% CI)	0.43 [-0.07, 0.93]
3.6 Calcipotriol twice daily vs. calcipotriol OM, clobetasone butyrate ON	1	344	Std. Mean Difference (IV, Random, 95% CI)	0.17 [-0.04, 0.38]
3.7 Calcipotriol twice daily vs. calcipotriol twice daily + clobetasol propionate twice daily	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
3.8 Calcipotriol twice daily vs. calcipotriol OM, diflucortolone valerate ON	1	116	Std. Mean Difference (IV, Random, 95% CI)	0.08 [-0.29, 0.44]
3.9 Calcipotriol OD vs. calcipotriol OM, fluocinonide acetonide ON	1	38	Std. Mean Difference (IV, Random, 95% CI)	0.53 [-0.11, 1.18]
3.10 Calcipotriol OD vs. combined calcipotriol + hydrocortisone OD	1	408	Std. Mean Difference (IV, Random, 95% CI)	0.08 [-0.11, 0.28]
3.11 Calcitriol twice daily vs. diflucortolone valerate OM, calcitriol ON	1	142	Std. Mean Difference (IV, Random, 95% CI)	0.24 [-0.09, 0.57]
3.12 Tacalcitol OD vs. combined calcipotriol + BMD OD	1	334	Std. Mean Difference (IV, Random, 95% CI)	0.47 [0.25, 0.69]
4 PAGI	2	399	Std. Mean Difference (IV, Random, 95% CI)	0.49 [0.29, 0.69]
4.1 Calcipotriol twice daily vs. calcipotriol OM, BMD ON	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
4.2 Calcipotriol OD vs. combined calcipotriol + BMD OD	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
4.3 Calcipotriol twice daily vs. combined calcipotriol + BMD OD	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
4.4 Calcipotriol twice daily vs. combined calcipotriol + BMD twice daily	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]

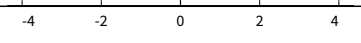
Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
4.5 Calcipotriol twice daily vs. calcipotriol OM, BMV ON	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
4.6 Calcipotriol twice daily vs. calcipotriol OM, clobetasone butyrate ON	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
4.7 Calcipotriol twice daily vs. calcipotriol twice daily + clobetasol propionate twice daily	1	65	Std. Mean Difference (IV, Random, 95% CI)	0.70 [0.16, 1.23]
4.8 Calcipotriol twice daily vs. calcipotriol OM, diflucortolone valerate ON	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
4.9 Calcipotriol OD vs. calcipotriol OM, fluocinonide acetonide ON	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
4.10 Calcipotriol OD vs. combined calcipotriol + hydrocortisone OD	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
4.11 Calcitriol twice daily vs. diflucortolone valerate OM, calcitriol ON	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
4.12 Tacalcitol OD vs. combined calcipotriol + BMD OD	1	334	Std. Mean Difference (IV, Random, 95% CI)	0.46 [0.24, 0.68]
5 Combined end point (IAGI/TSS/PASI/PAGI)	17		Std. Mean Difference (IV, Random, 95% CI)	Subtotals only
5.1 Calcipotriol twice daily vs. calcipotriol OM, BMD ON	1	154	Std. Mean Difference (IV, Random, 95% CI)	0.56 [0.23, 0.88]
5.2 Calcipotriol OD vs. combined calcipotriol + BMD OD	2	1194	Std. Mean Difference (IV, Random, 95% CI)	0.66 [0.31, 1.02]
5.3 Calcipotriol twice daily vs. combined calcipotriol + BMD OD	4	1204	Std. Mean Difference (IV, Random, 95% CI)	0.43 [0.20, 0.66]
5.4 Calcipotriol twice daily vs. combined calcipotriol + BMD twice daily	3	1804	Std. Mean Difference (IV, Random, 95% CI)	0.66 [0.40, 0.93]
5.5 Calcipotriol twice daily vs. calcipotriol OM, BMV ON	2	510	Std. Mean Difference (IV, Random, 95% CI)	0.27 [-0.19, 0.74]
5.6 Calcipotriol twice daily vs. calcipotriol OM, clobetasone butyrate ON	1	344	Std. Mean Difference (IV, Random, 95% CI)	0.27 [0.05, 0.48]
5.7 Calcipotriol twice daily vs. calcipotriol twice daily + clobetasol propionate twice daily	1	65	Std. Mean Difference (IV, Random, 95% CI)	0.88 [0.34, 1.42]
5.8 Calcipotriol twice daily vs. calcipotriol OM, diflucortolone valerate ON	1	116	Std. Mean Difference (IV, Random, 95% CI)	0.08 [-0.29, 0.44]
5.9 Calcipotriol OD vs. calcipotriol OM, fluocinonide acetonide ON	1	38	Std. Mean Difference (IV, Random, 95% CI)	0.53 [-0.11, 1.18]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
5.10 Calcipotriol OD vs. combined calcipotriol + hydrocortisone OD	1	408	Std. Mean Difference (IV, Random, 95% CI)	0.14 [-0.06, 0.33]
5.11 Calcitriol twice daily vs. diflucortolone valerate OM, calcitriol ON	1	142	Std. Mean Difference (IV, Random, 95% CI)	0.24 [-0.09, 0.57]
5.12 Tacalcitol OD vs. combined calcipotriol + BMD OD	1	334	Std. Mean Difference (IV, Random, 95% CI)	0.48 [0.26, 0.70]
6 Total withdrawals	15	5494	Risk Difference (M-H, Random, 95% CI)	0.03 [0.02, 0.05]
6.1 Talcipotriol vs. calcipotriol and corticosteroid	13	4985	Risk Difference (M-H, Random, 95% CI)	0.03 [0.01, 0.05]
6.2 Calcitriol vs. calcitriol and corticosteroid	1	142	Risk Difference (M-H, Random, 95% CI)	0.01 [-0.08, 0.10]
6.3 Tacalcitol vs. calcipotriol and corticosteroid	1	367	Risk Difference (M-H, Random, 95% CI)	0.05 [-0.01, 0.11]
7 Withdrawals due to adverse events	13	4081	Risk Difference (M-H, Random, 95% CI)	0.02 [0.01, 0.03]
7.1 Calcipotriol vs. calcipotriol and corticosteroid	11	3572	Risk Difference (M-H, Random, 95% CI)	0.02 [0.01, 0.03]
7.2 Calcitriol vs. calcitriol and corticosteroid	1	142	Risk Difference (M-H, Random, 95% CI)	0.03 [-0.02, 0.07]
7.3 Tacalcitol vs. calcipotriol and corticosteroid	1	367	Risk Difference (M-H, Random, 95% CI)	0.01 [-0.02, 0.03]
8 Withdrawals due to treatment failure	7	1925	Risk Difference (M-H, Random, 95% CI)	0.01 [-0.00, 0.02]
8.1 Calcipotriol vs. calcipotriol and corticosteroid	7	1925	Risk Difference (M-H, Random, 95% CI)	0.01 [-0.00, 0.02]
8.2 Calcitriol vs. calcitriol and corticosteroid	0	0	Risk Difference (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
8.3 Tacalcitol vs. calcipotriol and corticosteroid	0	0	Risk Difference (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
9 Adverse events (local)	15	5581	Risk Difference (M-H, Random, 95% CI)	0.06 [0.05, 0.08]
9.1 Calcipotriol vs. calcipotriol and corticosteroid	13	5084	Risk Difference (M-H, Random, 95% CI)	0.06 [0.04, 0.08]
9.2 Calcitriol vs. calcitriol and corticosteroid	1	131	Risk Difference (M-H, Random, 95% CI)	0.10 [0.02, 0.19]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
9.3 Tacalcitol vs. calcipotriol and corticosteroid	1	366	Risk Difference (M-H, Random, 95% CI)	0.09 [0.02, 0.15]
10 Adverse events (systemic)	6	2099	Risk Difference (M-H, Random, 95% CI)	0.00 [-0.00, 0.00]
10.1 Calcipotriol vs. calcipotriol and corticosteroid	5	1968	Risk Difference (M-H, Random, 95% CI)	0.00 [-0.00, 0.00]
10.2 Calcitriol vs. calcitriol and corticosteroid	1	131	Risk Difference (M-H, Random, 95% CI)	0.0 [-0.03, 0.03]
10.3 Tacalcitol vs. calcipotriol and corticosteroid	0	0	Risk Difference (M-H, Random, 95% CI)	0.0 [0.0, 0.0]

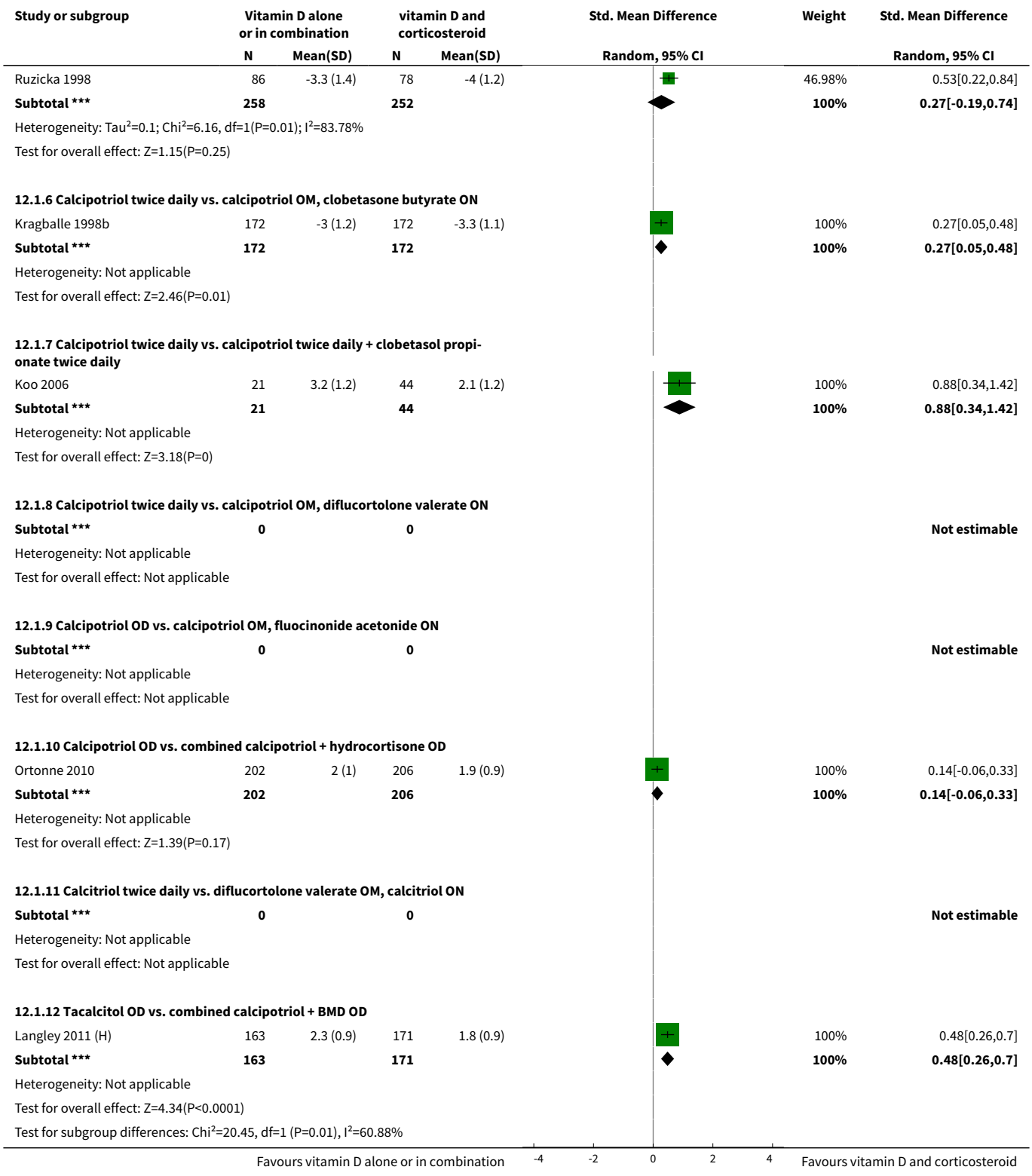
Analysis 12.1. Comparison 12 Vitamin D alone or in combination versus vitamin D + corticosteroid, Outcome 1 IAGI.

Study or subgroup	Vitamin D alone or in combination		vitamin D and corticosteroid		Std. Mean Difference	Weight	Std. Mean Difference
	N	Mean(SD)	N	Mean(SD)	Random, 95% CI		Random, 95% CI
12.1.1 Calcipotriol twice daily vs. calcipotriol OM, BMD ON							
Ortonne 1994	80	-3.6 (1)	74	-4.1 (0.8)		100%	0.56[0.23,0.88]
Subtotal ***	**80**		**74**			**100%**	**0.56[0.23,0.88]**
Heterogeneity: Not applicable							
Test for overall effect: Z=3.39(P=0)							
12.1.2 Calcipotriol OD vs. combined calcipotriol + BMD OD							
Fleming 2010 (H)	74	2.3 (0.8)	150	1.9 (1.1)		43.85%	0.46[0.18,0.74]
Kaufmann 2002 (H)	480	2.2 (0.9)	490	1.5 (0.9)		56.15%	0.82[0.69,0.95]
Subtotal ***	**554**		**640**			**100%**	**0.66[0.31,1.02]**
Heterogeneity: Tau^2=0.05; Chi^2=5.24, df=1(P=0.02); I^2=80.91%							
Test for overall effect: Z=3.68(P=0)							
12.1.3 Calcipotriol twice daily vs. combined calcipotriol + BMD OD							
Guenther 2002 (H)	227	-3.3 (1.1)	150	-3.6 (1)		100%	0.27[0.06,0.48]
Subtotal ***	**227**		**150**			**100%**	**0.27[0.06,0.48]**
Heterogeneity: Not applicable							
Test for overall effect: Z=2.55(P=0.01)							
12.1.4 Calcipotriol twice daily vs. combined calcipotriol + BMD twice daily							
Douglas 2002	365	-3.1 (1.1)	369	-3.7 (1)		34.32%	0.58[0.44,0.73]
Guenther 2002 (H)	227	-3.3 (1.1)	234	-3.8 (1)		32.36%	0.47[0.28,0.65]
Papp 2003 (H)	308	-2.8 (1.2)	301	-3.8 (0.9)		33.32%	0.93[0.76,1.1]
Subtotal ***	**900**		**904**			**100%**	**0.66[0.4,0.93]**
Heterogeneity: Tau^2=0.05; Chi^2=15.28, df=2(P=0); I^2=86.91%							
Test for overall effect: Z=4.89(P<0.0001)							
12.1.5 Calcipotriol twice daily vs. calcipotriol OM, BMV ON							
Kragballe 1998b	172	-3 (1.2)	174	-3 (1.2)		53.02%	0.05[-0.16,0.26]

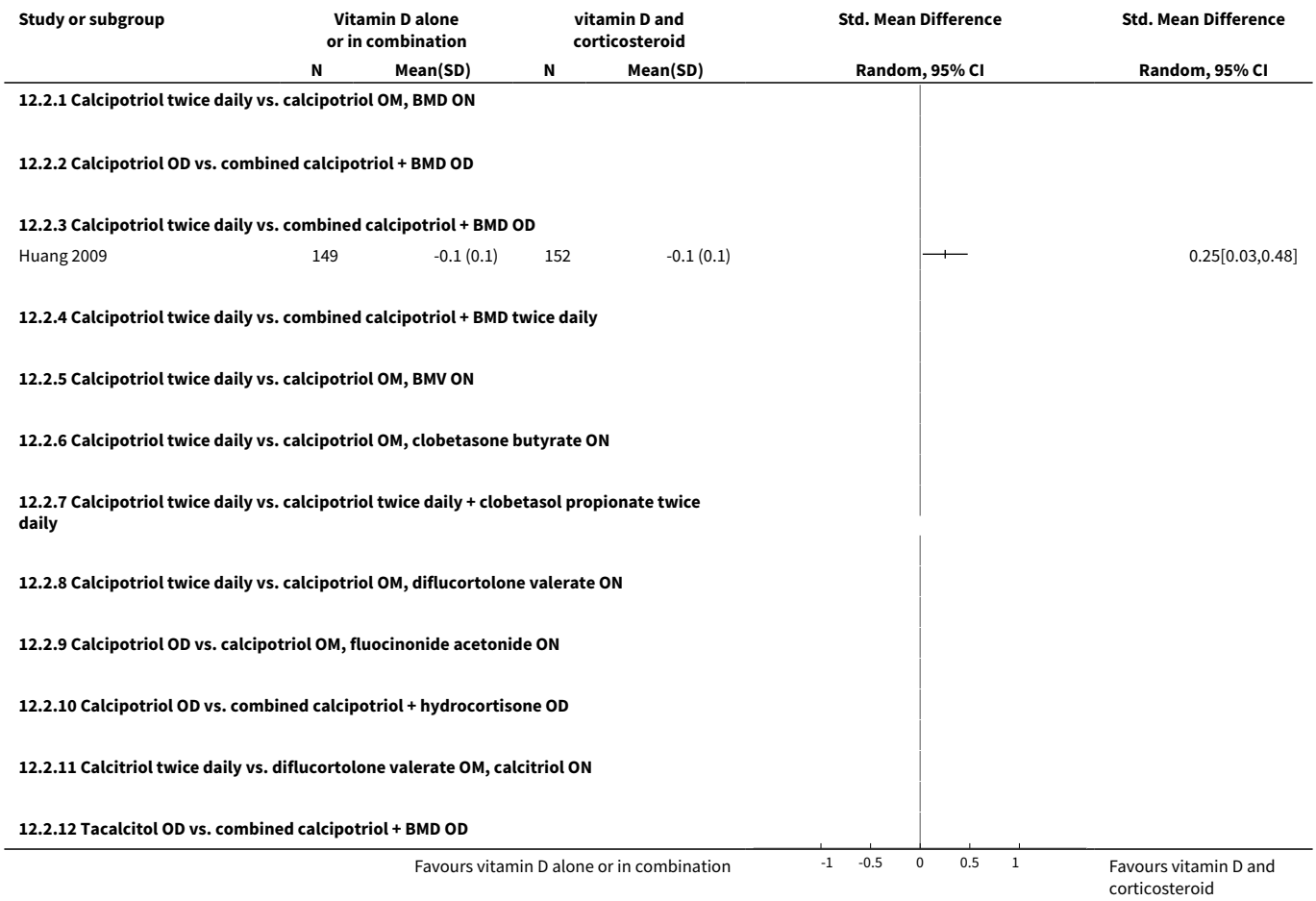


Favours vitamin D alone or in combination

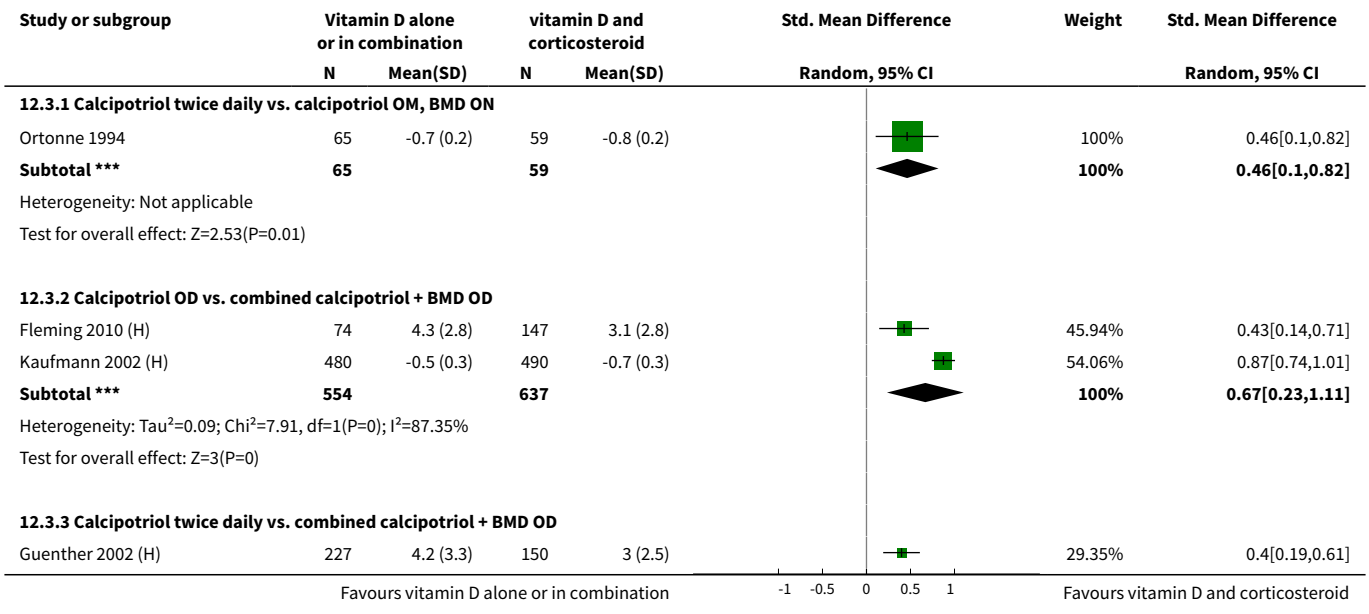
Favours vitamin D and corticosteroid



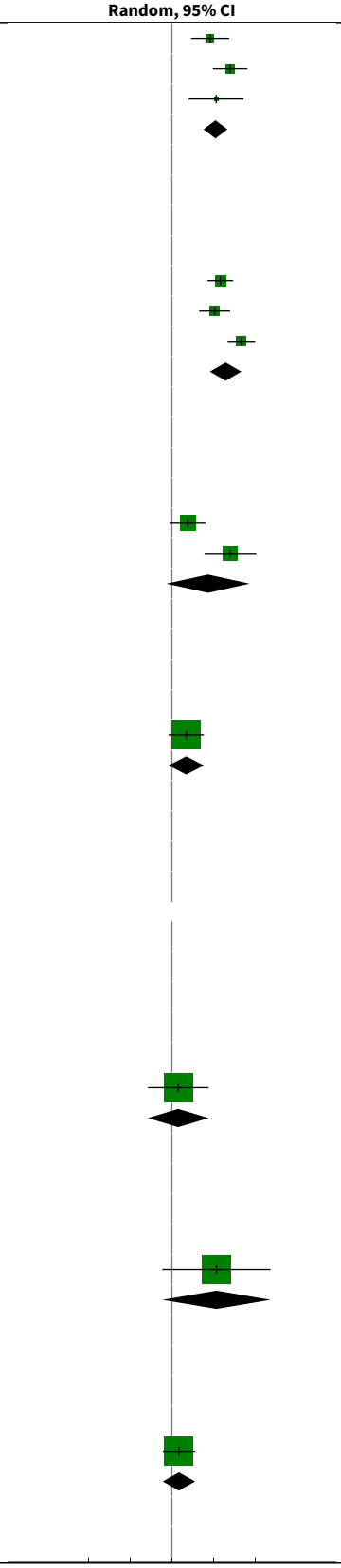
Analysis 12.2. Comparison 12 Vitamin D alone or in combination versus vitamin D + corticosteroid, Outcome 2 TSS.



Analysis 12.3. Comparison 12 Vitamin D alone or in combination versus vitamin D + corticosteroid, Outcome 3 PASI.

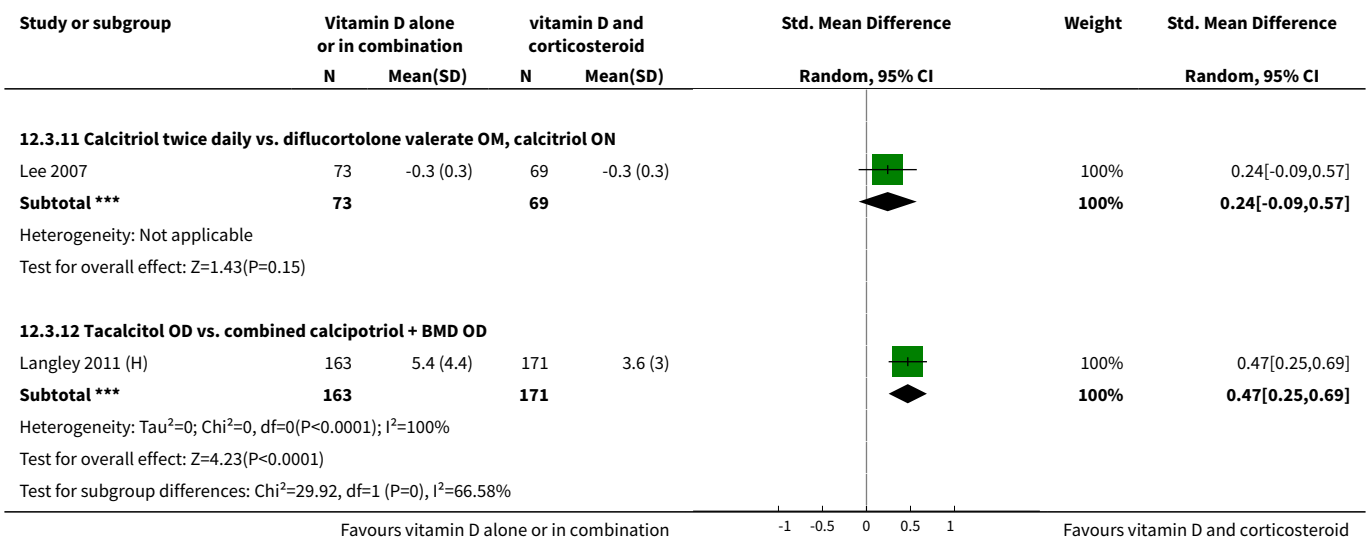


Study or subgroup	Vitamin D alone or in combination		vitamin D and corticosteroid		Std. Mean Difference	Weight	Std. Mean Difference
	N	Mean(SD)	N	Mean(SD)	Random, 95% CI		Random, 95% CI
Huang 2009	149	-0.7 (0.2)	152	-0.8 (0.2)		25.97%	0.46[0.23,0.69]
Jorizzo 2007	186	-0.4 (0.3)	193	-0.6 (0.3)		29.48%	0.7[0.49,0.91]
Saraceno 2007	73	4.1 (3.3)	74	2.5 (2.5)		15.2%	0.53[0.2,0.86]
Subtotal ***	**635**		**569**			**100%**	**0.52[0.38,0.67]**
Heterogeneity: Tau^2=0.01; Chi^2=4.43, df=3(P=0.22); I^2=32.29%							
Test for overall effect: Z=7.16(P<0.0001)							
12.3.4 Calcipotriol twice daily vs. combined calcipotriol + BMD twice daily							
Douglas 2002	332	4.4 (3.9)	342	2.5 (2.5)		34.83%	0.58[0.43,0.74]
Guenther 2002 (H)	227	4.2 (3.3)	234	2.7 (2.5)		31.55%	0.51[0.33,0.7]
Papp 2003 (H)	308	-0.5 (0.3)	301	-0.7 (0.3)		33.63%	0.83[0.67,1]
Subtotal ***	**867**		**877**			**100%**	**0.64[0.46,0.83]**
Heterogeneity: Tau^2=0.02; Chi^2=7.59, df=2(P=0.02); I^2=73.65%							
Test for overall effect: Z=6.68(P<0.0001)							
12.3.5 Calcipotriol twice daily vs. calcipotriol OM, BMV ON							
Kragballe 1998b	172	4 (3.4)	174	3.4 (3.1)		52.61%	0.19[-0.02,0.4]
Ruzicka 1998	87	1.9 (1.6)	82	1 (0.8)		47.39%	0.7[0.39,1.01]
Subtotal ***	**259**		**256**			**100%**	**0.43[-0.07,0.93]**
Heterogeneity: Tau^2=0.11; Chi^2=7.08, df=1(P=0.01); I^2=85.87%							
Test for overall effect: Z=1.7(P=0.09)							
12.3.6 Calcipotriol twice daily vs. calcipotriol OM, clobetasone butyrate ON							
Kragballe 1998b	172	4 (3.4)	172	3.5 (2.9)		100%	0.17[-0.04,0.38]
Subtotal ***	**172**		**172**			**100%**	**0.17[-0.04,0.38]**
Heterogeneity: Not applicable							
Test for overall effect: Z=1.59(P=0.11)							
12.3.7 Calcipotriol twice daily vs. calcipotriol twice daily + clobetasol propionate twice daily							
Subtotal ***	**0**		**0**				**Not estimable**
Heterogeneity: Not applicable							
Test for overall effect: Not applicable							
12.3.8 Calcipotriol twice daily vs. calcipotriol OM, diflucortolone valerate ON							
Salmhofer 2000	58	1.9 (1.4)	58	1.8 (1.2)		100%	0.08[-0.29,0.44]
Subtotal ***	**58**		**58**			**100%**	**0.08[-0.29,0.44]**
Heterogeneity: Not applicable							
Test for overall effect: Z=0.41(P=0.68)							
12.3.9 Calcipotriol OD vs. calcipotriol OM, fluocinonide acetonide ON							
Wozel 2001	19	8.9 (5.1)	19	6.3 (4.6)		100%	0.53[-0.11,1.18]
Subtotal ***	**19**		**19**			**100%**	**0.53[-0.11,1.18]**
Heterogeneity: Not applicable							
Test for overall effect: Z=1.62(P=0.11)							
12.3.10 Calcipotriol OD vs. combined calcipotriol + hydrocortisone OD							
Ortonne 2010	202	4.4 (3.9)	206	4.1 (3.9)		100%	0.08[-0.11,0.28]
Subtotal ***	**202**		**206**			**100%**	**0.08[-0.11,0.28]**
Heterogeneity: Tau^2=0; Chi^2=0, df=0(P<0.0001); I^2=100%							
Test for overall effect: Z=0.85(P=0.39)							

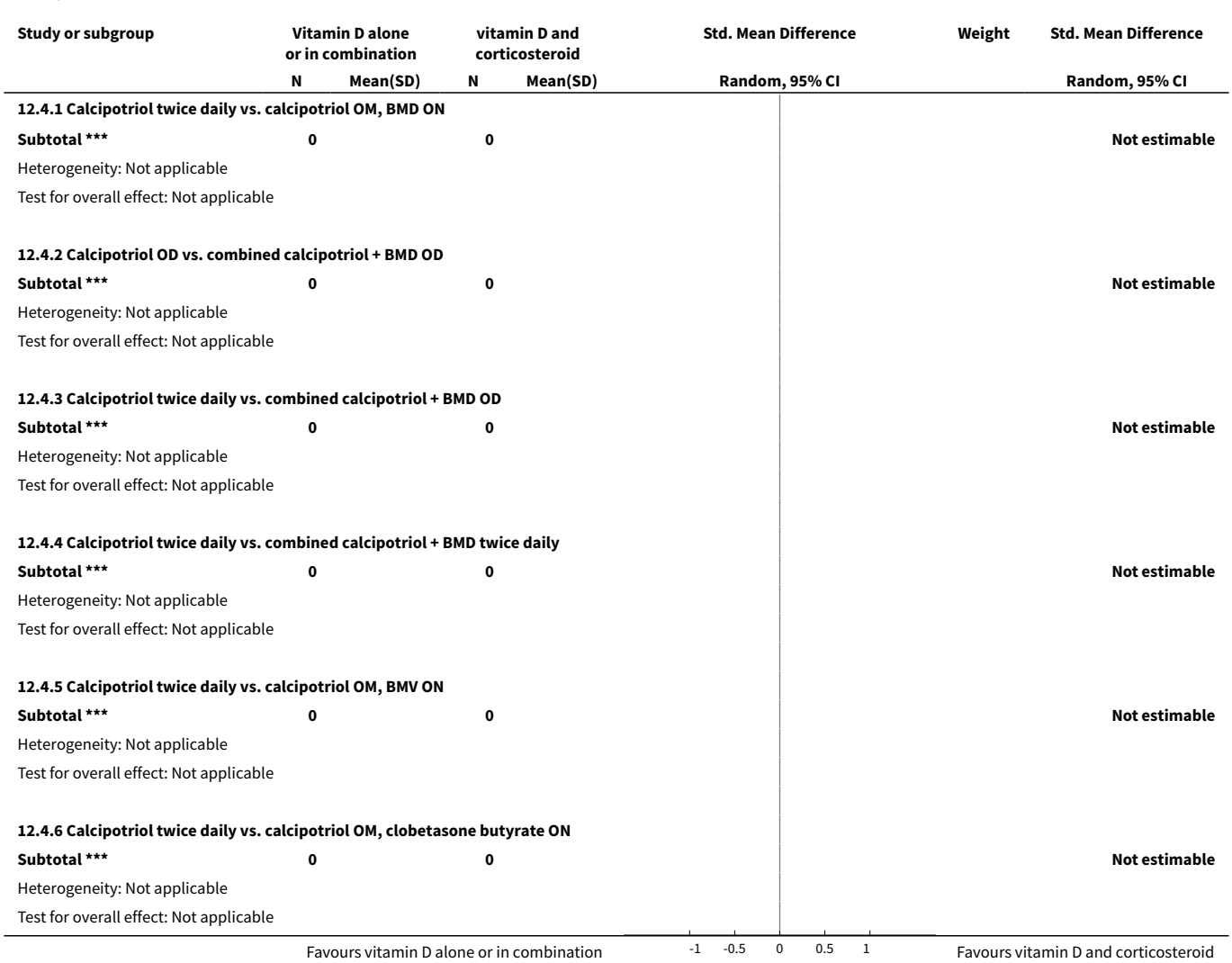


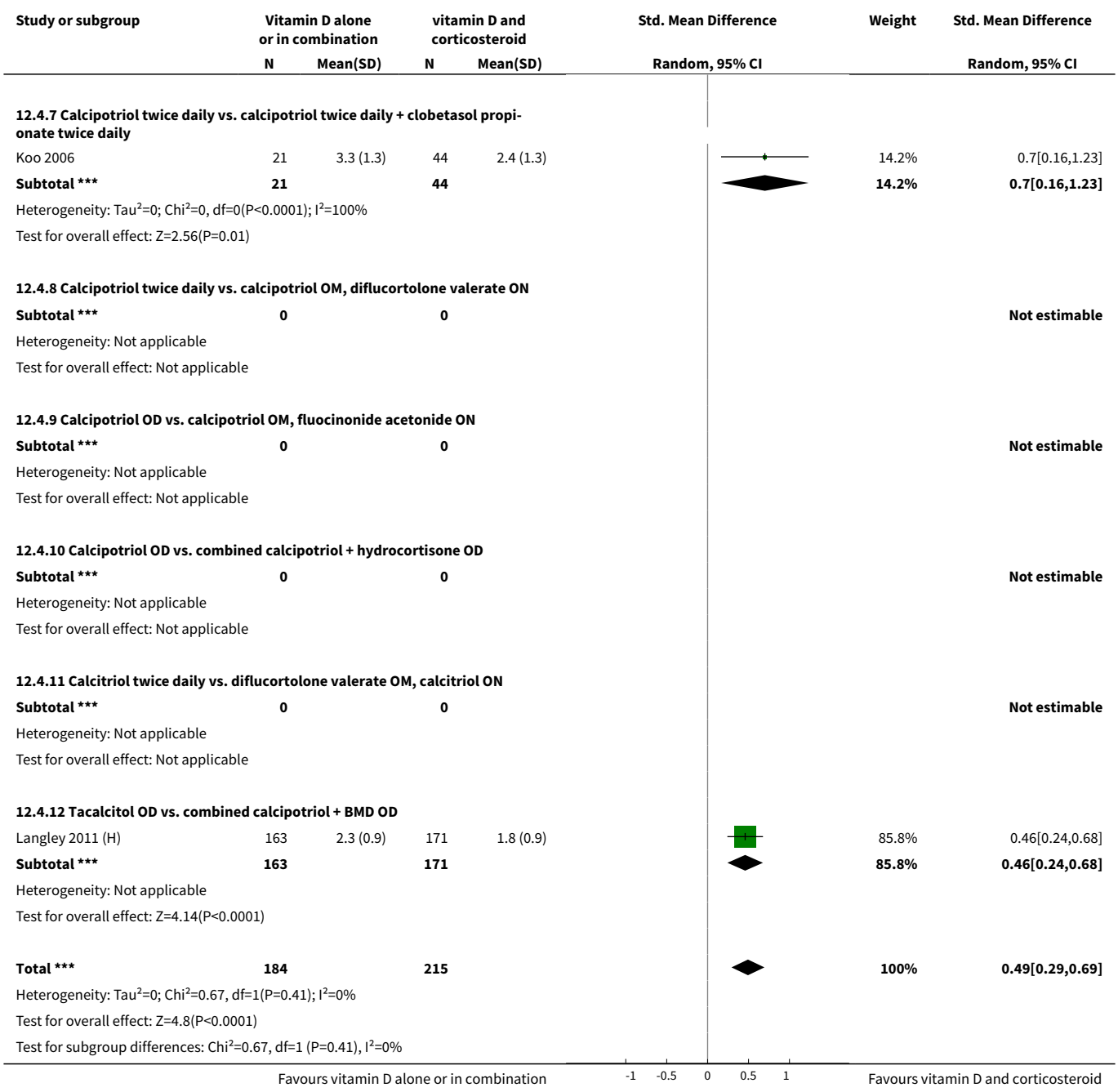
Favours vitamin D alone or in combination

Favours vitamin D and corticosteroid

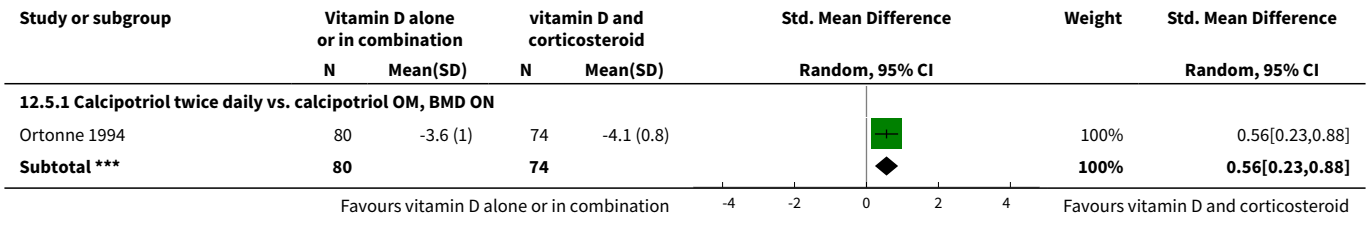


Analysis 12.4. Comparison 12 Vitamin D alone or in combination versus vitamin D + corticosteroid, Outcome 4 PAGI.

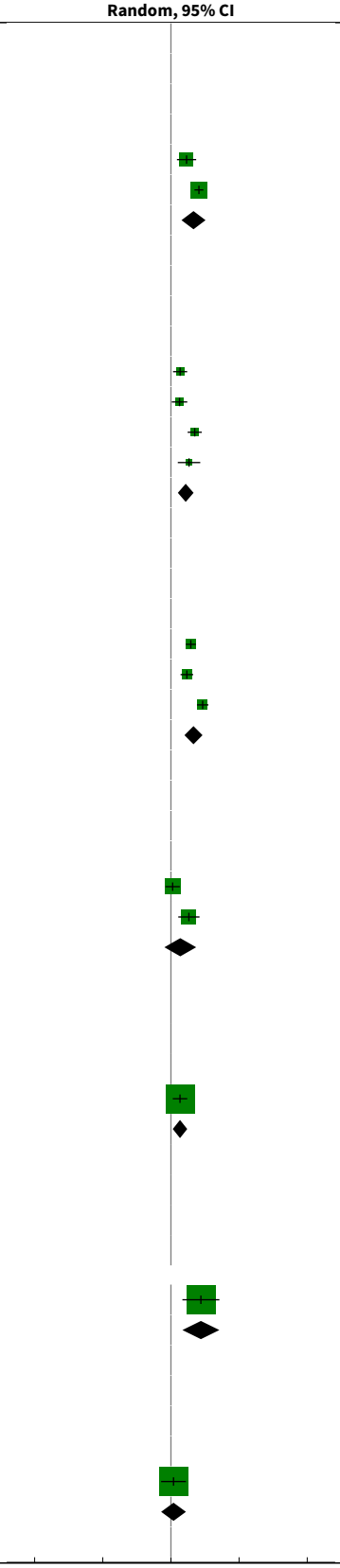


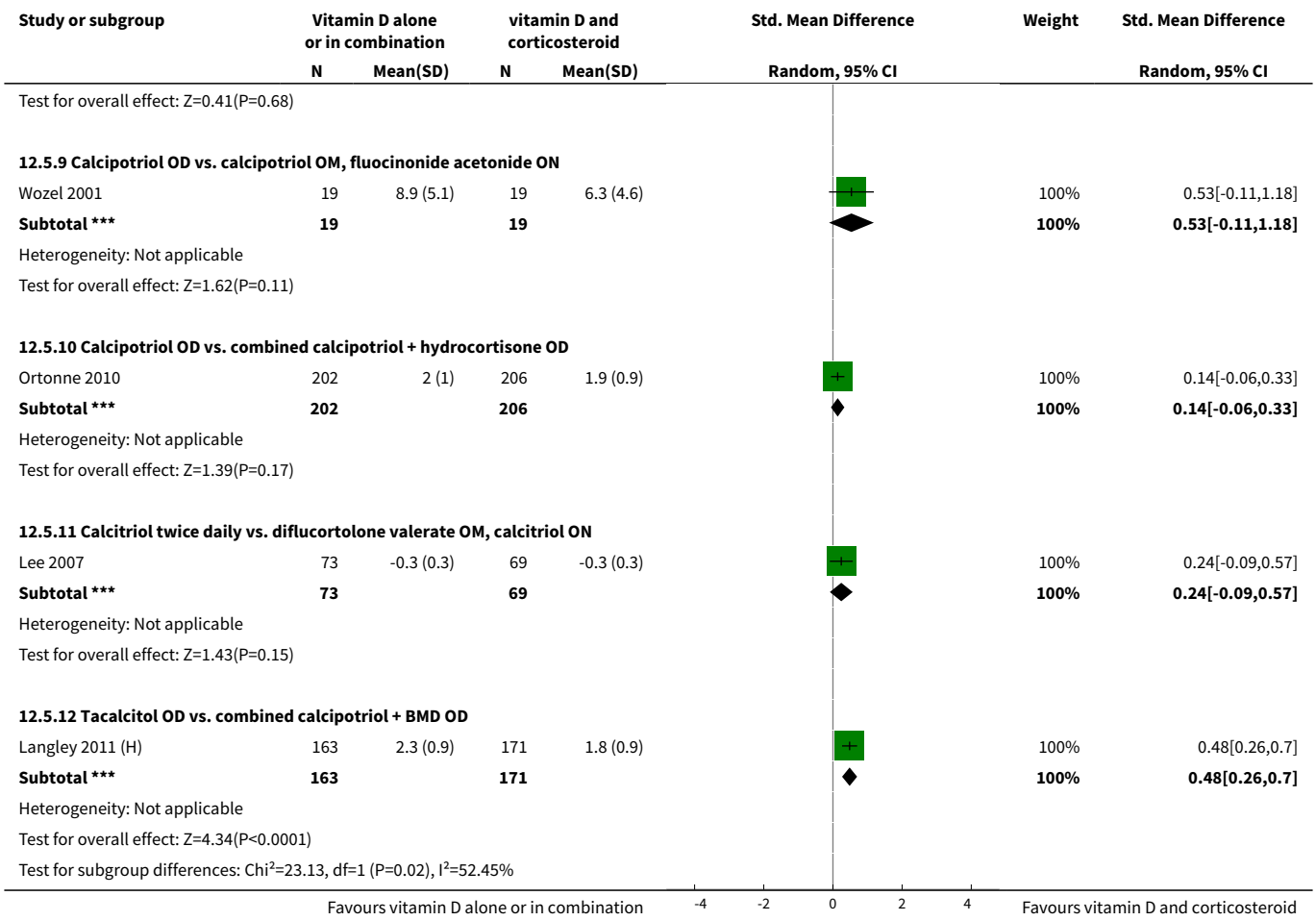


Analysis 12.5. Comparison 12 Vitamin D alone or in combination versus vitamin D + corticosteroid, Outcome 5 Combined end point (IAGI/TSS/PASI/PAGI).

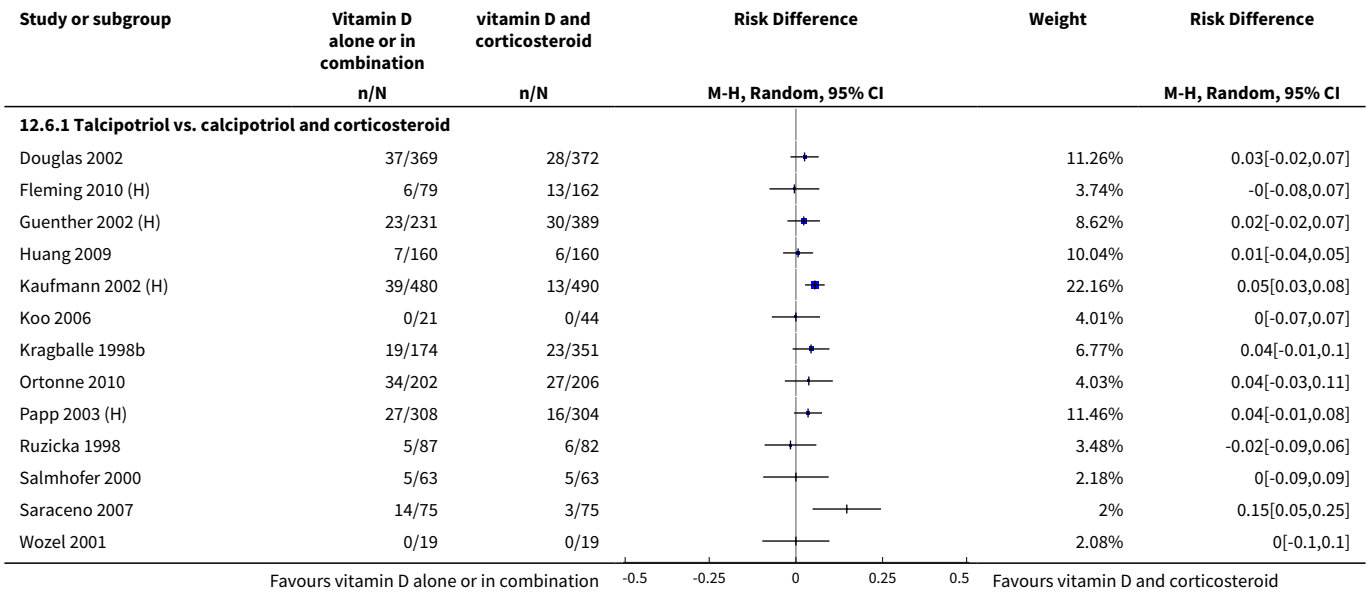


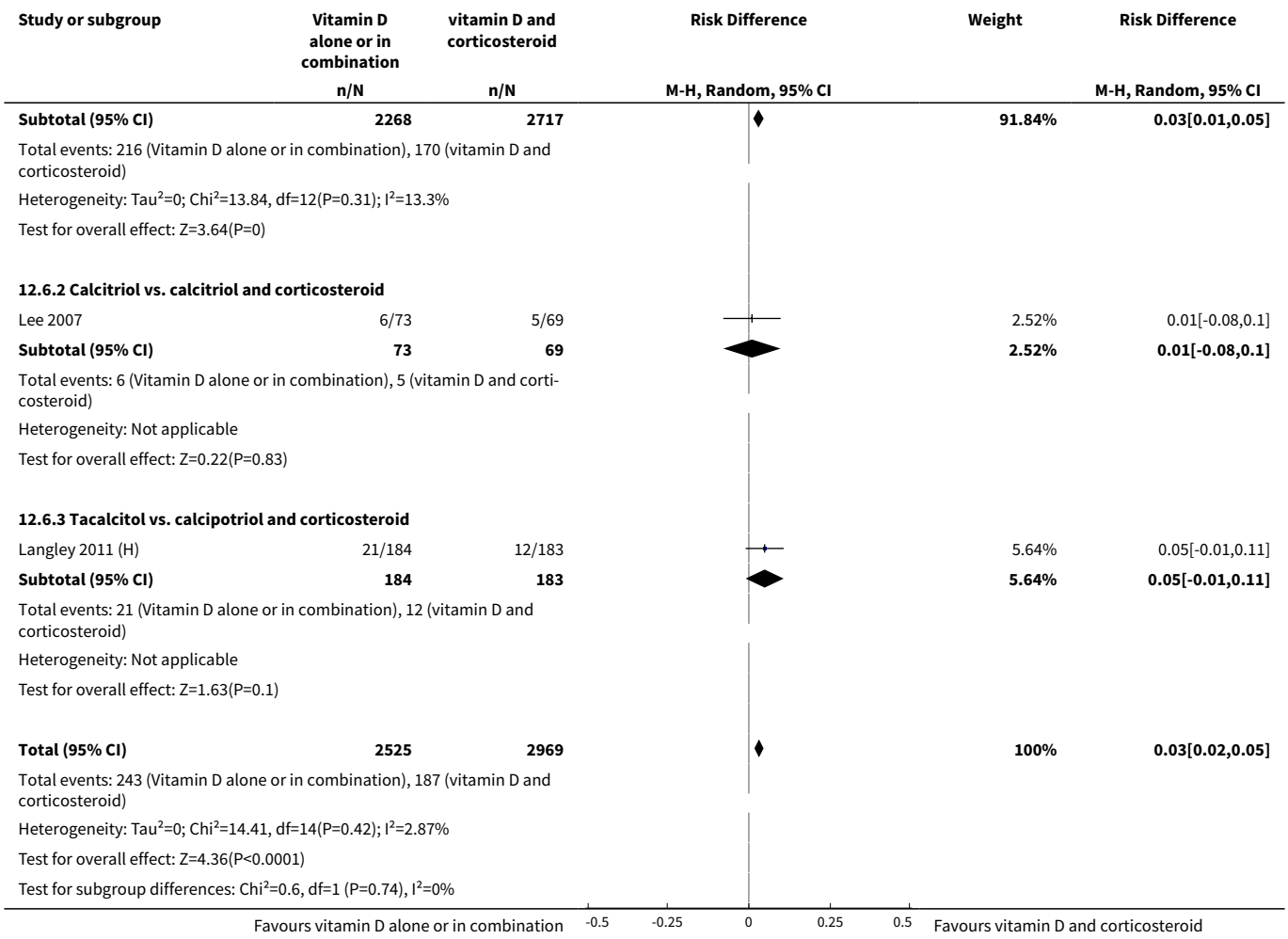
Study or subgroup	Vitamin D alone or in combination N	Mean(SD)	vitamin D and corticosteroid N	Mean(SD)	Std. Mean Difference Random, 95% CI	Weight	Std. Mean Difference Random, 95% CI
Heterogeneity: Not applicable							
Test for overall effect: Z=3.39(P=0)							
12.5.2 Calcipotriol OD vs. combined calcipotriol + BMD OD							
Fleming 2010 (H)	74	2.3 (0.8)	150	1.9 (1.1)		43.85%	0.46[0.18,0.74]
Kaufmann 2002 (H)	480	2.2 (0.9)	490	1.5 (0.9)		56.15%	0.82[0.69,0.95]
Subtotal ***	**554**		**640**			**100%**	**0.66[0.31,1.02]**
Heterogeneity: Tau^2=0.05; Chi^2=5.24, df=1(P=0.02); I^2=80.91%							
Test for overall effect: Z=3.68(P=0)							
12.5.3 Calcipotriol twice daily vs. combined calcipotriol + BMD OD							
Guenther 2002 (H)	227	-3.3 (1.1)	150	-3.6 (1)		26.96%	0.27[0.06,0.48]
Huang 2009	149	-0.1 (0.1)	152	-0.1 (0.1)		25.84%	0.25[0.03,0.48]
Jorizzo 2007	186	-0.4 (0.3)	193	-0.6 (0.3)		26.94%	0.7[0.49,0.91]
Saraceno 2007	73	4.1 (3.3)	74	2.5 (2.5)		20.26%	0.53[0.2,0.86]
Subtotal ***	**635**		**569**			**100%**	**0.43[0.2,0.66]**
Heterogeneity: Tau^2=0.04; Chi^2=11.46, df=3(P=0.01); I^2=73.83%							
Test for overall effect: Z=3.68(P=0)							
12.5.4 Calcipotriol twice daily vs. combined calcipotriol + BMD twice daily							
Douglas 2002	365	-3.1 (1.1)	369	-3.7 (1)		34.32%	0.58[0.44,0.73]
Guenther 2002 (H)	227	-3.3 (1.1)	234	-3.8 (1)		32.36%	0.47[0.28,0.65]
Papp 2003 (H)	308	-2.8 (1.2)	301	-3.8 (0.9)		33.32%	0.93[0.76,1.1]
Subtotal ***	**900**		**904**			**100%**	**0.66[0.4,0.93]**
Heterogeneity: Tau^2=0.05; Chi^2=15.28, df=2(P=0); I^2=86.91%							
Test for overall effect: Z=4.89(P<0.0001)							
12.5.5 Calcipotriol twice daily vs. calcipotriol OM, BMV ON							
Kragballe 1998b	172	-3 (1.2)	174	-3 (1.2)		53.02%	0.05[-0.16,0.26]
Ruzicka 1998	86	-3.3 (1.4)	78	-4 (1.2)		46.98%	0.53[0.22,0.84]
Subtotal ***	**258**		**252**			**100%**	**0.27[-0.19,0.74]**
Heterogeneity: Tau^2=0.1; Chi^2=6.16, df=1(P=0.01); I^2=83.78%							
Test for overall effect: Z=1.15(P=0.25)							
12.5.6 Calcipotriol twice daily vs. calcipotriol OM, clobetasone butyrate ON							
Kragballe 1998b	172	-3 (1.2)	172	-3.3 (1.1)		100%	0.27[0.05,0.48]
Subtotal ***	**172**		**172**			**100%**	**0.27[0.05,0.48]**
Heterogeneity: Not applicable							
Test for overall effect: Z=2.46(P=0.01)							
12.5.7 Calcipotriol twice daily vs. calcipotriol twice daily + clobetasol propionate twice daily							
Koo 2006	21	3.2 (1.2)	44	2.1 (1.2)		100%	0.88[0.34,1.42]
Subtotal ***	**21**		**44**			**100%**	**0.88[0.34,1.42]**
Heterogeneity: Not applicable							
Test for overall effect: Z=3.18(P=0)							
12.5.8 Calcipotriol twice daily vs. calcipotriol OM, diflucortolone valerate ON							
Salmhofer 2000	58	1.9 (1.4)	58	1.8 (1.2)		100%	0.08[-0.29,0.44]
Subtotal ***	**58**		**58**			**100%**	**0.08[-0.29,0.44]**
Heterogeneity: Not applicable							



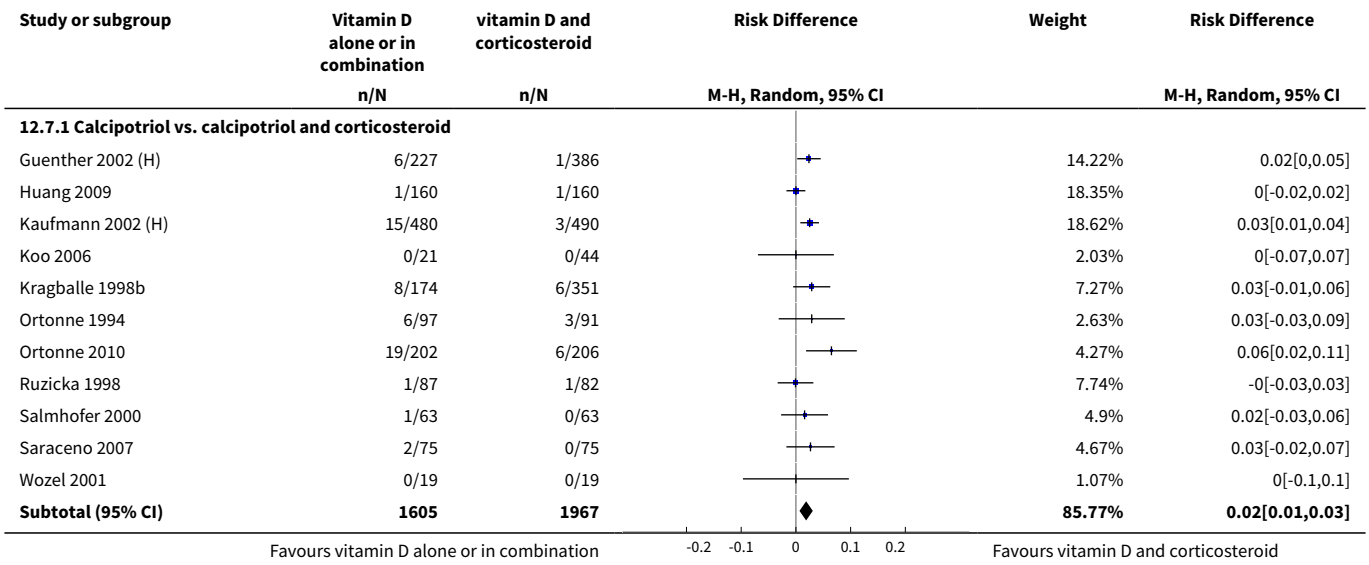


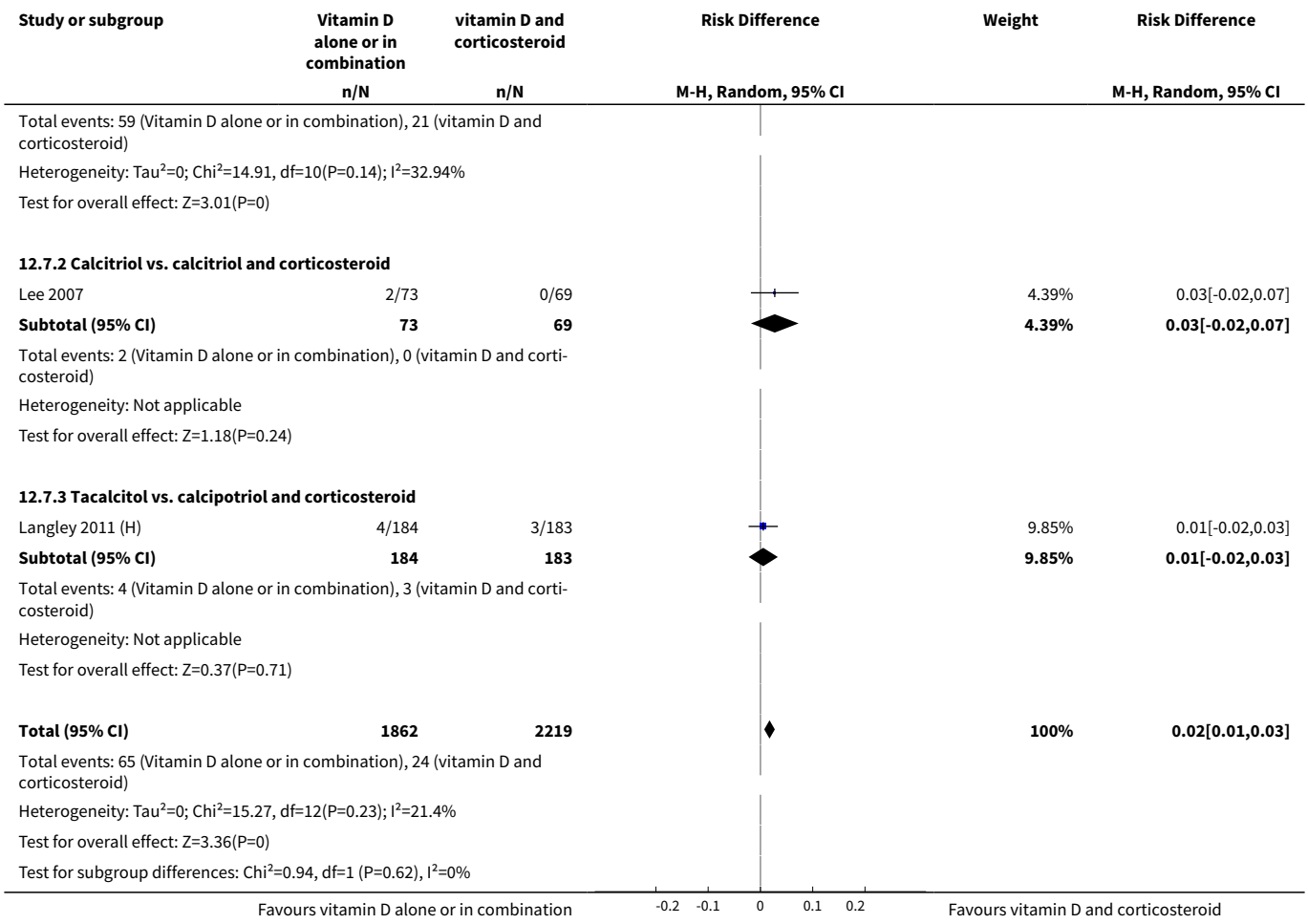
Analysis 12.6. Comparison 12 Vitamin D alone or in combination versus vitamin D + corticosteroid, Outcome 6 Total withdrawals.



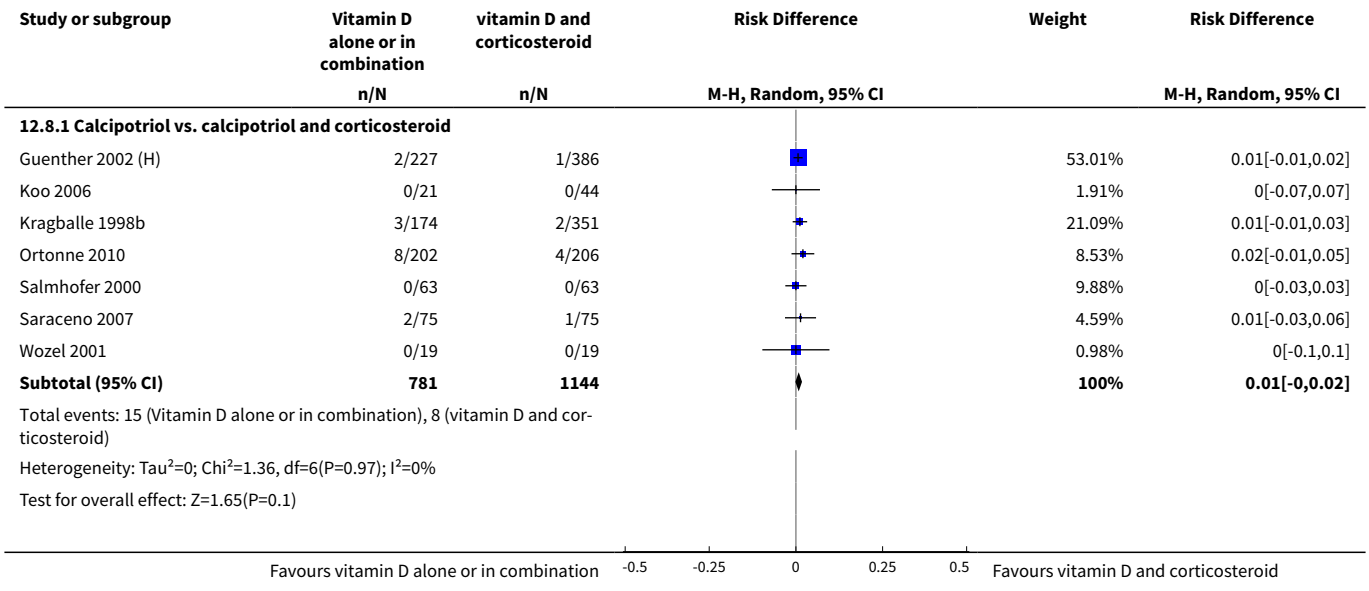


Analysis 12.7. Comparison 12 Vitamin D alone or in combination versus vitamin D + corticosteroid, Outcome 7 Withdrawals due to adverse events.

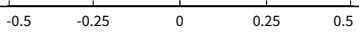




Analysis 12.8. Comparison 12 Vitamin D alone or in combination versus vitamin D + corticosteroid, Outcome 8 Withdrawals due to treatment failure.



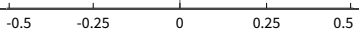
Study or subgroup	Vitamin D alone or in combination	vitamin D and corticosteroid	Risk Difference	Weight	Risk Difference
	n/N	n/N	M-H, Random, 95% CI		M-H, Random, 95% CI
12.8.2 Calcitriol vs. calcitriol and corticosteroid					
Subtotal (95% CI)	**0**	**0**			**Not estimable**
Total events: 0 (Vitamin D alone or in combination), 0 (vitamin D and corticosteroid)					
Heterogeneity: Not applicable					
Test for overall effect: Not applicable					
12.8.3 Tacalcitol vs. calcipotriol and corticosteroid					
Subtotal (95% CI)	**0**	**0**			**Not estimable**
Total events: 0 (Vitamin D alone or in combination), 0 (vitamin D and corticosteroid)					
Heterogeneity: Not applicable					
Test for overall effect: Not applicable					
Total (95% CI)	**781**	**1144**		**100%**	**0.01[-0,0.02]**
Total events: 15 (Vitamin D alone or in combination), 8 (vitamin D and corticosteroid)					
Heterogeneity: Tau^2=0; Chi^2=1.36, df=6(P=0.97); I^2=0%					
Test for overall effect: Z=1.65(P=0.1)					
Test for subgroup differences: Not applicable					



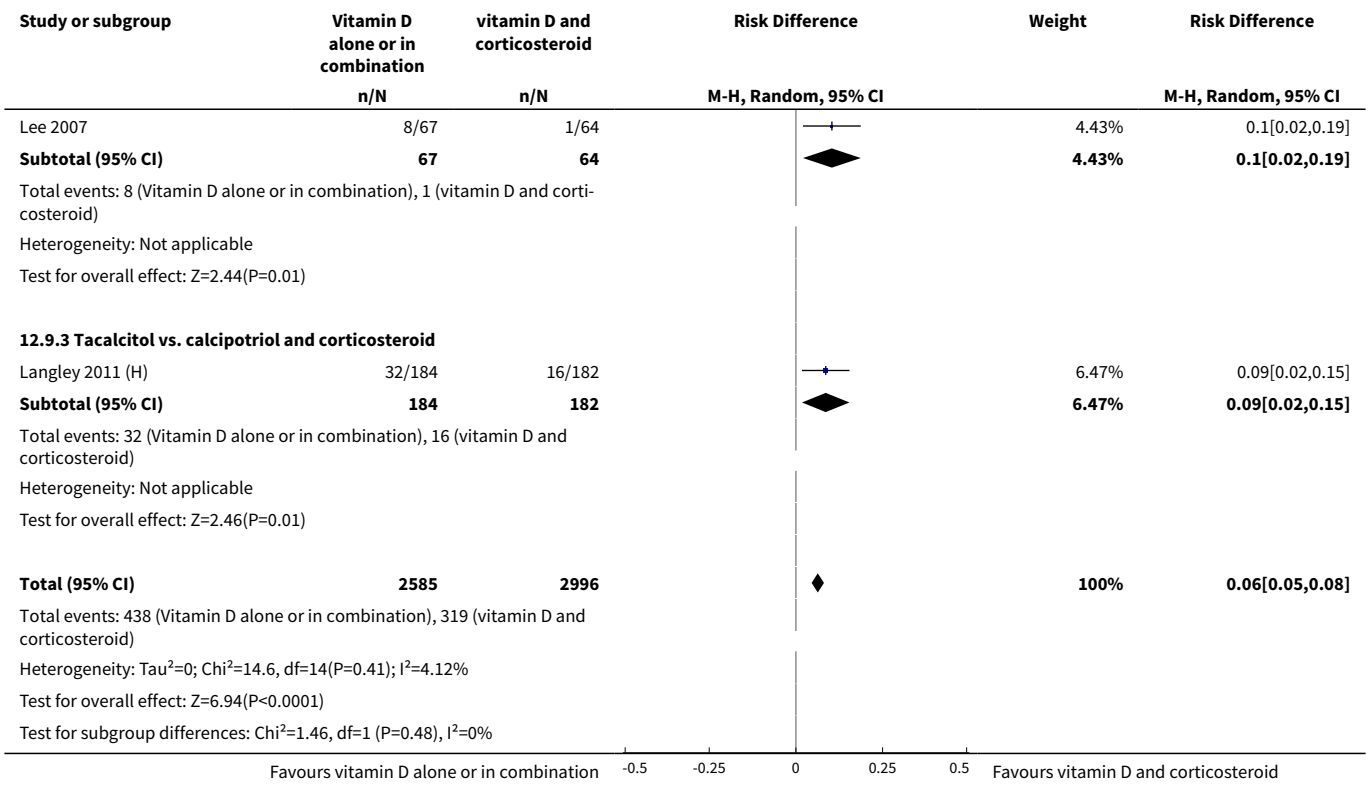
Favours vitamin D alone or in combination — Favours vitamin D and corticosteroid

Analysis 12.9. Comparison 12 Vitamin D alone or in combination versus vitamin D + corticosteroid, Outcome 9 Adverse events (local).

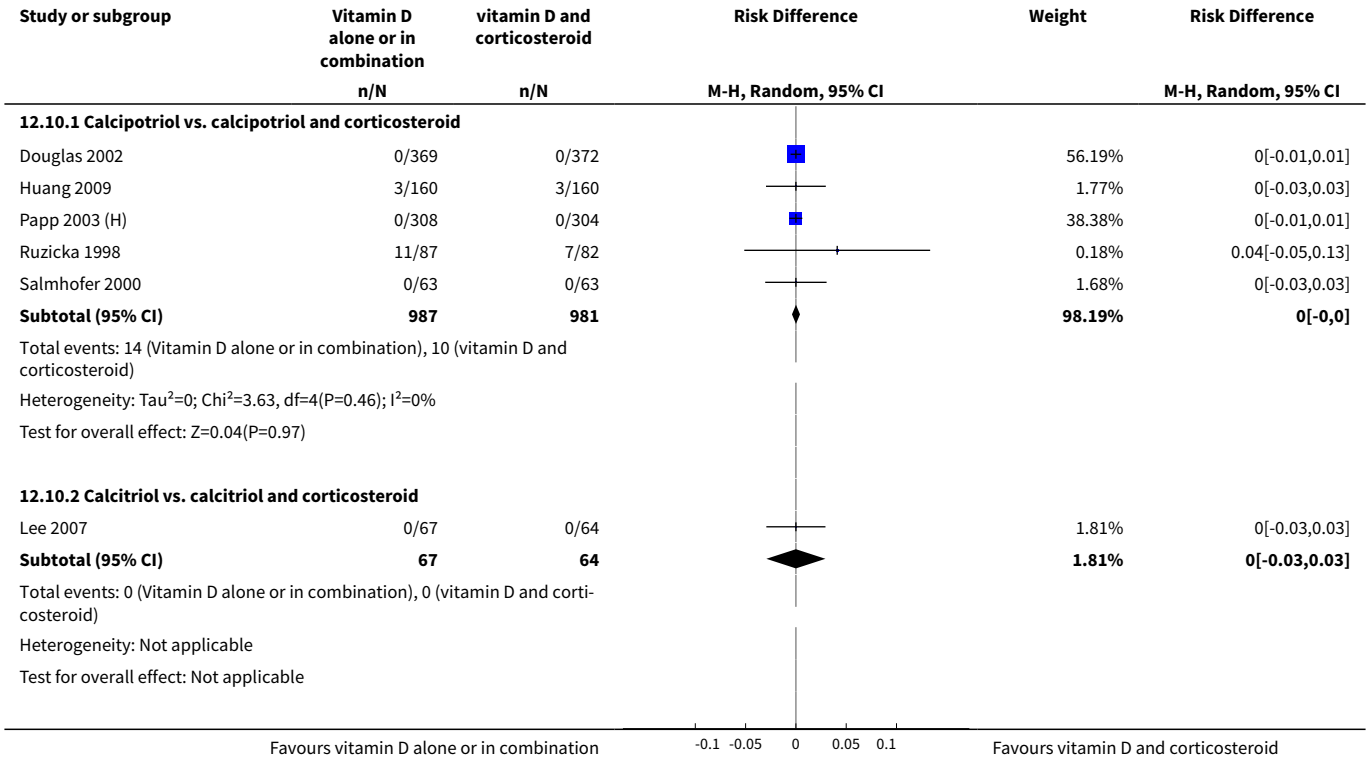
Study or subgroup	Vitamin D alone or in combination	vitamin D and corticosteroid	Risk Difference	Weight	Risk Difference
	n/N	n/N	M-H, Random, 95% CI		M-H, Random, 95% CI
12.9.1 Calcipotriol vs. calcipotriol and corticosteroid					
Douglas 2002	44/369	30/372		15.38%	0.04[-0,0.08]
Fleming 2010 (H)	8/79	12/160		5.03%	0.03[-0.05,0.1]
Guenther 2002 (H)	45/227	40/386		8.3%	0.09[0.03,0.15]
Huang 2009	25/160	17/160		5.61%	0.05[-0.02,0.12]
Kaufmann 2002 (H)	54/480	29/490		22.05%	0.05[0.02,0.09]
Kragballe 1998b	54/173	71/347		4.68%	0.11[0.03,0.19]
Ortonne 1994	24/94	11/88		2.48%	0.13[0.02,0.24]
Ortonne 2010	63/200	40/204		4.33%	0.12[0.03,0.2]
Papp 2003 (H)	53/308	30/304		10.21%	0.07[0.02,0.13]
Ruzicka 1998	13/87	6/82		3.52%	0.08[-0.02,0.17]
Salmhofer 2000	6/63	8/63		2.59%	-0.03[-0.14,0.08]
Saraceno 2007	8/75	7/75		3.36%	0.01[-0.08,0.11]
Wozel 2001	1/19	1/19		1.55%	0[-0.14,0.14]
Subtotal (95% CI)	**2334**	**2750**		**89.1%**	**0.06[0.04,0.08]**
Total events: 398 (Vitamin D alone or in combination), 302 (vitamin D and corticosteroid)					
Heterogeneity: Tau^2=0; Chi^2=13.26, df=12(P=0.35); I^2=9.5%					
Test for overall effect: Z=5.92(P<0.0001)					
12.9.2 Calcitriol vs. calcitriol and corticosteroid					

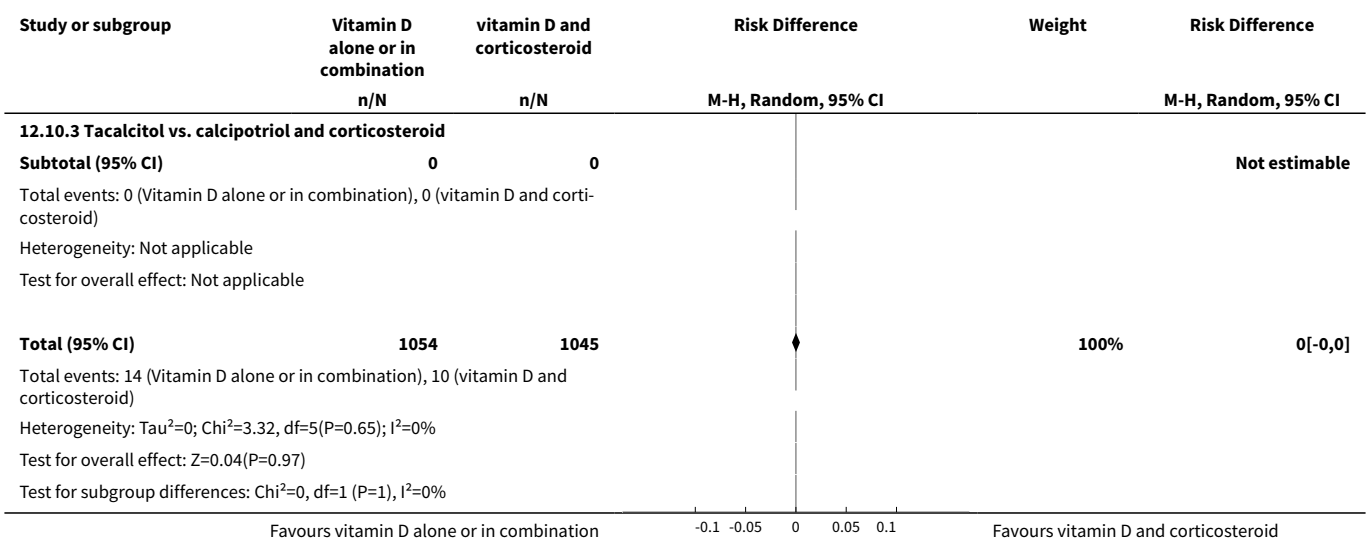


Favours vitamin D alone or in combination — Favours vitamin D and corticosteroid



Analysis 12.10. Comparison 12 Vitamin D alone or in combination versus vitamin D + corticosteroid, Outcome 10 Adverse events (systemic).





Comparison 13. Vitamin D alone or in combination versus other treatments: complex regimens

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 IAGI	7		Std. Mean Difference (IV, Random, 95% CI)	Subtotals only
1.1 Calcipotriol (12 wks) vs. combined calcipotriol + BMD (8 wks); then calcipotriol (4 wks)	1	577	Std. Mean Difference (IV, Random, 95% CI)	-0.12 [-0.29, 0.04]
1.2 Calcipotriol (12 wks) vs. combined calcipotriol + BMD (4 wks); then calcipotriol (8 wks)	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
1.3 Calcipotriol (12 wks) vs. combined calcipotriol + BMD (4 wks); then calcipotriol (w/dy) & combined calcipotriol + BMD (w/e) (8 wks)	1	585	Std. Mean Difference (IV, Random, 95% CI)	0.13 [-0.04, 0.29]
1.4 Calcipotriol (6 wks) vs. clobetasol propionate (2 wks); then calcipotriol (4 wks)	1	92	Std. Mean Difference (IV, Random, 95% CI)	0.60 [0.18, 1.02]
1.5 Calcipotriol (6 wks) vs. calcipotriol OM, fluocinonide acetonide ON (2 wks); then calcipotriol twice daily (4 wks)	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
1.6 Calcipotriol (6 wks) vs. halometasone OM, calcipotriol ON (2 wks); then calcipotriol twice daily (w/dy), halometasone (w/e) (2 wks); then calcipotriol twice daily (2wks)	1	76	Std. Mean Difference (IV, Random, 95% CI)	0.41 [-0.05, 0.86]
1.7 Calcipotriol ON, clobetasol propionate OM (2 to 4 wks); then calcipotriol twice daily (to wk 12)	1	125	Std. Mean Difference (IV, Random, 95% CI)	-0.19 [-0.54, 0.16]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
vs. calcitriol ON, clobetasol propionate OM (2 to 4 wks); then calcitriol twice daily (to wk 12)				
1.8 Combined calcipotriol + BMD (4 wks); then placebo ointment twice daily (8 wks) vs. combined calcipotriol + BMD (4 wks); then calcipotriol ointment twice daily (8 wks)	1	759	Std. Mean Difference (IV, Random, 95% CI)	0.27 [0.12, 0.41]
1.9 Combined calcipotriol + BMD (4 wks); then placebo ointment twice daily (8 wks) vs. combined calcipotriol + BMD (4 wks); then calcipotriol (w/dy)+ combined calcipotriol + BMD (w/e) (8 wks)	1	753	Std. Mean Difference (IV, Random, 95% CI)	0.51 [0.37, 0.66]
1.10 Combined calcipotriol + BMD (4 wks); then calcipotriol ointment twice daily (8 wks) vs. combined calcipotriol + BMD (4 wks); then calcipotriol (w/dy)+ combined calcipotriol + BMD (w/e) (8 wks)	1	760	Std. Mean Difference (IV, Random, 95% CI)	0.26 [0.11, 0.40]
1.11 Combined calcipotriol + BMD (8 wks); then calcipotriol (4 wks) vs. combined calcipotriol + BMD (4 wks); then calcipotriol (w/dy) & combined calcipotriol + BMD (w/e) (8 wks)	1	596	Std. Mean Difference (IV, Random, 95% CI)	0.24 [0.08, 0.40]
1.12 Tacalcitol (8 wks) vs. combined calcipotriol + BMD (4 wks); then calcipotriol (4 wks)	1	493	Std. Mean Difference (IV, Random, 95% CI)	0.54 [0.36, 0.72]
2 TSS	1		Std. Mean Difference (IV, Random, 95% CI)	Subtotals only
2.1 Calcipotriol (12 wks) vs. combined calcipotriol + BMD (8 wks); then calcipotriol (4 wks)	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
2.2 Calcipotriol (12 wks) vs. combined calcipotriol + BMD (4 wks); then calcipotriol (8 wks)	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
2.3 Calcipotriol (12 wks) vs. combined calcipotriol + BMD (4 wks); then calcipotriol (w/dy) & combined calcipotriol + BMD (w/e) (8 wks)	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
2.4 Calcipotriol (6 wks) vs. clobetasol propionate (2wks); then calcipotriol (4 wks)	1	92	Std. Mean Difference (IV, Random, 95% CI)	0.63 [0.21, 1.05]
2.5 Calcipotriol (6 wks) vs. calcipotriol OM, fluocinonide acetonide ON (2 wks); then calcipotriol twice daily (4 wks)	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
2.6 Calcipotriol (6 wks) vs. halometasone OM, calcipotriol ON (2 wks); then calcipotriol twice	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
daily (w/dy), halometasone (w/e) (2 wks); then calcipotriol twice daily (2 wks)				
2.7 Calcipotriol ON, clobetasol propionate OM (2 to 4 wks); then calcipotriol twice daily (to wk 12) vs. calcitriol ON, clobetasol propionate OM (2 to 4 wks); then calcitriol twice daily (to wk 12)	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
2.8 Combined calcipotriol + BMD (4 wks); then placebo ointment twice daily (8 wks) vs. combined calcipotriol + BMD (4 wks); then calcipotriol ointment twice daily (8 wks)	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
2.9 Combined calcipotriol + BMD (4 wks); then placebo ointment twice daily (8 wks) vs. combined calcipotriol + BMD (4 wks); then calcipotriol (w/dy) + combined calcipotriol + BMD (w/e) (8 wks)	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
2.10 Combined calcipotriol + BMD (4 wks); then calcipotriol ointment twice daily (8 wks) vs. combined calcipotriol + BMD (4 wks); then calcipotriol (w/dy) + combined calcipotriol + BMD (w/e) (8 wks)	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
2.11 Combined calcipotriol + BMD (8 wks); then calcipotriol (4 wks) vs. combined calcipotriol + BMD (4 wks); then calcipotriol (w/dy) & combined calcipotriol + BMD (w/e) (8 wks)	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
2.12 Tacalcitol (8 wks) vs. combined calcipotriol + BMD (4 wks); then calcipotriol (4 wks)	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
3 PASI	8		Std. Mean Difference (IV, Random, 95% CI)	Subtotals only
3.1 Calcipotriol (12 wks) vs. combined calcipotriol + BMD (8 wks); then calcipotriol (4 wks)	1	649	Std. Mean Difference (IV, Random, 95% CI)	-0.04 [-0.19, 0.11]
3.2 Calcipotriol (12 wks) vs. combined calcipotriol + BMD (4 wks); then calcipotriol (8 wks)	1	143	Std. Mean Difference (IV, Random, 95% CI)	0.29 [-0.04, 0.62]
3.3 Calcipotriol (12 wks) vs. combined calcipotriol + BMD (4 wks); then calcipotriol (w/dy) & combined calcipotriol + BMD (w/e) (8 wks)	1	650	Std. Mean Difference (IV, Random, 95% CI)	0.10 [-0.05, 0.25]
3.4 Calcipotriol (6 wks) vs. clobetasol propionate (2 wks); then calcipotriol (4 wks)	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
3.5 Calcipotriol (6 wks) vs. calcipotriol OM, fluocinonide acetonide ON (2 wks); then calcipotriol twice daily (4 wks)	1	38	Std. Mean Difference (IV, Random, 95% CI)	0.66 [0.01, 1.32]
3.6 Calcipotriol (6 wks) vs. halometasone OM, calcipotriol ON (2 wks); then calcipotriol twice daily (w/dy), halometasone (w/e) (2 wks); then calcipotriol twice daily (2 wks)	1	76	Std. Mean Difference (IV, Random, 95% CI)	1.13 [0.64, 1.62]
3.7 Calcipotriol ON, clobetasol propionate OM (2 to 4 wks); then calcipotriol twice daily (to wk 12) vs. calcitriol ON, clobetasol propionate OM (2 to 4 wks); then calcitriol twice daily (to wk 12)	1	125	Std. Mean Difference (IV, Random, 95% CI)	-0.27 [-0.62, 0.09]
3.8 Combined calcipotriol + BMD (4 wks); then placebo ointment twice daily (8 wks) vs. combined calcipotriol + BMD (4 wks); then calcipotriol ointment twice daily (8 wks)	1	759	Std. Mean Difference (IV, Random, 95% CI)	0.25 [0.10, 0.39]
3.9 Combined calcipotriol + BMD (4 wks); then placebo ointment twice daily (8 wks) vs. combined calcipotriol + BMD (4 wks); then calcipotriol (w/dy) + combined calcipotriol + BMD (w/e) (8 wks)	1	753	Std. Mean Difference (IV, Random, 95% CI)	0.59 [0.45, 0.74]
3.10 Combined calcipotriol + BMD (4 wks); then calcipotriol ointment twice daily (8 wks) vs. combined calcipotriol + BMD (4 wks); then calcipotriol (w/dy) + combined calcipotriol + BMD (w/e) (8 wks)	1	760	Std. Mean Difference (IV, Random, 95% CI)	0.30 [0.16, 0.45]
3.11 Combined calcipotriol + BMD (8 wks); then calcipotriol (4 wks) vs. combined calcipotriol + BMD (4 wks); then calcipotriol (w/dy) & combined calcipotriol + BMD (w/e) (8 wks)	1	645	Std. Mean Difference (IV, Random, 95% CI)	0.15 [-0.01, 0.30]
3.12 Tacalcitol (8 wks) vs. combined calcipotriol + BMD (4 wks); then calcipotriol (4 wks)	1	501	Std. Mean Difference (IV, Random, 95% CI)	0.49 [0.31, 0.67]
4 PAGI	4		Std. Mean Difference (IV, Random, 95% CI)	Subtotals only
4.1 Calcipotriol (12 wks) vs. combined calcipotriol + BMD (8 wks); then calcipotriol (4 wks)	1	577	Std. Mean Difference (IV, Random, 95% CI)	-0.14 [-0.30, 0.02]
4.2 Calcipotriol (12 wks) vs. combined calcipotriol + BMD (4 wks); then calcipotriol (8 wks)	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
4.3 Calcipotriol (12 wks) vs. combined calcipotriol + BMD (4 wks); then calcipotriol (w/dy) & combined calcipotriol + BMD (w/e) (8 wks)	1	585	Std. Mean Difference (IV, Random, 95% CI)	0.10 [-0.06, 0.26]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
4.4 Calcipotriol (6 wks) vs. clobetasol propionate (2 wks); then calcipotriol (4 wks)	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
4.5 Calcipotriol (6 wks) vs. calcipotriol OM, fluocinonide acetonide ON (2 wks); then calcipotriol twice daily (4 wks)	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
4.6 Calcipotriol (6 wks) vs. halometasone OM, calcipotriol ON (2 wks); then calcipotriol twice daily (w/dy), halometasone (w/e) (2 wks); then calcipotriol twice daily (2 wks)	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
4.7 Calcipotriol ON, clobetasol propionate OM (2 to 4 wks); then calcipotriol twice daily (to wk 12) vs. calcitriol ON, clobetasol propionate OM (2 to 4 wks); then calcitriol twice daily (to wk 12)	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
4.8 Combined calcipotriol + BMD (4 wks); then placebo ointment twice daily (8 wks) vs. combined calcipotriol + BMD (4 wks); then calcipotriol ointment twice daily (8 wks)	1	759	Std. Mean Difference (IV, Random, 95% CI)	0.28 [0.13, 0.42]
4.9 Combined calcipotriol + BMD (4 wks); then placebo ointment twice daily (8 wks) vs. combined calcipotriol + BMD (4 wks); then calcipotriol (w/dy) + combined calcipotriol + BMD (w/e) (8 wks)	1	753	Std. Mean Difference (IV, Random, 95% CI)	0.71 [0.56, 0.85]
4.10 Combined calcipotriol + BMD (4 wks); then calcipotriol ointment twice daily (8 wks) vs. combined calcipotriol + BMD (4 wks); then calcipotriol (w/dy) + combined calcipotriol + BMD (w/e) (8 wks)	1	760	Std. Mean Difference (IV, Random, 95% CI)	0.44 [0.29, 0.58]
4.11 Combined calcipotriol + BMD (8 wks); then calcipotriol (4 wks) vs. combined calcipotriol + BMD (4 wks); then calcipotriol (w/dy) & combined calcipotriol + BMD (w/e) (8 wks)	1	596	Std. Mean Difference (IV, Random, 95% CI)	0.23 [0.07, 0.39]
4.12 Tacalcitol (8 wks) vs. combined calcipotriol + BMD (4 wks); then calcipotriol (4 wks)	1	493	Std. Mean Difference (IV, Random, 95% CI)	0.54 [0.36, 0.72]
5 Combined end point (IAGI/TSS/PASI/PAGI)	9		Std. Mean Difference (IV, Random, 95% CI)	Subtotals only
5.1 Calcipotriol (12 wks) vs. combined calcipotriol + BMD (8 wks); then calcipotriol (4 wks)	1	577	Std. Mean Difference (IV, Random, 95% CI)	-0.12 [-0.29, 0.04]
5.2 Calcipotriol (12 wks) vs. combined calcipotriol + BMD (4 wks); then calcipotriol (8 wks)	1	143	Std. Mean Difference (IV, Random, 95% CI)	0.29 [-0.04, 0.62]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
5.3 Calcipotriol (12 wks) vs. combined calcipotriol + BMD (4 wks); then calcipotriol (w/dy) & combined calcipotriol + BMD (w/e) (8 wks)	1	585	Std. Mean Difference (IV, Random, 95% CI)	0.13 [-0.04, 0.29]
5.4 Calcipotriol (6 wks) vs. clobetasol propionate (2 wks); then calcipotriol (4 wks)	1	92	Std. Mean Difference (IV, Random, 95% CI)	0.60 [0.18, 1.02]
5.5 Calcipotriol (6 wks) vs. calcipotriol OM, fluocinonide acetonide ON (2 wks); then calcipotriol twice daily (4 wks)	1	38	Std. Mean Difference (IV, Random, 95% CI)	0.66 [0.01, 1.32]
5.6 Calcipotriol (6 wks) vs. halometasone OM, calcipotriol ON (2 wks); then calcipotriol twice daily (w/dy), halometasone (w/e) (2 wks); then calcipotriol twice daily (2 wks)	1	76	Std. Mean Difference (IV, Random, 95% CI)	0.41 [-0.05, 0.86]
5.7 Calcipotriol ON, clobetasol propionate OM (2 to 4 wks); then calcipotriol twice daily (to wk 12) vs. calcitriol ON, clobetasol propionate OM (2 to 4 wks); then calcitriol twice daily (to wk 12)	1	125	Std. Mean Difference (IV, Random, 95% CI)	-0.19 [-0.54, 0.16]
5.8 Combined calcipotriol + BMD (4 wks); then placebo ointment twice daily (8 wks) vs. combined calcipotriol + BMD (4 wks); then calcipotriol ointment twice daily (8 wks)	1	759	Std. Mean Difference (IV, Random, 95% CI)	0.27 [0.12, 0.41]
5.9 Combined calcipotriol + BMD (4 wks); then placebo ointment twice daily (8 wks) vs. combined calcipotriol + BMD (4 wks); then calcipotriol (w/dy)+ combined calcipotriol + BMD (w/e) (8 wks)	1	753	Std. Mean Difference (IV, Random, 95% CI)	0.51 [0.37, 0.66]
5.10 Combined calcipotriol + BMD (4 wks); then calcipotriol ointment twice daily (8 wks) vs. combined calcipotriol + BMD (4 wks); then calcipotriol (w/dy) + combined calcipotriol + BMD (w/e) (8 wks)	1	760	Std. Mean Difference (IV, Random, 95% CI)	0.26 [0.11, 0.40]
5.11 Combined calcipotriol + BMD (8 wks); then calcipotriol (4 wks) vs. combined calcipotriol + BMD (4 wks); then calcipotriol (w/dy) & combined calcipotriol + BMD (w/e) (8 wks)	1	596	Std. Mean Difference (IV, Random, 95% CI)	0.24 [0.08, 0.40]
5.12 Tacalcitol (8 wks) vs. combined calcipotriol + BMD (4 wks); then calcipotriol (4 wks)	1	493	Std. Mean Difference (IV, Random, 95% CI)	0.54 [0.36, 0.72]
6 Total withdrawals	9		Risk Difference (M-H, Random, 95% CI)	Subtotals only
6.1 Calcipotriol (12 wks) vs. combined calcipotriol + BMD (8 wks); then calcipotriol (4 wks)	1	649	Risk Difference (M-H, Random, 95% CI)	0.05 [0.00, 0.10]
6.2 Calcipotriol (12 wks) vs. combined calcipotriol + BMD (4 wks); then calcipotriol (8 wks)	1	150	Risk Difference (M-H, Random, 95% CI)	0.04 [-0.09, 0.17]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
6.3 Calcipotriol (12 wks) vs. combined calcipotriol + BMD (4 wks); then calcipotriol (w/dy) & combined calcipotriol + BMD (w/e) (8 wks)	1	649	Risk Difference (M-H, Random, 95% CI)	0.08 [0.03, 0.13]
6.4 Calcipotriol (6 wks) vs. clobetasol propionate (2 wks); then calcipotriol (4 wks)	1	98	Risk Difference (M-H, Random, 95% CI)	0.0 [-0.09, 0.09]
6.5 Calcipotriol (6 wks) vs. calcipotriol OM, fluocinonide acetonide ON (2 wks); then calcipotriol twice daily (4 wks)	1	38	Risk Difference (M-H, Random, 95% CI)	0.0 [-0.10, 0.10]
6.6 Calcipotriol (6 wks) vs. halometasone OM, calcipotriol ON (2 wks); then calcipotriol twice daily (w/dy), halometasone (w/e) (2 wks); then calcipotriol twice daily (2 wks)	1	76	Risk Difference (M-H, Random, 95% CI)	0.0 [-0.05, 0.05]
6.7 Calcipotriol ON, clobetasol propionate OM (2 to 4 wks); then calcipotriol twice daily (to wk 12) vs. calcitriol ON, clobetasol propionate OM (2 to 4 wks); then calcitriol twice daily (to wk 12)	1	125	Risk Difference (M-H, Random, 95% CI)	-0.01 [-0.12, 0.11]
6.8 Combined calcipotriol + BMD (4 wks); then placebo ointment twice daily (8 wks) vs. combined calcipotriol + BMD (4 wks); then calcipotriol ointment twice daily (8 wks)	1	759	Risk Difference (M-H, Random, 95% CI)	0.08 [0.03, 0.14]
6.9 Combined calcipotriol + BMD (4 wks); then placebo ointment twice daily (8 wks) vs. combined calcipotriol + BMD (4 wks); then calcipotriol (w/dy) + combined calcipotriol + BMD (w/e) (8 wks)	1	753	Risk Difference (M-H, Random, 95% CI)	0.11 [0.06, 0.17]
6.10 Combined calcipotriol + BMD (4 wks); then calcipotriol ointment twice daily (8 wks) vs. combined calcipotriol + BMD (4 wks); then calcipotriol (w/dy) + combined calcipotriol + BMD (w/e) (8 wks)	1	760	Risk Difference (M-H, Random, 95% CI)	0.03 [-0.01, 0.07]
6.11 Combined calcipotriol + BMD (8 wks); then calcipotriol (4 wks) vs. combined calcipotriol + BMD (4 wks); then calcipotriol (w/dy) & combined calcipotriol + BMD (w/e) (8 wks)	1	644	Risk Difference (M-H, Random, 95% CI)	0.03 [-0.01, 0.07]
6.12 Tacalcitol (8 wks) vs. combined calcipotriol + BMD (4 wks); then calcipotriol (4 wks)	1	501	Risk Difference (M-H, Random, 95% CI)	0.05 [-0.01, 0.12]
7 Withdrawals due to adverse events	8		Risk Difference (M-H, Random, 95% CI)	Subtotals only
7.1 Calcipotriol (12 wks) vs. combined calcipotriol + BMD (8 wks); then calcipotriol (4 wks)	0	0	Risk Difference (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
7.2 Calcipotriol (12 wks) vs. combined calcipotriol + BMD (4 wks); then calcipotriol (8 wks)	1	150	Risk Difference (M-H, Random, 95% CI)	-0.04 [-0.09, 0.01]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
7.3 Calcipotriol (12 wks) vs. combined calcipotriol + BMD (4 wks); then calcipotriol (w/dy) & combined calcipotriol + BMD (w/e) (8 wks)	0	0	Risk Difference (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
7.4 Calcipotriol (6 wks) vs. clobetasol propionate (2 wks); then calcipotriol (4 wks)	1	98	Risk Difference (M-H, Random, 95% CI)	0.0 [-0.04, 0.04]
7.5 Calcipotriol (6 wks) vs. calcipotriol OM, fluocinonide acetonide ON (2 wks); then calcipotriol twice daily (4 wks)	1	38	Risk Difference (M-H, Random, 95% CI)	0.0 [-0.10, 0.10]
7.6 Calcipotriol (6 wks) vs. halometasone OM, calcipotriol ON (2 wks); then calcipotriol twice daily (w/dy), halometasone (w/e) (2 wks); then calcipotriol twice daily (2 wks)	1	76	Risk Difference (M-H, Random, 95% CI)	0.0 [-0.05, 0.05]
7.7 Calcipotriol ON, clobetasol propionate OM (2 to 4 wks); then calcipotriol twice daily (to wk 12) vs. calcitriol ON, clobetasol propionate OM (2 to 4 wks); then calcitriol twice daily (to wk 12)	1	125	Risk Difference (M-H, Random, 95% CI)	-0.02 [-0.06, 0.03]
7.8 Combined calcipotriol + BMD (4 wks); then placebo ointment twice daily (8 wks) vs. combined calcipotriol + BMD (4 wks); then calcipotriol ointment twice daily (8 wks)	1	759	Risk Difference (M-H, Random, 95% CI)	0.01 [-0.01, 0.02]
7.9 Combined calcipotriol + BMD (4 wks); then placebo ointment twice daily (8 wks) vs. combined calcipotriol + BMD (4 wks); then calcipotriol (w/dy) + combined calcipotriol + BMD (w/e) (8 wks)	1	753	Risk Difference (M-H, Random, 95% CI)	-0.00 [-0.02, 0.02]
7.10 Combined calcipotriol + BMD (4 wks); then calcipotriol ointment twice daily (8 wks) vs. combined calcipotriol + BMD (4 wks); then calcipotriol (w/dy) + combined calcipotriol + BMD (w/e) (8 wks)	1	760	Risk Difference (M-H, Random, 95% CI)	-0.01 [-0.03, 0.01]
7.11 Combined calcipotriol + BMD (8 wks); then calcipotriol (4 wks) vs. combined calcipotriol + BMD (4 wks); then calcipotriol (w/dy) & combined calcipotriol + BMD (w/e) (8 wks)	0	0	Risk Difference (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
7.12 Tacalcitol (8 wks) vs. combined calcipotriol + BMD (4 wks); then calcipotriol (4 wks)	1	501	Risk Difference (M-H, Random, 95% CI)	0.02 [-0.01, 0.05]
8 Withdrawals due to treatment failure	6		Risk Difference (M-H, Random, 95% CI)	Subtotals only
8.1 Calcipotriol (12 wks) vs. combined calcipotriol + BMD (8 wks); then calcipotriol (4 wks)	0	0	Risk Difference (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
8.2 Calcipotriol (12 wks) vs. combined calcipotriol + BMD (4 wks); then calcipotriol (8 wks)	1	150	Risk Difference (M-H, Random, 95% CI)	0.21 [0.10, 0.33]

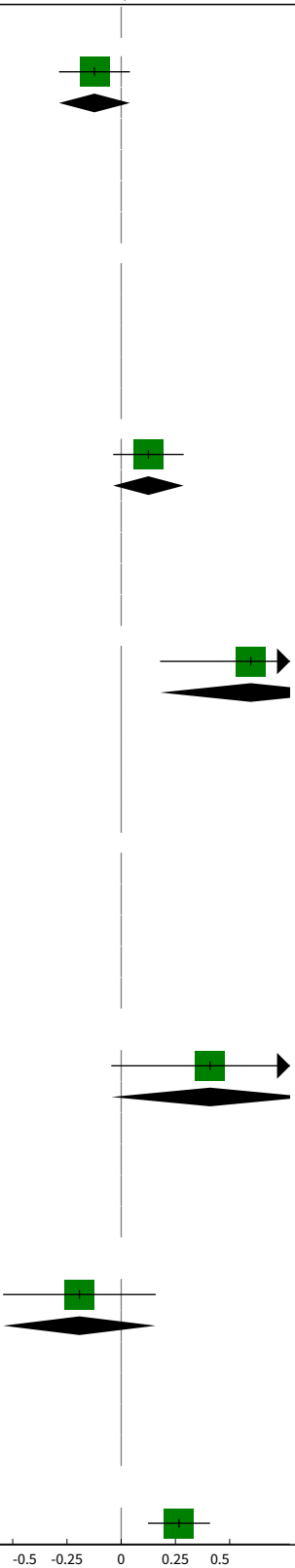
Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
8.3 Calcipotriol (12 wks) vs. combined calcipotriol + BMD (4 wks); then calcipotriol (w/dy) & combined calcipotriol + BMD (w/e) (8 wks)	0	0	Risk Difference (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
8.4 Calcipotriol (6 wks) vs. clobetasol propionate (2 wks); then calcipotriol (4 wks)	1	98	Risk Difference (M-H, Random, 95% CI)	0.0 [-0.04, 0.04]
8.5 Calcipotriol (6 wks) vs. calcipotriol OM, fluocinonide acetonide ON (2 wks); then calcipotriol twice daily (4 wks)	1	38	Risk Difference (M-H, Random, 95% CI)	0.0 [-0.10, 0.10]
8.6 Calcipotriol (6 wks) vs. halometasone OM, calcipotriol ON (2 wks); then calcipotriol twice daily (w/dy), halometasone (w/e) (2 wks); then calcipotriol twice daily (2 wks)	1	76	Risk Difference (M-H, Random, 95% CI)	0.0 [-0.05, 0.05]
8.7 Calcipotriol ON, clobetasol propionate OM (2 to 4 wks); then calcipotriol twice daily (to wk 12) vs. calcitriol ON, clobetasol propionate OM (2 to 4 wks); then calcitriol twice daily (to wk 12)	1	125	Risk Difference (M-H, Random, 95% CI)	0.03 [-0.04, 0.10]
8.8 Combined calcipotriol + BMD (4 wks); then placebo ointment twice daily (8 wks) vs. combined calcipotriol + BMD (4 wks); then calcipotriol ointment twice daily (8 wks)	0	0	Risk Difference (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
8.9 Combined calcipotriol + BMD (4 wks); then placebo ointment twice daily (8 wks) vs. combined calcipotriol + BMD (4 wks); then calcipotriol (w/dy) + combined calcipotriol + BMD (w/e) (8 wks)	0	0	Risk Difference (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
8.10 Combined calcipotriol + BMD (4 wks); then calcipotriol ointment twice daily (8 wks) vs. combined calcipotriol + BMD (4 wks); then calcipotriol (w/dy)+ combined calcipotriol + BMD (w/e) (8 wks)	0	0	Risk Difference (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
8.11 Combined calcipotriol + BMD (8 wks); then calcipotriol (4 wks) vs. combined calcipotriol + BMD (4 wks); then calcipotriol (w/dy) & combined calcipotriol + BMD (w/e) (8 wks)	0	0	Risk Difference (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
8.12 Tacalcitol (8 wks) vs. combined calcipotriol + BMD (4 wks); then calcipotriol (4 wks)	1	501	Risk Difference (M-H, Random, 95% CI)	0.05 [0.02, 0.08]
9 Adverse events (local)	8		Risk Difference (M-H, Random, 95% CI)	Subtotals only
9.1 Calcipotriol (12 wks) vs. combined calcipotriol + BMD (8 wks); then calcipotriol (4 wks)	1	649	Risk Difference (M-H, Random, 95% CI)	0.11 [0.06, 0.17]
9.2 Calcipotriol (12 wks) vs. combined calcipotriol + BMD (4 wks); then calcipotriol (8 wks)	0	0	Risk Difference (M-H, Random, 95% CI)	0.0 [0.0, 0.0]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
9.3 Calcipotriol (12 wks) vs. combined calcipotriol + BMD (4 wks); then calcipotriol (w/dy) & combined calcipotriol + BMD (w/e) (8 wks)	1	649	Risk Difference (M-H, Random, 95% CI)	0.11 [0.05, 0.17]
9.4 Calcipotriol (6 wks) vs. clobetasol propionate (2 wks); then calcipotriol (4 wks)	1	98	Risk Difference (M-H, Random, 95% CI)	0.02 [-0.08, 0.12]
9.5 Calcipotriol (6 wks) vs. calcipotriol OM, fluocinonide acetonide ON (2 wks); then calcipotriol twice daily (4 wks)	1	38	Risk Difference (M-H, Random, 95% CI)	0.0 [-0.14, 0.14]
9.6 Calcipotriol (6 wks) vs. halometasone OM, calcipotriol ON (2 wks); then calcipotriol twice daily (w/dy), halometasone (w/e) (2 wks); then calcipotriol twice daily (2 wks)	1	76	Risk Difference (M-H, Random, 95% CI)	0.26 [0.07, 0.45]
9.7 Calcipotriol ON, clobetasol propionate OM (2 to 4 wks); then calcipotriol twice daily (to wk 12) vs. calcitriol ON, clobetasol propionate OM (2 to 4 wks); then calcitriol twice daily (to wk 12)	1	125	Risk Difference (M-H, Random, 95% CI)	-0.02 [-0.10, 0.06]
9.8 Combined calcipotriol + BMD (4 wks); then placebo ointment twice daily (8 wks) vs. combined calcipotriol + BMD (4 wks); then calcipotriol ointment twice daily (8 wks)	1	752	Risk Difference (M-H, Random, 95% CI)	-0.03 [-0.07, 0.02]
9.9 Combined calcipotriol + BMD (4 wks); then placebo ointment twice daily (8 wks) vs. combined calcipotriol + BMD (4 wks); then calcipotriol (w/dy) + combined calcipotriol + BMD (w/e) (8 wks)	1	743	Risk Difference (M-H, Random, 95% CI)	0.01 [-0.03, 0.05]
9.10 Combined calcipotriol + BMD (4 wks); then calcipotriol ointment twice daily (8 wks) vs. combined calcipotriol + BMD (4 wks); then calcipotriol (w/dy) + combined calcipotriol + BMD (w/e) (8 wks)	1	749	Risk Difference (M-H, Random, 95% CI)	0.04 [-0.00, 0.08]
9.11 Combined calcipotriol + BMD (8 wks); then calcipotriol (4 wks) vs. combined calcipotriol + BMD (4 wks); then calcipotriol (w/dy) & combined calcipotriol + BMD (w/e) (8 wks)	1	644	Risk Difference (M-H, Random, 95% CI)	-0.01 [-0.05, 0.04]
9.12 Tacalcitol (8 wks) vs. combined calcipotriol + BMD (4 wks); then calcipotriol (4 wks)	1	501	Risk Difference (M-H, Random, 95% CI)	0.06 [0.01, 0.11]
10 Adverse events (systemic)	0	0	Risk Difference (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
10.1 Calcipotriol (12 wks) vs. combined calcipotriol + BMD (8 wks); then calcipotriol (4 wks)	0	0	Risk Difference (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
10.2 Calcipotriol (12 wks) vs. combined calcipotriol + BMD (4 wks); then calcipotriol (8 wks)	0	0	Risk Difference (M-H, Random, 95% CI)	0.0 [0.0, 0.0]

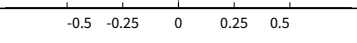
Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
10.3 Calcipotriol (12 wks) vs. combined calcipotriol + BMD (4 wks); then calcipotriol (w/dy) & combined calcipotriol + BMD (w/e) (8 wks)	0	0	Risk Difference (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
10.4 Calcipotriol (6 wks) vs. clobetasol propionate (2 wks); then calcipotriol (4 wks)	0	0	Risk Difference (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
10.5 Calcipotriol (6 wks) vs. calcipotriol OM, fluocinonide acetonide ON (2 wks); then calcipotriol twice daily (4 wks)	0	0	Risk Difference (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
10.6 Calcipotriol (6 wks) vs. halometasone OM, calcipotriol ON (2 wks); then calcipotriol twice daily (w/dy), halometasone (w/e) (2 wks); then calcipotriol twice daily (2 wks)	0	0	Risk Difference (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
10.7 Calcipotriol ON, clobetasol propionate OM (2 to 4 wks); then calcipotriol twice daily (to wk 12) vs. calcitriol ON, clobetasol propionate OM (2 to 4 wks); then calcitriol twice daily (to wk 12)	0	0	Risk Difference (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
10.8 Combined calcipotriol + BMD (4 wks); then placebo ointment twice daily (8 wks) vs. combined calcipotriol + BMD (4 wks); then calcipotriol ointment twice daily (8 wks)	0	0	Risk Difference (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
10.9 Combined calcipotriol + BMD (4 wks); then placebo ointment twice daily (8 wks) vs. combined calcipotriol + BMD (4 wks); then calcipotriol (w/dy) + combined calcipotriol + BMD (w/e) (8 wks)	0	0	Risk Difference (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
10.10 Combined calcipotriol + BMD (4 wks); then calcipotriol ointment twice daily (8 wks) vs. combined calcipotriol + BMD (4 wks); then calcipotriol (w/dy) + combined calcipotriol + BMD (w/e) (8 wks)	0	0	Risk Difference (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
10.11 Combined calcipotriol + BMD (8 wks); then calcipotriol (4 wks) vs. combined calcipotriol + BMD (4 wks); then calcipotriol (w/dy) & combined calcipotriol + BMD (w/e) (8 wks)	0	0	Risk Difference (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
10.12 Tacalcitol (8 wks) vs. combined calcipotriol + BMD (4 wks); then calcipotriol (4 wks)	0	0	Risk Difference (M-H, Random, 95% CI)	0.0 [0.0, 0.0]

Analysis 13.1. Comparison 13 Vitamin D alone or in combination versus other treatments: complex regimens, Outcome 1 IAGI.

Study or subgroup	Vitamin D regimen N	Vitamin D regimen Mean(SD)	Complex regimen N	Complex regimen Mean(SD)	Std. Mean Difference Random, 95% CI	Weight	Std. Mean Difference Random, 95% CI
13.1.1 Calcipotriol (12 wks) vs. combined calcipotriol + BMD (8 wks); then calcipotriol (4 wks)							
Kragballe 2004	283	1.6 (0.9)	294	1.7 (0.9)		100%	-0.12[-0.29,0.04]
Subtotal ***	**283**		**294**			**100%**	**-0.12[-0.29,0.04]**
Heterogeneity: Tau^2=0; Chi^2=0, df=0(P<0.0001); I^2=100%							
Test for overall effect: Z=1.48(P=0.14)							
13.1.2 Calcipotriol (12 wks) vs. combined calcipotriol + BMD (4 wks); then calcipotriol (8 wks)							
Subtotal ***	**0**		**0**				**Not estimable**
Heterogeneity: Not applicable							
Test for overall effect: Not applicable							
13.1.3 Calcipotriol (12 wks) vs. combined calcipotriol + BMD (4 wks); then calcipotriol (w/dy) & combined calcipotriol + BMD (w/e) (8 wks)							
Kragballe 2004	283	1.6 (0.9)	302	1.5 (0.9)		100%	0.13[-0.04,0.29]
Subtotal ***	**283**		**302**			**100%**	**0.13[-0.04,0.29]**
Heterogeneity: Not applicable							
Test for overall effect: Z=1.51(P=0.13)							
13.1.4 Calcipotriol (6 wks) vs. clobetasol propionate (2 wks); then calcipotriol (4 wks)							
Austad 1998	46	-3.2 (0.8)	46	-3.7 (0.8)		100%	0.6[0.18,1.02]
Subtotal ***	**46**		**46**			**100%**	**0.6[0.18,1.02]**
Heterogeneity: Not applicable							
Test for overall effect: Z=2.8(P=0.01)							
13.1.5 Calcipotriol (6 wks) vs. calcipotriol OM, fluocinonide acetonide ON (2 wks); then calcipotriol twice daily (4 wks)							
Subtotal ***	**0**		**0**				**Not estimable**
Heterogeneity: Not applicable							
Test for overall effect: Not applicable							
13.1.6 Calcipotriol (6 wks) vs. halometasone OM, calcipotriol ON (2 wks); then calcipotriol twice daily (w/dy), halometasone (w/e) (2 wks); then calcipotriol twice daily (2wks)							
Yang 2009	36	-1.9 (0.9)	40	-2.2 (0.9)		100%	0.41[-0.05,0.86]
Subtotal ***	**36**		**40**			**100%**	**0.41[-0.05,0.86]**
Heterogeneity: Not applicable							
Test for overall effect: Z=1.76(P=0.08)							
13.1.7 Calcipotriol ON, clobetasol propionate OM (2 to 4 wks); then calcipotriol twice daily (to wk 12) vs. calcitriol ON, clobetasol propionate OM (2 to 4 wks); then calcitriol twice daily (to wk 12)							
Lahfa 2003	64	-4.7 (1.3)	61	-4.4 (1.3)		100%	-0.19[-0.54,0.16]
Subtotal ***	**64**		**61**			**100%**	**-0.19[-0.54,0.16]**
Heterogeneity: Not applicable							
Test for overall effect: Z=1.07(P=0.28)							
13.1.8 Combined calcipotriol + BMD (4 wks); then placebo ointment twice daily (8 wks) vs. combined calcipotriol + BMD (4 wks); then calcipotriol ointment twice daily (8 wks)							
White 2006 (P)	376	2.5 (1)	383	2.2 (1)		100%	0.27[0.12,0.41]



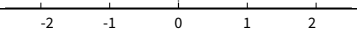
Study or subgroup	Vitamin D regimen N	Mean(SD)	Complex regimen N	Mean(SD)	Std. Mean Difference Random, 95% CI	Weight	Std. Mean Difference Random, 95% CI
Subtotal ***	**376**		**383**			**100%**	**0.27[0.12,0.41]**
Heterogeneity: Not applicable							
Test for overall effect: Z=3.65(P=0)							
13.1.9 Combined calcipotriol + BMD (4 wks); then placebo ointment twice daily (8 wks) vs. combined calcipotriol + BMD (4 wks); then calcipotriol (w/dy)+ combined calcipotriol + BMD (w/e) (8 wks)							
White 2006 (P)	376	2.5 (1)	377	2 (1)		100%	0.51[0.37,0.66]
Subtotal ***	**376**		**377**			**100%**	**0.51[0.37,0.66]**
Heterogeneity: Not applicable							
Test for overall effect: Z=6.95(P<0.0001)							
13.1.10 Combined calcipotriol + BMD (4 wks); then calcipotriol ointment twice daily (8 wks) vs. combined calcipotriol + BMD (4 wks); then calcipotriol (w/dy)+ combined calcipotriol + BMD (w/e) (8 wks)							
White 2006 (H)	383	2.2 (1)	377	2 (1)		100%	0.26[0.11,0.4]
Subtotal ***	**383**		**377**			**100%**	**0.26[0.11,0.4]**
Heterogeneity: Not applicable							
Test for overall effect: Z=3.52(P=0)							
13.1.11 Combined calcipotriol + BMD (8 wks); then calcipotriol (4 wks) vs. combined calcipotriol + BMD (4 wks); then calcipotriol (w/dy) & combined calcipotriol + BMD (w/e) (8 wks)							
Kragballe 2004	294	1.7 (0.9)	302	1.5 (0.9)		100%	0.24[0.08,0.4]
Subtotal ***	**294**		**302**			**100%**	**0.24[0.08,0.4]**
Heterogeneity: Not applicable							
Test for overall effect: Z=2.95(P=0)							
13.1.12 Tacalcitol (8 wks) vs. combined calcipotriol + BMD (4 wks); then calcipotriol (4 wks)							
Ortonne 2004	247	-2.4 (1.3)	246	-3.2 (1.3)		100%	0.54[0.36,0.72]
Subtotal ***	**247**		**246**			**100%**	**0.54[0.36,0.72]**
Heterogeneity: Not applicable							
Test for overall effect: Z=5.86(P<0.0001)							
Test for subgroup differences: Chi^2=54.06, df=1 (P<0.0001), I^2=83.35%							



Favours vitamin D regimen — Favours complex regimen

Analysis 13.2. Comparison 13 Vitamin D alone or in combination versus other treatments: complex regimens, Outcome 2 TSS.

Study or subgroup	Vitamin D regimen N	Mean(SD)	Complex regimen N	Mean(SD)	Std. Mean Difference Random, 95% CI	Weight	Std. Mean Difference Random, 95% CI
13.2.1 Calcipotriol (12 wks) vs. combined calcipotriol + BMD (8 wks); then calcipotriol (4 wks)							
Subtotal ***	**0**		**0**				**Not estimable**
Heterogeneity: Not applicable							
Test for overall effect: Not applicable							
13.2.2 Calcipotriol (12 wks) vs. combined calcipotriol + BMD (4 wks); then calcipotriol (8 wks)							
Subtotal ***	**0**		**0**				**Not estimable**
Heterogeneity: Not applicable							

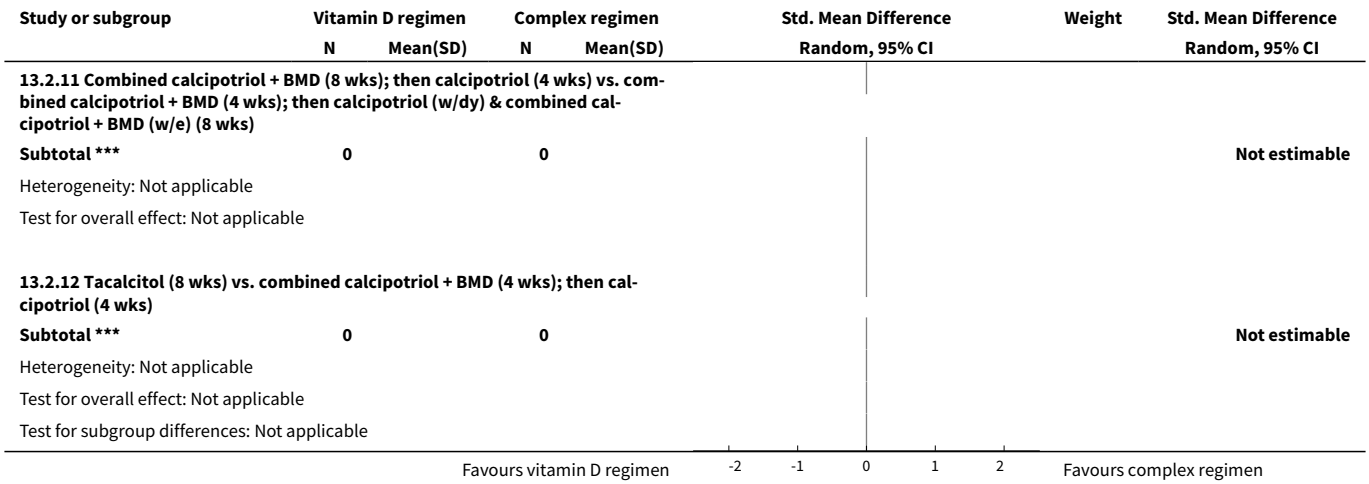


Favours vitamin D regimen — Favours complex regimen

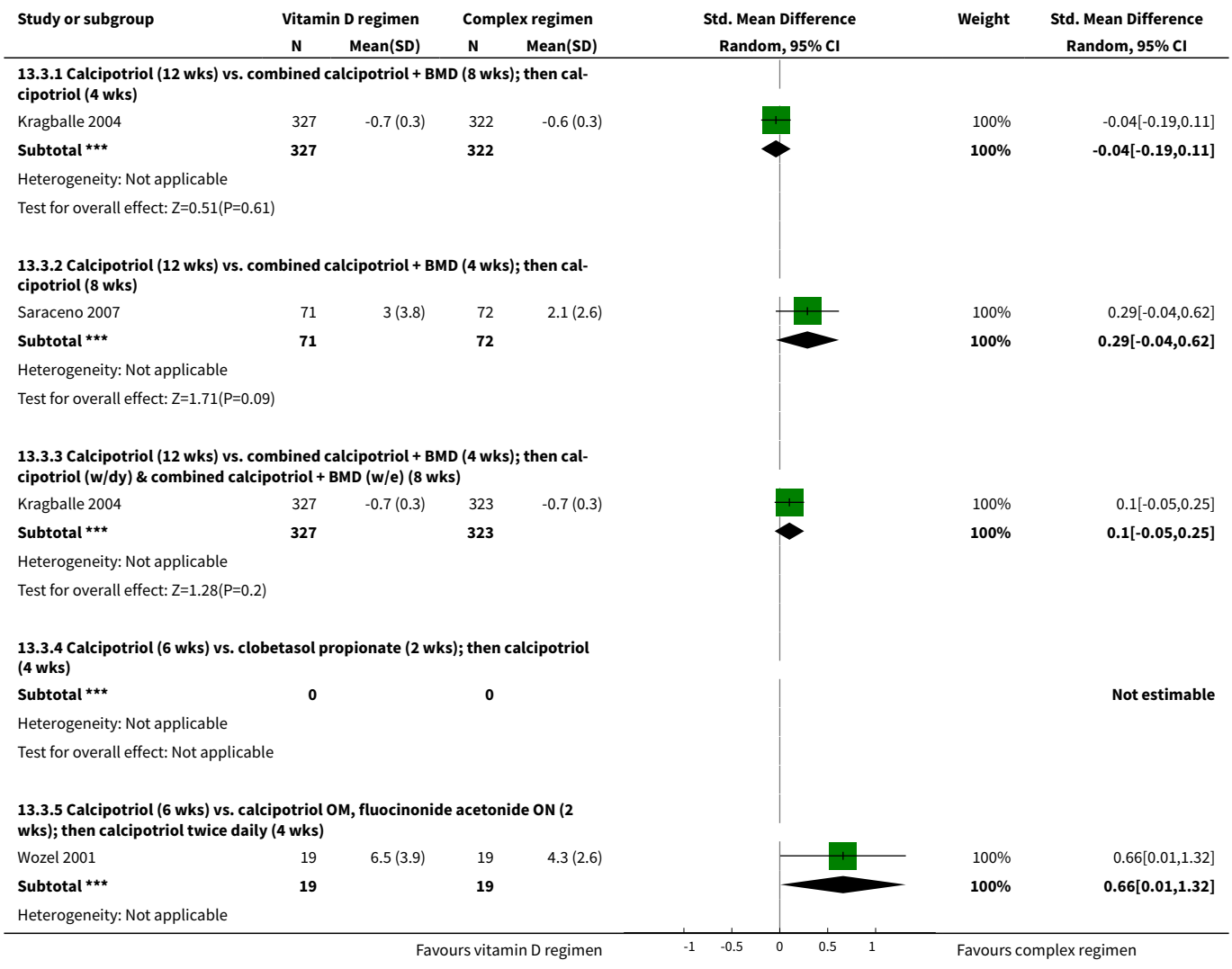
Study or subgroup	Vitamin D regimen N	Vitamin D regimen Mean(SD)	Complex regimen N	Complex regimen Mean(SD)	Std. Mean Difference Random, 95% CI	Weight	Std. Mean Difference Random, 95% CI
Test for overall effect: Not applicable							
13.2.3 Calcipotriol (12 wks) vs. combined calcipotriol + BMD (4 wks); then calcipotriol (w/dy) & combined calcipotriol + BMD (w/e) (8 wks)							
Subtotal ***	**0**		**0**				**Not estimable**
Heterogeneity: Not applicable							
Test for overall effect: Not applicable							
13.2.4 Calcipotriol (6 wks) vs. clobetasol propionate (2wks); then calcipotriol (4 wks)							
Austad 1998	46	2.5 (1.3)	46	1.7 (1.2)		100%	0.63[0.21,1.05]
Subtotal ***	**46**		**46**			**100%**	**0.63[0.21,1.05]**
Heterogeneity: Not applicable							
Test for overall effect: Z=2.96(P=0)							
13.2.5 Calcipotriol (6 wks) vs. calcipotriol OM, fluocinonide acetonide ON (2 wks); then calcipotriol twice daily (4 wks)							
Subtotal ***	**0**		**0**				**Not estimable**
Heterogeneity: Not applicable							
Test for overall effect: Not applicable							
13.2.6 Calcipotriol (6 wks) vs. halometasone OM, calcipotriol ON (2 wks); then calcipotriol twice daily (w/dy), halometasone (w/e) (2 wks); then calcipotriol twice daily (2 wks)							
Subtotal ***	**0**		**0**				**Not estimable**
Heterogeneity: Not applicable							
Test for overall effect: Not applicable							
13.2.7 Calcipotriol ON, clobetasol propionate OM (2 to 4 wks); then calcipotriol twice daily (to wk 12) vs. calcitriol ON, clobetasol propionate OM (2 to 4 wks); then calcitriol twice daily (to wk 12)							
Subtotal ***	**0**		**0**				**Not estimable**
Heterogeneity: Not applicable							
Test for overall effect: Not applicable							
13.2.8 Combined calcipotriol + BMD (4 wks); then placebo ointment twice daily (8 wks) vs. combined calcipotriol + BMD (4 wks); then calcipotriol ointment twice daily (8 wks)							
Subtotal ***	**0**		**0**				**Not estimable**
Heterogeneity: Not applicable							
Test for overall effect: Not applicable							
13.2.9 Combined calcipotriol + BMD (4 wks); then placebo ointment twice daily (8 wks) vs. combined calcipotriol + BMD (4 wks); then calcipotriol (w/dy) + combined calcipotriol + BMD (w/e) (8 wks)							
Subtotal ***	**0**		**0**				**Not estimable**
Heterogeneity: Not applicable							
Test for overall effect: Not applicable							
13.2.10 Combined calcipotriol + BMD (4 wks); then calcipotriol ointment twice daily (8 wks) vs. combined calcipotriol + BMD (4 wks); then calcipotriol (w/dy) + combined calcipotriol + BMD (w/e) (8 wks)							
Subtotal ***	**0**		**0**				**Not estimable**
Heterogeneity: Not applicable							
Test for overall effect: Not applicable							

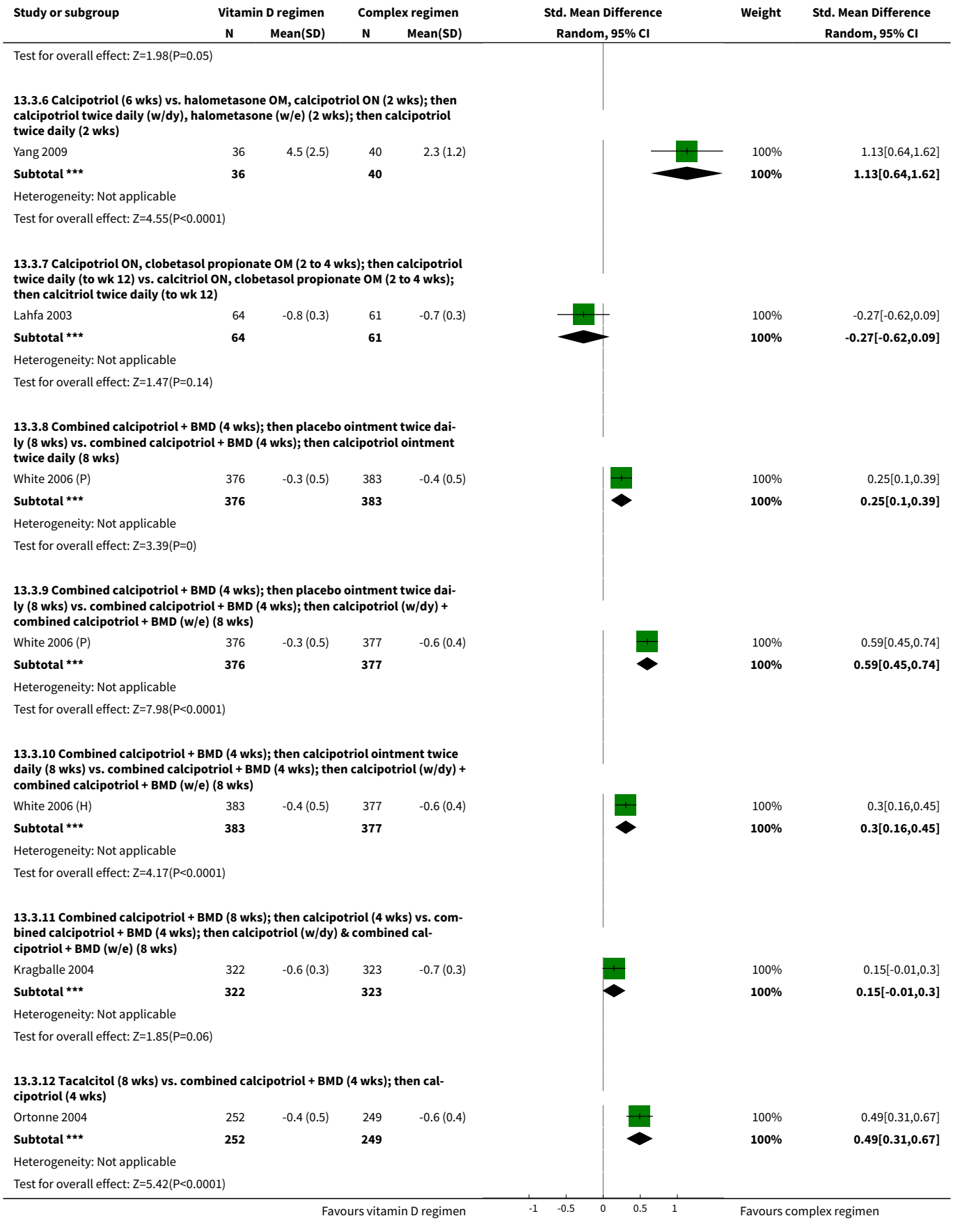
Favours vitamin D regimen

Favours complex regimen

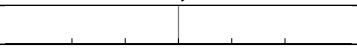


Analysis 13.3. Comparison 13 Vitamin D alone or in combination versus other treatments: complex regimens, Outcome 3 PASI.





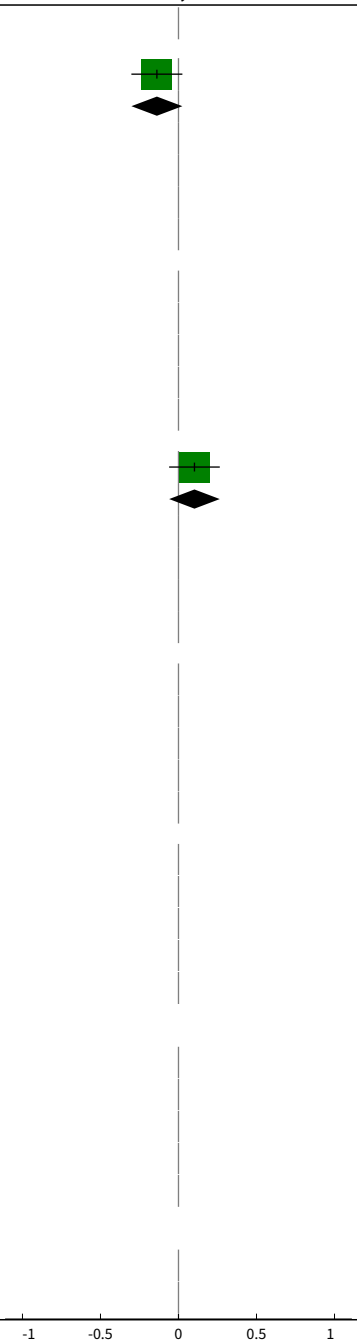
Study or subgroup	Vitamin D regimen N	Vitamin D regimen Mean(SD)	Complex regimen N	Complex regimen Mean(SD)	Std. Mean Difference Random, 95% CI	Weight	Std. Mean Difference Random, 95% CI
Test for subgroup differences: Chi^2=70.21, df=1 (P<0.0001), I^2=85.76%							



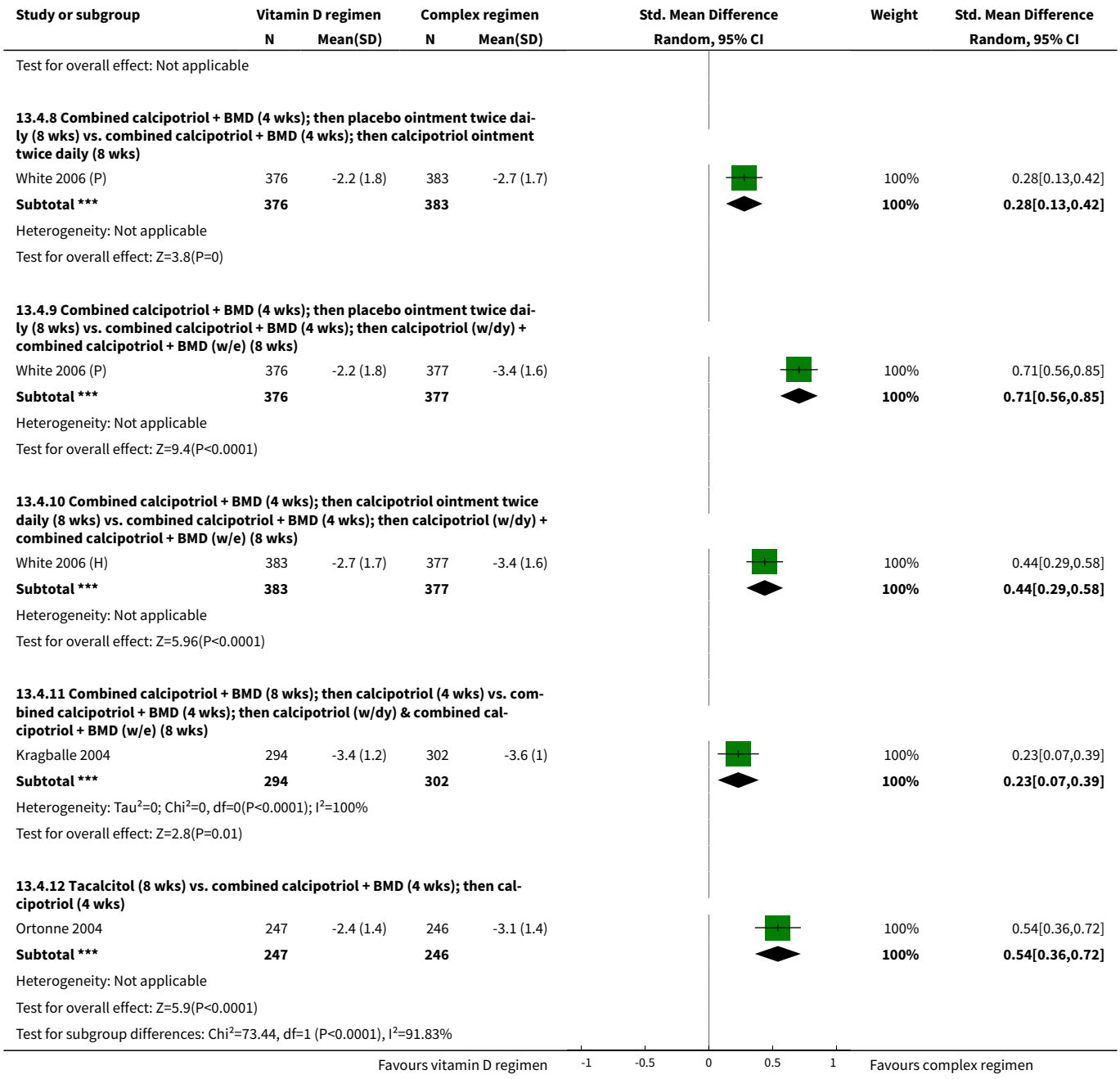
Favours vitamin D regimen | Favours complex regimen

Analysis 13.4. Comparison 13 Vitamin D alone or in combination versus other treatments: complex regimens, Outcome 4 PAGI.

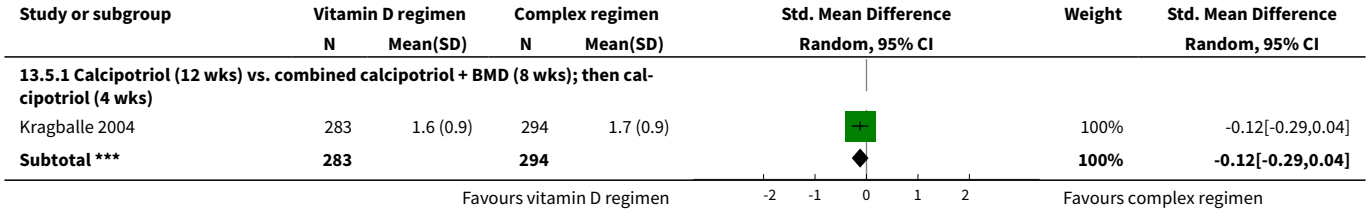
Study or subgroup	Vitamin D regimen N	Vitamin D regimen Mean(SD)	Complex regimen N	Complex regimen Mean(SD)	Std. Mean Difference Random, 95% CI	Weight	Std. Mean Difference Random, 95% CI
13.4.1 Calcipotriol (12 wks) vs. combined calcipotriol + BMD (8 wks); then calcipotriol (4 wks)							
Kragballe 2004	283	-3.5 (1)	294	-3.4 (1.2)		100%	-0.14[-0.3,0.02]
Subtotal ***	**283**		**294**			**100%**	**-0.14[-0.3,0.02]**
Heterogeneity: Not applicable							
Test for overall effect: Z=1.66(P=0.1)							
13.4.2 Calcipotriol (12 wks) vs. combined calcipotriol + BMD (4 wks); then calcipotriol (8 wks)							
Subtotal ***	**0**		**0**				**Not estimable**
Heterogeneity: Not applicable							
Test for overall effect: Not applicable							
13.4.3 Calcipotriol (12 wks) vs. combined calcipotriol + BMD (4 wks); then calcipotriol (w/dy) & combined calcipotriol + BMD (w/e) (8 wks)							
Kragballe 2004	283	-3.5 (1)	302	-3.6 (1)		100%	0.1[-0.06,0.26]
Subtotal ***	**283**		**302**			**100%**	**0.1[-0.06,0.26]**
Heterogeneity: Not applicable							
Test for overall effect: Z=1.24(P=0.22)							
13.4.4 Calcipotriol (6 wks) vs. clobetasol propionate (2 wks); then calcipotriol (4 wks)							
Subtotal ***	**0**		**0**				**Not estimable**
Heterogeneity: Not applicable							
Test for overall effect: Not applicable							
13.4.5 Calcipotriol (6 wks) vs. calcipotriol OM, fluocinonide acetonide ON (2 wks); then calcipotriol twice daily (4 wks)							
Subtotal ***	**0**		**0**				**Not estimable**
Heterogeneity: Not applicable							
Test for overall effect: Not applicable							
13.4.6 Calcipotriol (6 wks) vs. halometasone OM, calcipotriol ON (2 wks); then calcipotriol twice daily (w/dy), halometasone (w/e) (2 wks); then calcipotriol twice daily (2 wks)							
Subtotal ***	**0**		**0**				**Not estimable**
Heterogeneity: Not applicable							
Test for overall effect: Not applicable							
13.4.7 Calcipotriol ON, clobetasol propionate OM (2 to 4 wks); then calcipotriol twice daily (to wk 12) vs. calcitriol ON, clobetasol propionate OM (2 to 4 wks); then calcitriol twice daily (to wk 12)							
Subtotal ***	**0**		**0**				**Not estimable**
Heterogeneity: Not applicable							

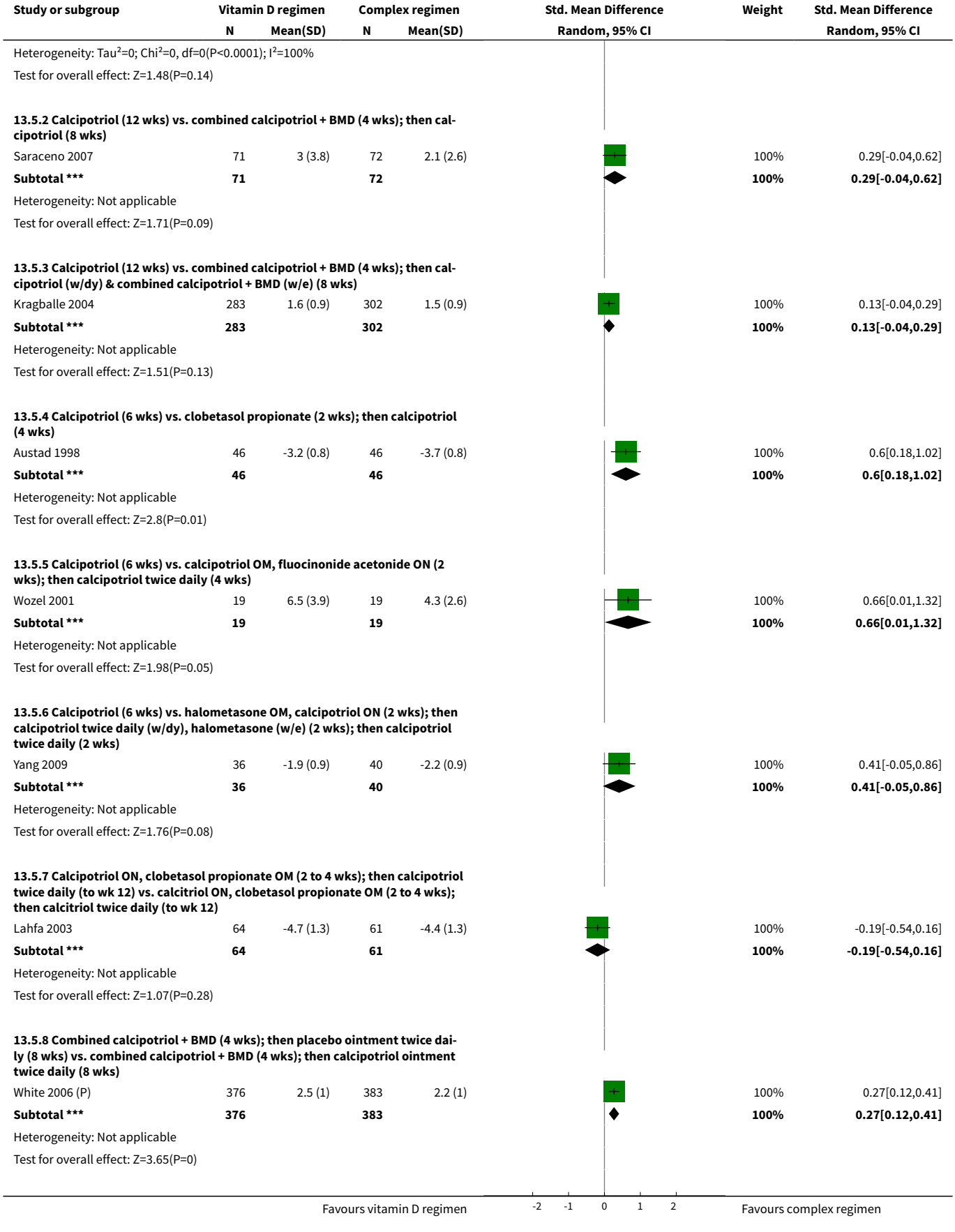


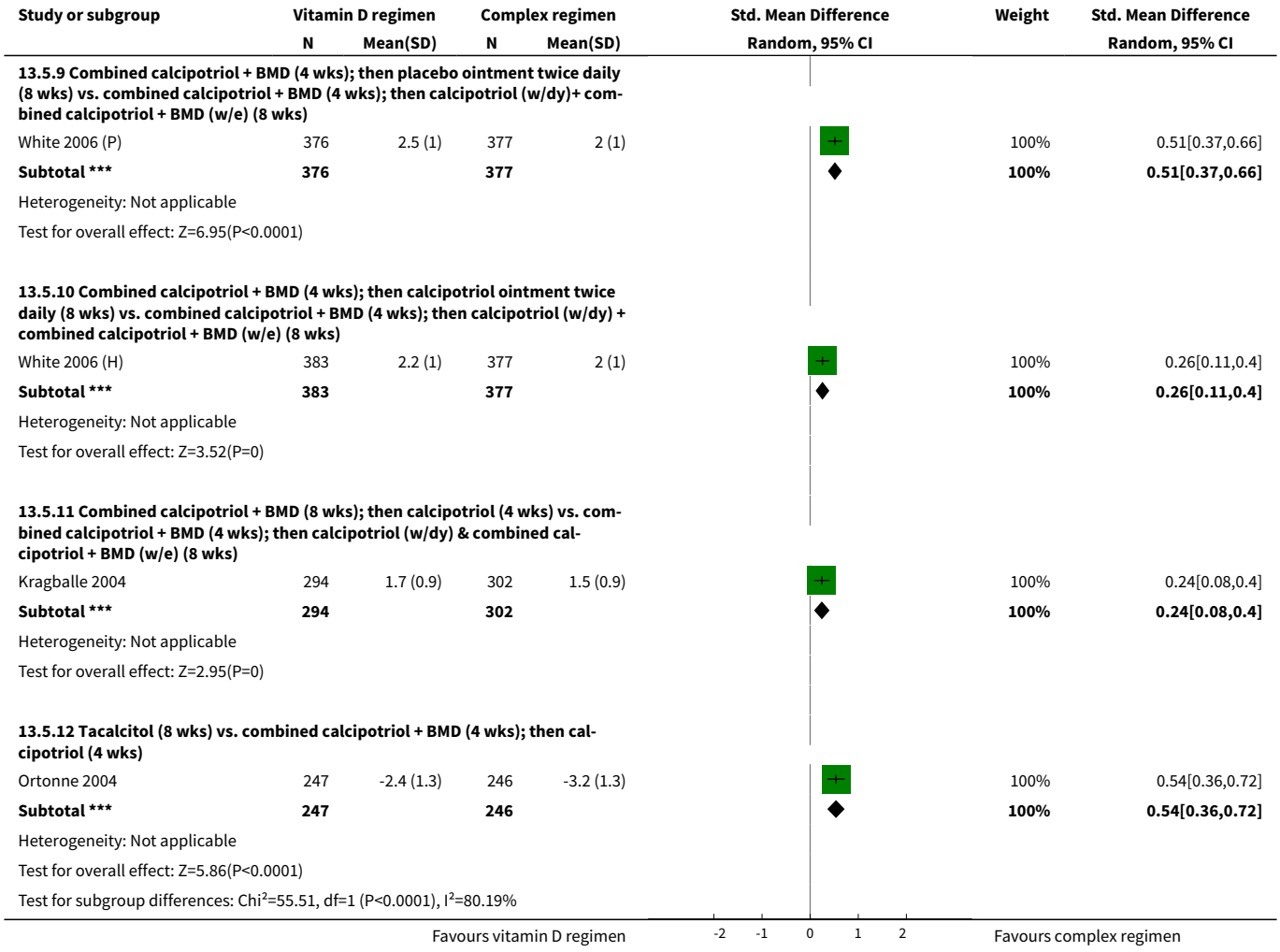
Favours vitamin D regimen | Favours complex regimen



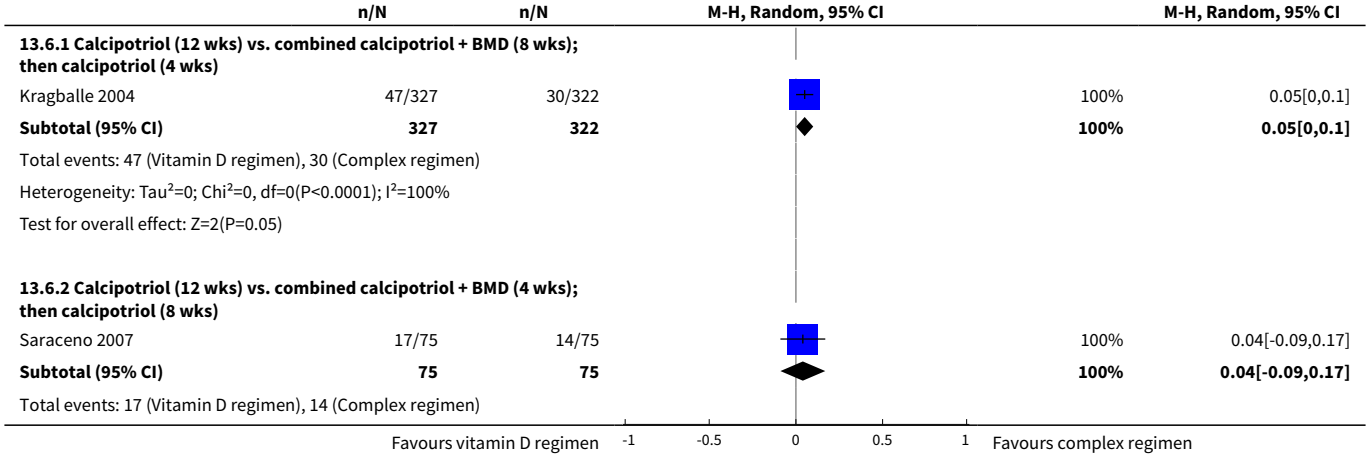
Analysis 13.5. Comparison 13 Vitamin D alone or in combination versus other treatments: complex regimens, Outcome 5 Combined end point (IAGI/TSS/PASI/PAGI).

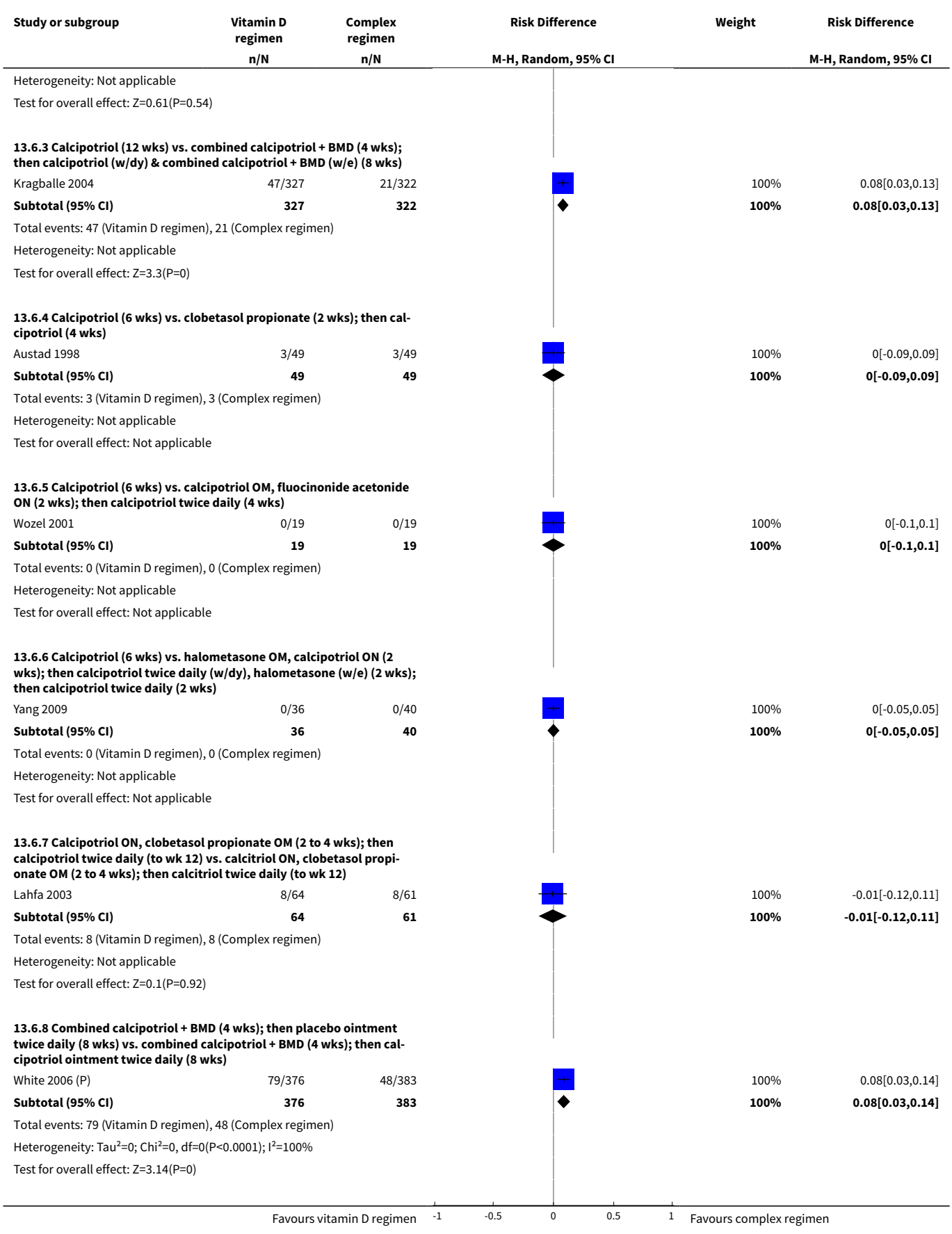


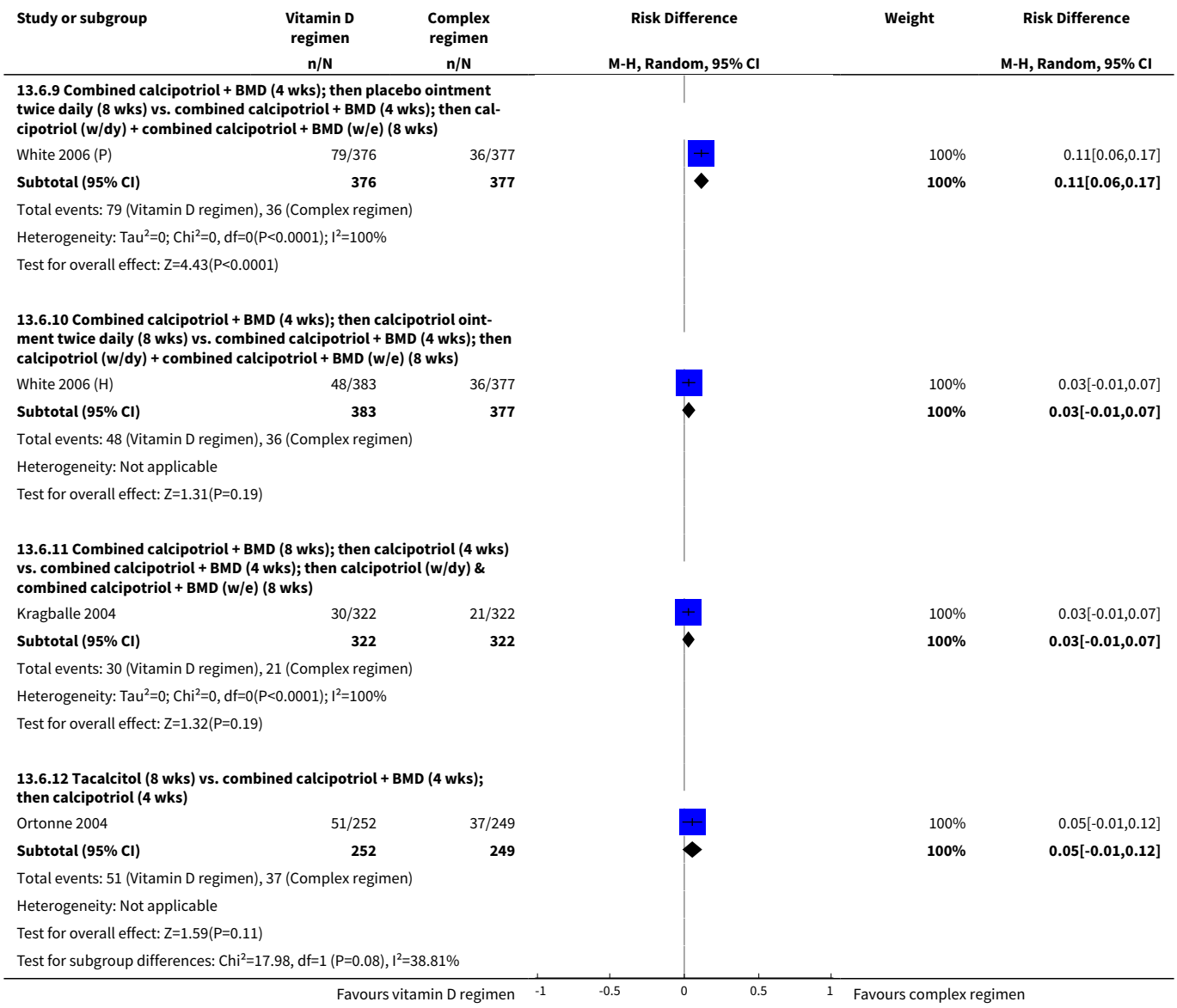




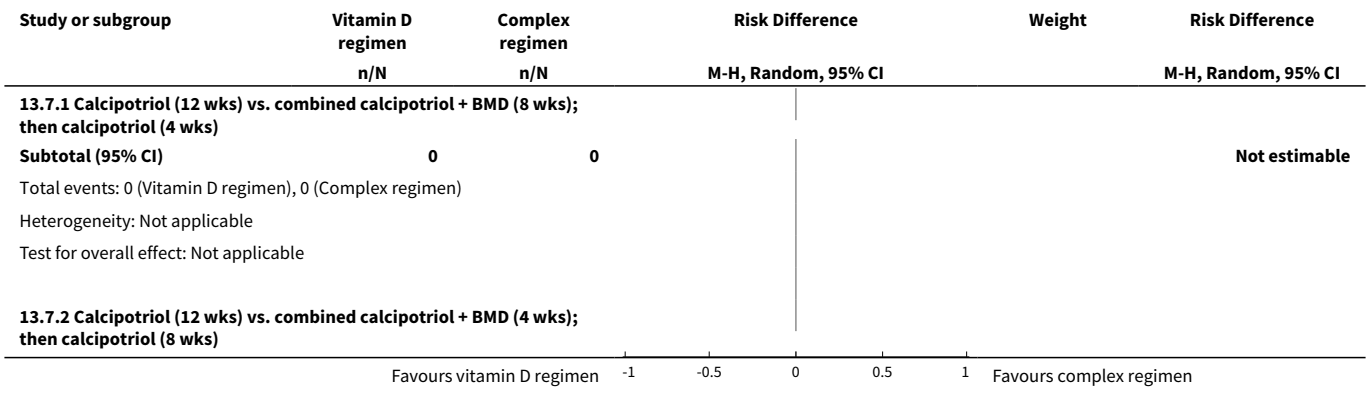
Analysis 13.6. Comparison 13 Vitamin D alone or in combination versus other treatments: complex regimens, Outcome 6 Total withdrawals.

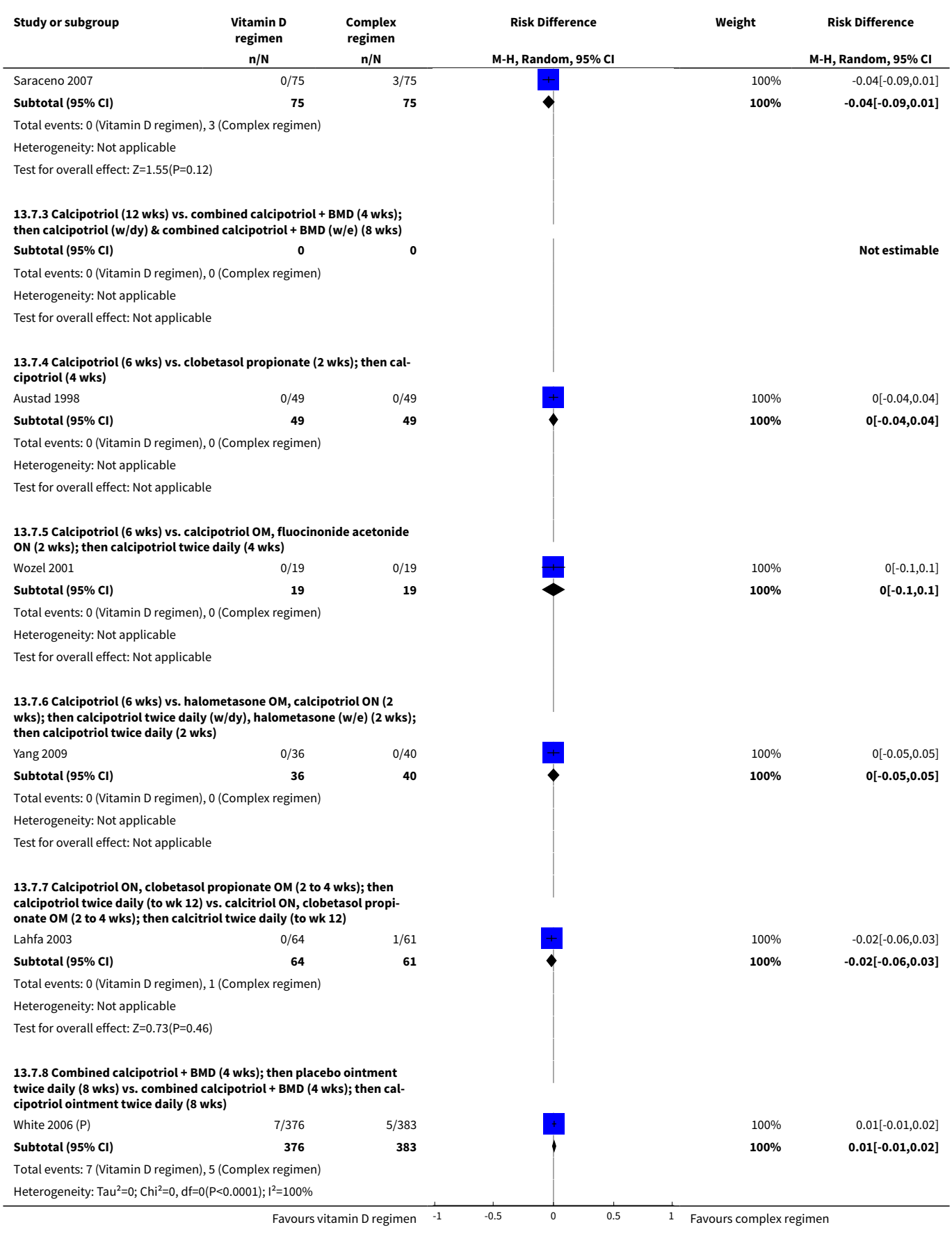




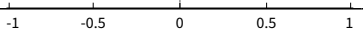


Analysis 13.7. Comparison 13 Vitamin D alone or in combination versus other treatments: complex regimens, Outcome 7 Withdrawals due to adverse events.





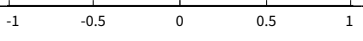
Study or subgroup	Vitamin D regimen n/N	Complex regimen n/N	Risk Difference M-H, Random, 95% CI	Weight	Risk Difference M-H, Random, 95% CI
Test for overall effect: Z=0.61(P=0.54)					
13.7.9 Combined calcipotriol + BMD (4 wks); then placebo ointment twice daily (8 wks) vs. combined calcipotriol + BMD (4 wks); then calcipotriol (w/dy) + combined calcipotriol + BMD (w/e) (8 wks)					
White 2006 (P)	7/376	8/377		100%	-0[-0.02,0.02]
Subtotal (95% CI)	**376**	**377**		**100%**	**-0[-0.02,0.02]**
Total events: 7 (Vitamin D regimen), 8 (Complex regimen)					
Heterogeneity: Not applicable					
Test for overall effect: Z=0.26(P=0.8)					
13.7.10 Combined calcipotriol + BMD (4 wks); then calcipotriol ointment twice daily (8 wks) vs. combined calcipotriol + BMD (4 wks); then calcipotriol (w/dy) + combined calcipotriol + BMD (w/e) (8 wks)					
White 2006 (H)	5/383	8/377		100%	-0.01[-0.03,0.01]
Subtotal (95% CI)	**383**	**377**		**100%**	**-0.01[-0.03,0.01]**
Total events: 5 (Vitamin D regimen), 8 (Complex regimen)					
Heterogeneity: Not applicable					
Test for overall effect: Z=0.87(P=0.39)					
13.7.11 Combined calcipotriol + BMD (8 wks); then calcipotriol (4 wks) vs. combined calcipotriol + BMD (4 wks); then calcipotriol (w/dy) & combined calcipotriol + BMD (w/e) (8 wks)					
Subtotal (95% CI)	**0**	**0**			**Not estimable**
Total events: 0 (Vitamin D regimen), 0 (Complex regimen)					
Heterogeneity: Not applicable					
Test for overall effect: Not applicable					
13.7.12 Tacalcitol (8 wks) vs. combined calcipotriol + BMD (4 wks); then calcipotriol (4 wks)					
Ortonne 2004	11/252	6/249		100%	0.02[-0.01,0.05]
Subtotal (95% CI)	**252**	**249**		**100%**	**0.02[-0.01,0.05]**
Total events: 11 (Vitamin D regimen), 6 (Complex regimen)					
Heterogeneity: Not applicable					
Test for overall effect: Z=1.21(P=0.23)					
Test for subgroup differences: Chi^2=5.51, df=1 (P=0.7), I^2=0%					



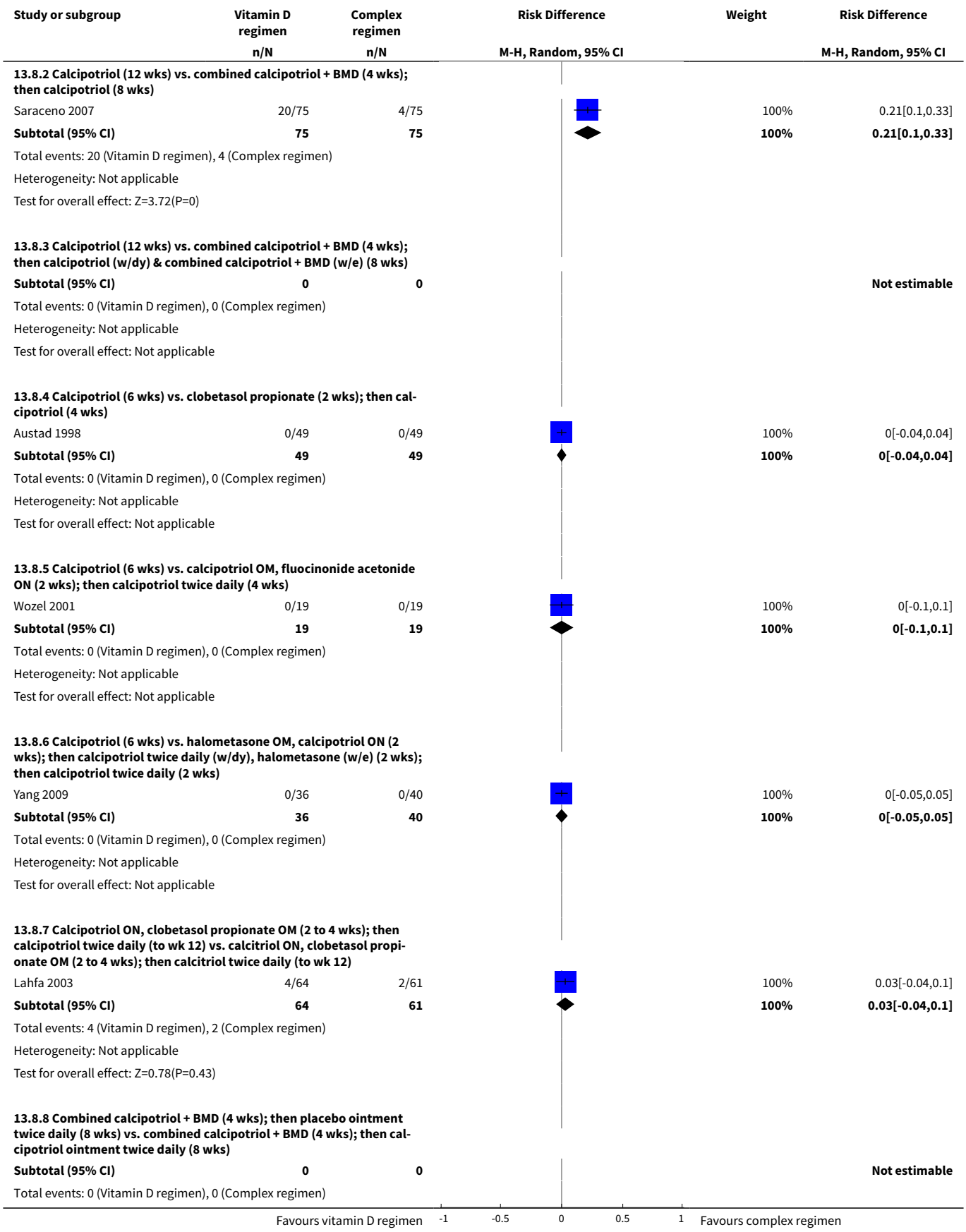
Favours vitamin D regimen — Favours complex regimen

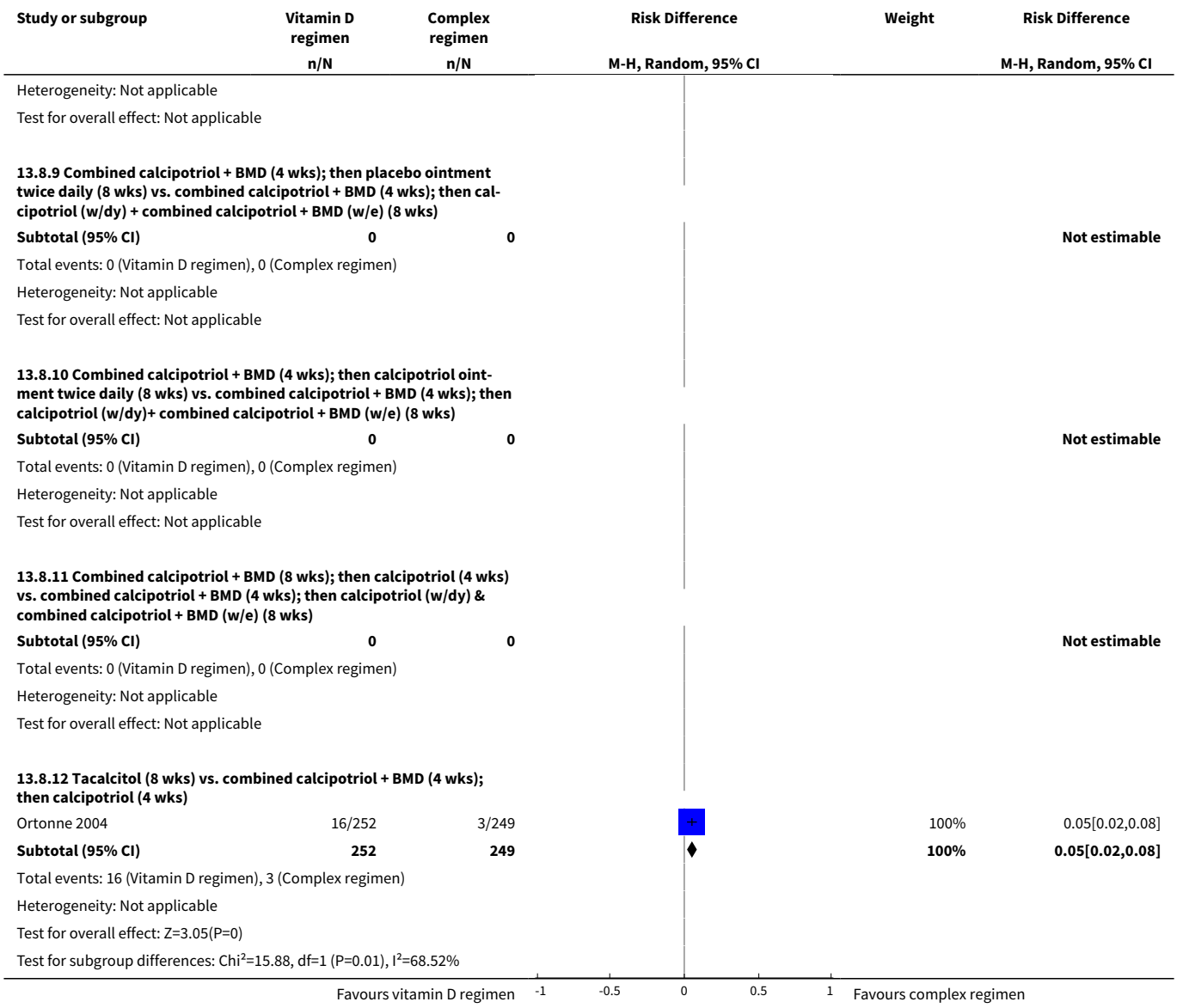
Analysis 13.8. Comparison 13 Vitamin D alone or in combination versus other treatments: complex regimens, Outcome 8 Withdrawals due to treatment failure.

Study or subgroup	Vitamin D regimen n/N	Complex regimen n/N	Risk Difference M-H, Random, 95% CI	Weight	Risk Difference M-H, Random, 95% CI
13.8.1 Calcipotriol (12 wks) vs. combined calcipotriol + BMD (8 wks); then calcipotriol (4 wks)					
Subtotal (95% CI)	**0**	**0**			**Not estimable**
Total events: 0 (Vitamin D regimen), 0 (Complex regimen)					
Heterogeneity: Not applicable					
Test for overall effect: Not applicable					

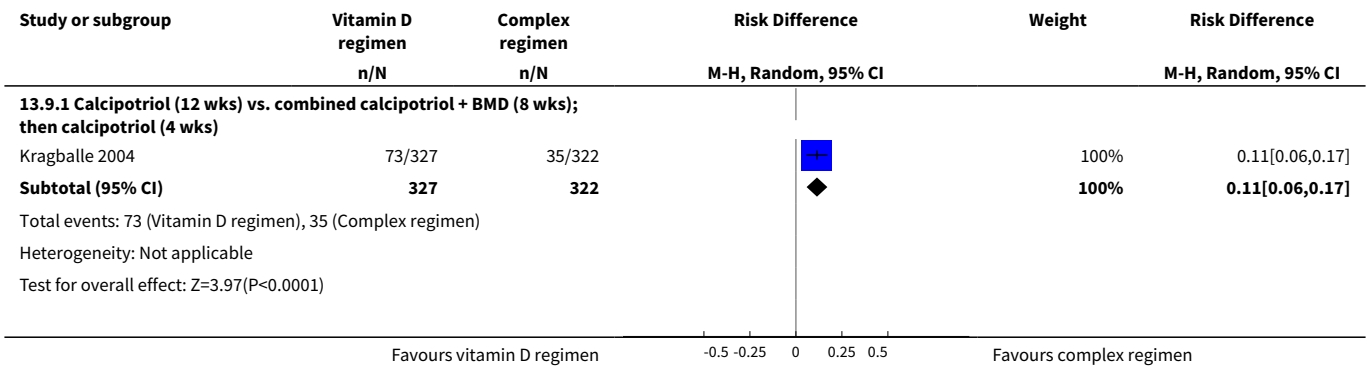


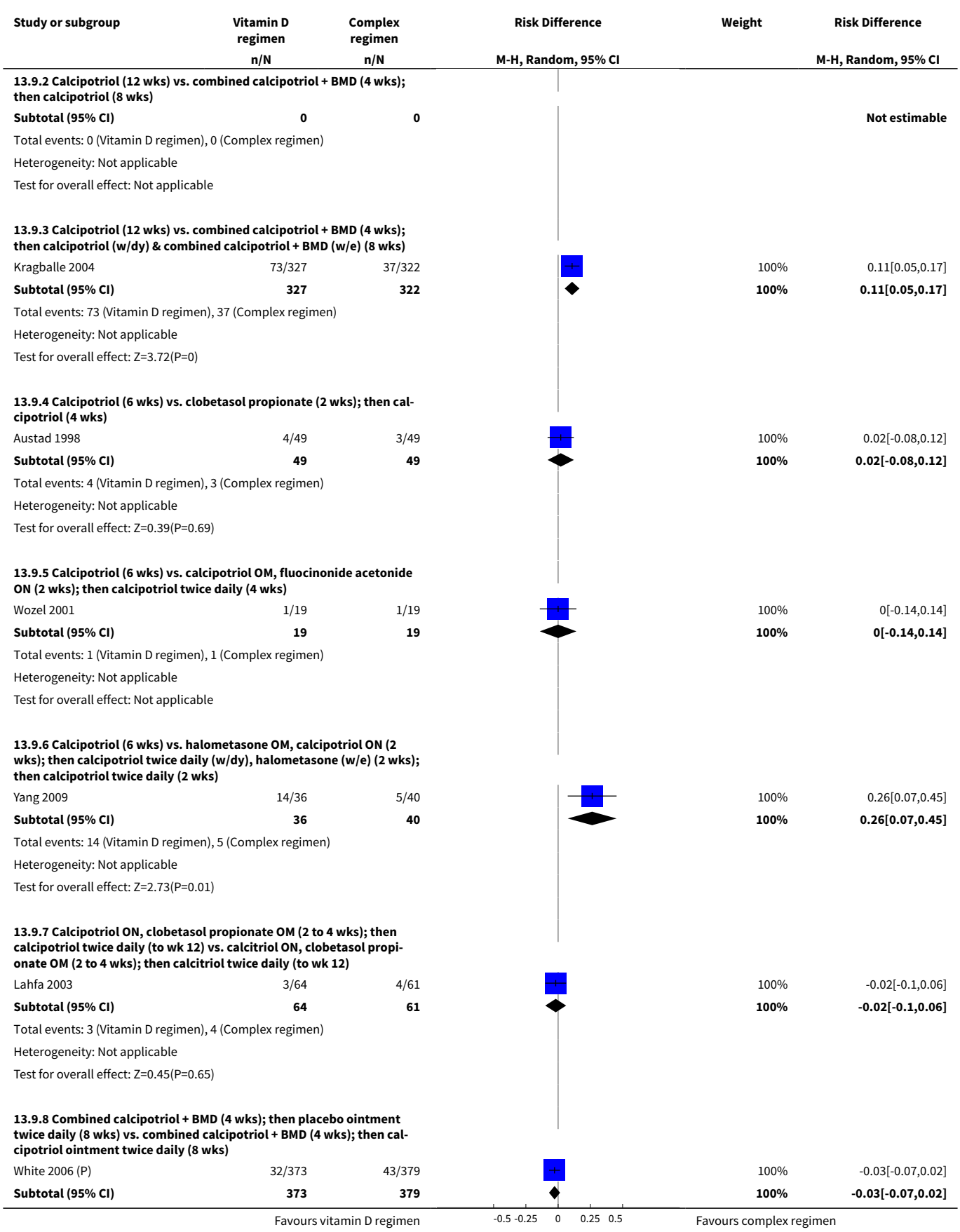
Favours vitamin D regimen — Favours complex regimen

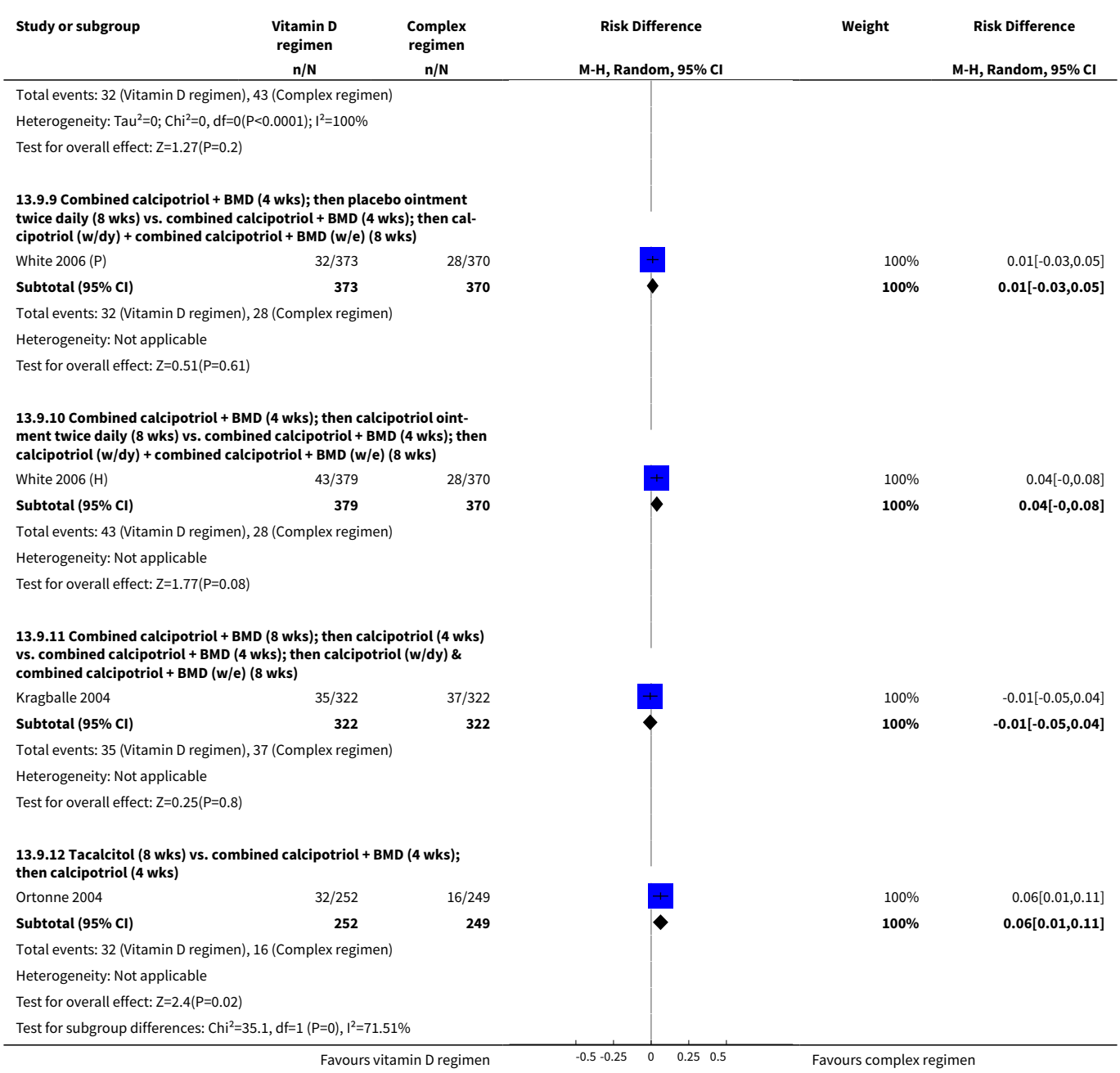




Analysis 13.9. Comparison 13 Vitamin D alone or in combination versus other treatments: complex regimens, Outcome 9 Adverse events (local).







Comparison 14. Vitamin D alone or in combination versus other treatment: long-term studies (> 24 wks)

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 IAGI	1		Std. Mean Difference (IV, Random, 95% CI)	Totals not selected
1.1 Combined calcipotriol + BMD (52 wks) vs. alternating: combined calcipotriol + BMD (4 wks); then calcipotriol (4 wks)	1		Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]

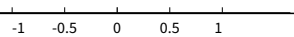
Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1.2 Combined calcipotriol + BMD (52 wks) vs. combined calcipotriol + BMD (4 wks); then calcipotriol (48 wks)	1		Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
1.3 Alternating: combined calcipotriol + BMD (4 wks); then calcipotriol (4 wks) vs. combined calcipotriol + BMD (4 wks); then calcipotriol (48 wks)	1		Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
2 TSS	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
2.1 Combined calcipotriol + BMD (52 wks) vs. alternating: combined calcipotriol + BMD (4 wks); then calcipotriol (4 wks)	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
2.2 Combined calcipotriol + BMD (52 wks) vs. combined calcipotriol + BMD (4 wks); then calcipotriol (48 wks)	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
2.3 Alternating: combined calcipotriol + BMD (4 wks); then calcipotriol (4 wks) vs. combined calcipotriol + BMD (4 wks); then calcipotriol (48 wks)	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
3 PASI	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
3.1 Combined calcipotriol + BMD (52 wks) vs. alternating: combined calcipotriol + BMD (4 wks); then calcipotriol (4 wks)	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
3.2 Combined calcipotriol + BMD (52 wks) vs. combined calcipotriol + BMD (4 wks); then calcipotriol (48 wks)	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
3.3 Alternating: combined calcipotriol + BMD (4 wks); then calcipotriol (4 wks) vs. combined calcipotriol + BMD (4 wks); then calcipotriol (48 wks)	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
4 PAGI	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
4.1 Combined calcipotriol + BMD (52 wks) vs. alternating: combined calcipotriol + BMD (4 wks); then calcipotriol (4 wks)	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
4.2 Combined calcipotriol + BMD (52 wks) vs. combined calcipotriol + BMD (4 wks); then calcipotriol (48 wks)	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
4.3 Alternating: combined calcipotriol + BMD (4 wks); then calcipotriol (4 wks) vs. combined calcipotriol + BMD (4 wks); then calcipotriol (48 wks)	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
5 Combined end point (IAGI/TSS/PASI/PAGI)	1		Std. Mean Difference (IV, Random, 95% CI)	Totals not selected
5.1 Combined calcipotriol + BMD (52 wks) vs. alternating: combined calcipotriol + BMD (4 wks); then calcipotriol (4 wks)	1		Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
5.2 Combined calcipotriol + BMD (52 wks) vs. combined calcipotriol + BMD (4 wks); then calcipotriol (48 wks)	1		Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
5.3 Alternating: combined calcipotriol + BMD (4 wks); then calcipotriol (4 wks) vs. combined calcipotriol + BMD (4 wks); then calcipotriol (48 wks)	1		Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
6 Total withdrawals	1		Risk Difference (M-H, Random, 95% CI)	Totals not selected
6.1 Combined calcipotriol + BMD (52 wks) vs. alternating: combined calcipotriol + BMD (4 wks); then calcipotriol (4 wks)	1		Risk Difference (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
6.2 Combined calcipotriol + BMD (52 wks) vs. combined calcipotriol + BMD (4 wks); then calcipotriol (48 wks)	1		Risk Difference (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
6.3 Alternating: combined calcipotriol + BMD (4 wks); then calcipotriol (4 wks) vs. combined calcipotriol + BMD (4 wks); then calcipotriol (48 wks)	1		Risk Difference (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
7 Withdrawals due to adverse events	1		Risk Difference (M-H, Random, 95% CI)	Totals not selected
7.1 Combined calcipotriol + BMD (52 wks) vs. alternating: combined calcipotriol + BMD (4 wks); then calcipotriol (4 wks)	1		Risk Difference (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
7.2 Combined calcipotriol + BMD (52 wks) vs. combined calcipotriol + BMD (4 wks); then calcipotriol (48 wks)	1		Risk Difference (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
7.3 Alternating: combined calcipotriol + BMD (4 wks); then calcipotriol (4 wks) vs. combined calcipotriol + BMD (4 wks); then calcipotriol (48 wks)	1		Risk Difference (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
8 Withdrawals due to treatment failure	1		Risk Difference (M-H, Random, 95% CI)	Totals not selected
8.1 Combined calcipotriol + BMD (52 wks) vs. alternating: combined calcipotriol + BMD (4 wks); then calcipotriol (4 wks)	1		Risk Difference (M-H, Random, 95% CI)	0.0 [0.0, 0.0]

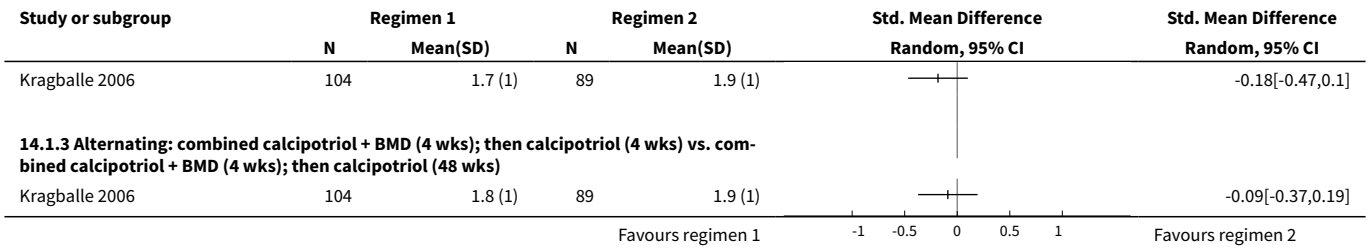
Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
8.2 Combined calcipotriol + BMD (52 wks) vs. combined calcipotriol + BMD (4 wks); then calcipotriol (48 wks)	1		Risk Difference (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
8.3 Alternating: combined calcipotriol + BMD (4 wks); then calcipotriol (4 wks) vs. combined calcipotriol + BMD (4 wks); then calcipotriol (48 wks)	1		Risk Difference (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
9 Adverse events (local)	1		Risk Difference (M-H, Random, 95% CI)	Totals not selected
9.1 Combined calcipotriol + BMD (52 wks) vs. alternating: combined calcipotriol + BMD (4 wks); then calcipotriol (4 wks)	1		Risk Difference (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
9.2 Combined calcipotriol + BMD (52 wks) vs. combined calcipotriol + BMD (4 wks); then calcipotriol (48 wks)	1		Risk Difference (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
9.3 Alternating: combined calcipotriol + BMD (4 wks); then calcipotriol (4 wks) vs. combined calcipotriol + BMD (4 wks); then calcipotriol (48 wks)	1		Risk Difference (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
10 Adverse events (systemic)	0		Risk Difference (M-H, Random, 95% CI)	Subtotals only
10.1 Combined calcipotriol + BMD (52 wks) vs. alternating: combined calcipotriol + BMD (4 wks); then calcipotriol (4 wks)	0	0	Risk Difference (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
10.2 Combined calcipotriol + BMD (52 wks) vs. combined calcipotriol + BMD (4 wks); then calcipotriol (48 wks)	0	0	Risk Difference (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
10.3 Alternating: combined calcipotriol + BMD (4 wks); then calcipotriol (4 wks) vs. combined calcipotriol + BMD (4 wks); then calcipotriol (48 wks)	0	0	Risk Difference (M-H, Random, 95% CI)	0.0 [0.0, 0.0]

Analysis 14.1. Comparison 14 Vitamin D alone or in combination versus other treatment: long-term studies (> 24 wks), Outcome 1 IAGI.

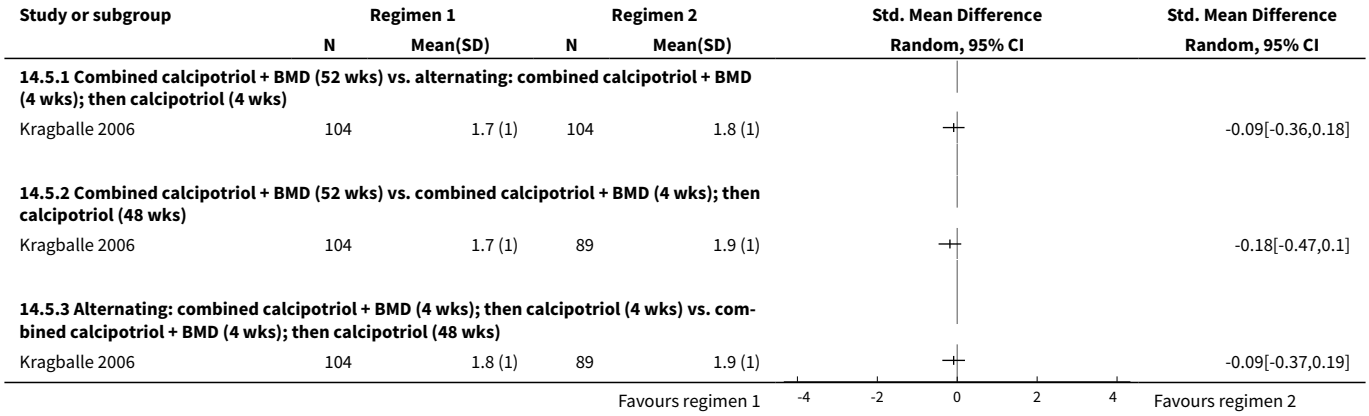
Study or subgroup	Regimen 1 N	Regimen 1 Mean(SD)	Regimen 2 N	Regimen 2 Mean(SD)	Std. Mean Difference Random, 95% CI	Std. Mean Difference Random, 95% CI
14.1.1 Combined calcipotriol + BMD (52 wks) vs. alternating: combined calcipotriol + BMD (4 wks); then calcipotriol (4 wks)						
Kragballe 2006	104	1.7 (1)	104	1.8 (1)		-0.09[-0.36,0.18]
14.1.2 Combined calcipotriol + BMD (52 wks) vs. combined calcipotriol + BMD (4 wks); then calcipotriol (48 wks)						



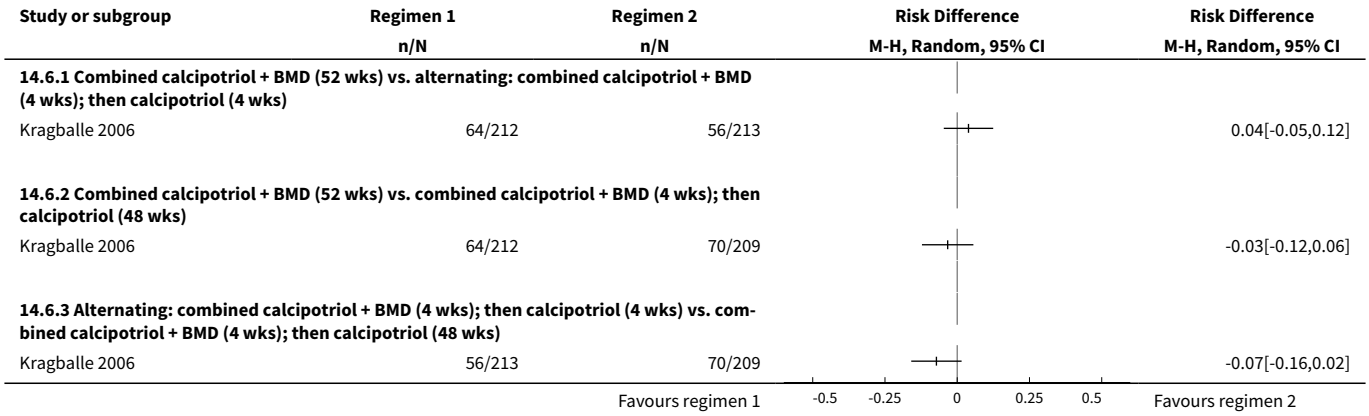
Favours regimen 1 — Favours regimen 2



Analysis 14.5. Comparison 14 Vitamin D alone or in combination versus other treatment: long-term studies (> 24 wks), Outcome 5 Combined end point (IAGI/TSS/PASI/PAGI).



Analysis 14.6. Comparison 14 Vitamin D alone or in combination versus other treatment: long-term studies (> 24 wks), Outcome 6 Total withdrawals.



Analysis 14.7. Comparison 14 Vitamin D alone or in combination versus other treatment: long-term studies (> 24 wks), Outcome 7 Withdrawals due to adverse events.

Study or subgroup	Regimen 1 n/N	Regimen 2 n/N	Risk Difference M-H, Random, 95% CI	Risk Difference M-H, Random, 95% CI
14.7.1 Combined calcipotriol + BMD (52 wks) vs. alternating: combined calcipotriol + BMD (4 wks); then calcipotriol (4 wks)				
Kragballe 2006	14/212	11/213		0.01[-0.03,0.06]
14.7.2 Combined calcipotriol + BMD (52 wks) vs. combined calcipotriol + BMD (4 wks); then calcipotriol (48 wks)				
Kragballe 2006	14/212	16/209		-0.01[-0.06,0.04]
14.7.3 Alternating: combined calcipotriol + BMD (4 wks); then calcipotriol (4 wks) vs. combined calcipotriol + BMD (4 wks); then calcipotriol (48 wks)				
Kragballe 2006	11/213	16/209		-0.02[-0.07,0.02]

Favours regimen 1 — Favours regimen 2

Analysis 14.8. Comparison 14 Vitamin D alone or in combination versus other treatment: long-term studies (> 24 wks), Outcome 8 Withdrawals due to treatment failure.

Study or subgroup	Regimen 1 n/N	Regimen 2 n/N	Risk Difference M-H, Random, 95% CI	Risk Difference M-H, Random, 95% CI
14.8.1 Combined calcipotriol + BMD (52 wks) vs. alternating: combined calcipotriol + BMD (4 wks); then calcipotriol (4 wks)				
Kragballe 2006	32/212	31/213		0.01[-0.06,0.07]
14.8.2 Combined calcipotriol + BMD (52 wks) vs. combined calcipotriol + BMD (4 wks); then calcipotriol (48 wks)				
Kragballe 2006	32/212	42/209		-0.05[-0.12,0.02]
14.8.3 Alternating: combined calcipotriol + BMD (4 wks); then calcipotriol (4 wks) vs. combined calcipotriol + BMD (4 wks); then calcipotriol (48 wks)				
Kragballe 2006	31/213	42/209		-0.06[-0.13,0.02]

Favours regimen 1 — Favours regimen 2

Analysis 14.9. Comparison 14 Vitamin D alone or in combination versus other treatment: long-term studies (> 24 wks), Outcome 9 Adverse events (local).

Study or subgroup	Regimen 1 n/N	Regimen 2 n/N	Risk Difference M-H, Random, 95% CI	Risk Difference M-H, Random, 95% CI
14.9.1 Combined calcipotriol + BMD (52 wks) vs. alternating: combined calcipotriol + BMD (4 wks); then calcipotriol (4 wks)				
Kragballe 2006	45/212	63/213		-0.08[-0.17,-0]
14.9.2 Combined calcipotriol + BMD (52 wks) vs. combined calcipotriol + BMD (4 wks); then calcipotriol (48 wks)				
Kragballe 2006	45/212	78/209		-0.16[-0.25,-0.08]
14.9.3 Alternating: combined calcipotriol + BMD (4 wks); then calcipotriol (4 wks) vs. combined calcipotriol + BMD (4 wks); then calcipotriol (48 wks)				
Kragballe 2006	63/213	78/209		-0.08[-0.17,0.01]

Favours regimen 1 — Favours regimen 2

Comparison 15. Vitamin D analogues versus other treatment

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 IAGI	10		Std. Mean Difference (IV, Random, 95% CI)	Subtotals only
1.1 Calcipotriol vs. coal tar	3	139	Std. Mean Difference (IV, Random, 95% CI)	-0.53 [-1.74, 0.68]
1.2 Calcipotriol vs. coal tar polytherapy	2	209	Std. Mean Difference (IV, Random, 95% CI)	-0.59 [-0.87, -0.31]
1.3 Calcipotriol vs. nicotinamide 1.4%, twice daily	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
1.4 Calcipotriol vs. calcipotriol + nicotinamide 1.4%, twice daily	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
1.5 Calcipotriol vs. corticosteroid + salicylic acid	1	200	Std. Mean Difference (IV, Random, 95% CI)	-0.06 [-0.33, 0.22]
1.6 Calcipotriol vs. propylthiouracil cream	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
1.7 Calcipotriol vs. tazarotene	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
1.8 Calcipotriol vs. tacrolimus ointment	1	124	Std. Mean Difference (IV, Random, 95% CI)	-0.22 [-0.60, 0.16]
1.9 Calcipotriol vs. tazarotene gel plus mometasone furoate cream	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
1.10 Calcipotriol vs. vitamin B12 cream	1	26	Std. Mean Difference (IV, Random, 95% CI)	-0.55 [-1.33, 0.24]
1.11 Head-to-head vitamin D alone or in combination: twice daily vs OD	2	728	Std. Mean Difference (IV, Random, 95% CI)	-0.24 [-0.38, -0.09]
1.12 Head-to-head vitamin D alone or in combination: no occlusion vs. occlusion	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
2 TSS	7		Std. Mean Difference (IV, Random, 95% CI)	Subtotals only
2.1 Calcipotriol vs. coal tar	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
2.2 Calcipotriol vs. coal tar polytherapy	1	132	Std. Mean Difference (IV, Random, 95% CI)	-0.51 [-0.86, -0.16]
2.3 Calcipotriol vs. nicotinamide 1.4%, twice daily	1	96	Std. Mean Difference (IV, Random, 95% CI)	-0.09 [-0.49, 0.31]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
2.4 Calcipotriol vs. calcipotriol+nicotinamide (0.05%, 0.1%, 0.7%, or 1.4%), twice daily	1	192	Std. Mean Difference (IV, Random, 95% CI)	0.19 [-0.14, 0.52]
2.5 Calcipotriol vs. corticosteroid + salicylic acid	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
2.6 Calcipotriol vs. propylthiouracil cream	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
2.7 Calcipotriol vs. tacrolimus ointment	2	171	Std. Mean Difference (IV, Random, 95% CI)	-0.35 [-1.51, 0.81]
2.8 Calcipotriol vs. tazarotene	1	199	Std. Mean Difference (IV, Random, 95% CI)	-0.05 [-0.33, 0.23]
2.9 Calcipotriol vs. tazarotene gel plus mometasone furoate cream	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
2.10 Calcipotriol vs. vitamin B12 cream	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
2.11 Head-to-head vitamin D alone or in combination: twice daily vs OD	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
2.12 Head-to-head vitamin D alone or in combination: no occlusion vs. occlusion	2	247	Std. Mean Difference (IV, Random, 95% CI)	-0.18 [-2.04, 1.68]
3 PASI	9		Std. Mean Difference (IV, Random, 95% CI)	Subtotals only
3.1 Calcipotriol vs. coal tar	2	109	Std. Mean Difference (IV, Random, 95% CI)	-0.10 [-1.54, 1.35]
3.2 Calcipotriol vs. coal tar polytherapy	1	87	Std. Mean Difference (IV, Random, 95% CI)	-0.63 [-1.06, -0.20]
3.3 Calcipotriol vs. nicotinamide 1.4%, twice daily	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
3.4 Calcipotriol vs. calcipotriol + nicotinamide 1.4%, twice daily	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
3.5 Calcipotriol vs. corticosteroid + salicylic acid	1	160	Std. Mean Difference (IV, Random, 95% CI)	-0.05 [-0.36, 0.26]
3.6 Calcipotriol vs. propylthiouracil cream	1	27	Std. Mean Difference (IV, Random, 95% CI)	-2.24 [-3.23, -1.25]
3.7 Calcipotriol vs. tacrolimus ointment	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
3.8 Calcipotriol vs. tazarotene	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
3.9 Calcipotriol vs. tazarotene gel plus mometasone furoate cream	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
3.10 Calcipotriol vs. vitamin B12 cream	1	26	Std. Mean Difference (IV, Random, 95% CI)	-0.01 [-0.78, 0.75]
3.11 Head-to-head vitamin D alone or in combination: twice daily vs OD	3	989	Std. Mean Difference (IV, Random, 95% CI)	-0.12 [-0.25, 0.00]
3.12 Head-to-head vitamin D alone or in combination: no occlusion vs. occlusion	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
4 PAGI	6		Std. Mean Difference (IV, Random, 95% CI)	Subtotals only
4.1 Calcipotriol vs. coal tar	1	54	Std. Mean Difference (IV, Random, 95% CI)	-1.51 [-2.12, -0.90]
4.2 Calcipotriol vs. coal tar polytherapy	1	87	Std. Mean Difference (IV, Random, 95% CI)	-0.56 [-0.99, -0.13]
4.3 Calcipotriol vs. nicotinamide 1.4%, twice daily	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
4.4 Calcipotriol vs. calcipotriol + nicotinamide 1.4%, twice daily	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
4.5 Calcipotriol vs. corticosteroid + salicylic acid	1	186	Std. Mean Difference (IV, Random, 95% CI)	-0.49 [-0.79, -0.20]
4.6 Calcipotriol vs. propylthiouracil cream	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
4.7 Calcipotriol vs. tacrolimus ointment	1	124	Std. Mean Difference (IV, Random, 95% CI)	-0.13 [-0.51, 0.24]
4.8 Calcipotriol vs. tazarotene	1	38	Std. Mean Difference (IV, Random, 95% CI)	-0.35 [-0.99, 0.29]
4.9 Calcipotriol vs. tazarotene gel plus mometasone furoate cream	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
4.10 Calcipotriol vs. vitamin B12 cream	1	26	Std. Mean Difference (IV, Random, 95% CI)	-0.55 [-1.33, 0.24]
4.11 Head-to-head vitamin D alone or in combination: twice daily vs OD	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
4.12 Head-to-head vitamin D alone or in combination: no occlusion vs. occlusion	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
5 Combined end point (IAGI/TSS/PASI/PAGI)	19		Std. Mean Difference (IV, Random, 95% CI)	Subtotals only

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
5.1 Calcipotriol vs. coal tar	3	139	Std. Mean Difference (IV, Random, 95% CI)	-0.53 [-1.74, 0.68]
5.2 Calcipotriol vs. coal tar polytherapy	2	209	Std. Mean Difference (IV, Random, 95% CI)	-0.59 [-0.87, -0.31]
5.3 Calcipotriol vs. nicotinamide 1.4%, twice daily	1	96	Std. Mean Difference (IV, Random, 95% CI)	-0.09 [-0.49, 0.31]
5.4 Calcipotriol vs. calcipotriol + nicotinamide (0.05%, 0.1%, 0.7%, or 1.4%), twice daily	1	192	Std. Mean Difference (IV, Random, 95% CI)	0.19 [-0.14, 0.52]
5.5 Calcipotriol vs. corticosteroid + salicylic acid	2	360	Std. Mean Difference (IV, Random, 95% CI)	-0.05 [-0.26, 0.15]
5.6 Calcipotriol vs. propylthiouracil cream	1	27	Std. Mean Difference (IV, Random, 95% CI)	-2.24 [-3.23, -1.25]
5.7 Calcipotriol vs. tacrolimus ointment	2	171	Std. Mean Difference (IV, Random, 95% CI)	-0.55 [-1.28, 0.17]
5.8 Calcipotriol vs. tazarotene	2	237	Std. Mean Difference (IV, Random, 95% CI)	-0.10 [-0.35, 0.16]
5.9 Calcipotriol vs. tazarotene gel plus mometasone furoate cream	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
5.10 Calcipotriol vs. vitamin B12 cream	1	26	Std. Mean Difference (IV, Random, 95% CI)	-0.55 [-1.33, 0.24]
5.11 Head-to-head vitamin D alone or in combination: twice daily vs OD	3	988	Std. Mean Difference (IV, Random, 95% CI)	-0.20 [-0.32, -0.07]
5.12 Head-to-head vitamin D alone or in combination: no occlusion vs. occlusion	2	247	Std. Mean Difference (IV, Random, 95% CI)	-0.18 [-2.04, 1.68]
6 Total withdrawals	15		Risk Difference (M-H, Random, 95% CI)	Subtotals only
6.1 Calcipotriol vs. coal tar	2	120	Risk Difference (M-H, Random, 95% CI)	-0.02 [-0.12, 0.08]
6.2 Calcipotriol vs. coal tar polytherapy	2	220	Risk Difference (M-H, Random, 95% CI)	-0.03 [-0.10, 0.04]
6.3 Calcipotriol vs. nicotinamide 1.4%, twice daily	1	96	Risk Difference (M-H, Random, 95% CI)	0.02 [-0.05, 0.09]
6.4 Calcipotriol vs. calcipotriol + nicotinamide (0.05%, 0.1%, 0.7%, or 1.4%), twice daily	1	192	Risk Difference (M-H, Random, 95% CI)	0.01 [-0.06, 0.07]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
6.5 Calcipotriol vs. corticosteroid + salicylic acid	1	160	Risk Difference (M-H, Random, 95% CI)	0.04 [-0.09, 0.17]
6.6 Calcipotriol vs. propylthiouracil cream	1	28	Risk Difference (M-H, Random, 95% CI)	0.07 [-0.16, 0.30]
6.7 Calcipotriol vs. tacrolimus ointment	1	124	Risk Difference (M-H, Random, 95% CI)	-0.13 [-0.25, -0.01]
6.8 Calcipotriol vs. tazarotene	2	254	Risk Difference (M-H, Random, 95% CI)	-0.04 [-0.10, 0.01]
6.9 Calcipotriol vs. tazarotene gel plus mometasone furoate cream	1	120	Risk Difference (M-H, Random, 95% CI)	-0.03 [-0.15, 0.08]
6.10 Calcipotriol vs. vitamin B12 cream	1	26	Risk Difference (M-H, Random, 95% CI)	0.0 [-0.14, 0.14]
6.11 Head-to-head vitamin D alone or in combination: twice daily vs OD	3	1001	Risk Difference (M-H, Random, 95% CI)	0.01 [-0.03, 0.05]
6.12 Head-to-head vitamin D alone or in combination: no occlusion vs. occlusion	0	0	Risk Difference (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
7 Withdrawals due to adverse events	15		Risk Difference (M-H, Random, 95% CI)	Subtotals only
7.1 Calcipotriol vs. coal tar	2	120	Risk Difference (M-H, Random, 95% CI)	0.01 [-0.04, 0.06]
7.2 Calcipotriol vs. coal tar polytherapy	2	210	Risk Difference (M-H, Random, 95% CI)	-0.02 [-0.07, 0.03]
7.3 Calcipotriol vs. nicotinamide 1.4%, twice daily	1	96	Risk Difference (M-H, Random, 95% CI)	0.0 [-0.04, 0.04]
7.4 Calcipotriol vs. calcipotriol + nicotinamide (0.05%, 0.1%, 0.7%, or 1.4%), twice daily	1	192	Risk Difference (M-H, Random, 95% CI)	0.0 [-0.03, 0.03]
7.5 Calcipotriol vs. corticosteroid + salicylic acid	1	160	Risk Difference (M-H, Random, 95% CI)	0.05 [-0.00, 0.10]
7.6 Calcipotriol vs. propylthiouracil cream	1	28	Risk Difference (M-H, Random, 95% CI)	0.07 [-0.16, 0.30]
7.7 Calcipotriol vs. tacrolimus ointment	1	124	Risk Difference (M-H, Random, 95% CI)	0.02 [-0.08, 0.11]
7.8 Calcipotriol vs. tazarotene	2	254	Risk Difference (M-H, Random, 95% CI)	-0.05 [-0.16, 0.05]
7.9 Calcipotriol vs. tazarotene gel plus mometasone furoate cream	1	120	Risk Difference (M-H, Random, 95% CI)	-0.02 [-0.10, 0.07]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
7.10 Calcipotriol vs. vitamin B12 cream	1	26	Risk Difference (M-H, Random, 95% CI)	0.0 [-0.14, 0.14]
7.11 Head-to-head vitamin D alone or in combination: twice daily vs OD	3	998	Risk Difference (M-H, Random, 95% CI)	0.01 [-0.01, 0.02]
7.12 Head-to-head vitamin D alone or in combination: no occlusion vs. occlusion	0	0	Risk Difference (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
8 Withdrawals due to treatment failure	12		Risk Difference (M-H, Random, 95% CI)	Subtotals only
8.1 Calcipotriol vs. coal tar	1	60	Risk Difference (M-H, Random, 95% CI)	0.0 [-0.06, 0.06]
8.2 Calcipotriol vs. coal tar polytherapy	1	88	Risk Difference (M-H, Random, 95% CI)	0.00 [-0.06, 0.07]
8.3 Calcipotriol vs. nicotinamide 1.4%, twice daily	1	96	Risk Difference (M-H, Random, 95% CI)	0.0 [-0.04, 0.04]
8.4 Calcipotriol vs. calcipotriol + nicotinamide (0.05%, 0.1%, 0.7%, or 1.4%), twice daily	1	192	Risk Difference (M-H, Random, 95% CI)	0.0 [-0.03, 0.03]
8.5 Calcipotriol vs. corticosteroid + salicylic acid	1	160	Risk Difference (M-H, Random, 95% CI)	-0.02 [-0.07, 0.02]
8.6 Calcipotriol vs. propylthiouracil cream	1	28	Risk Difference (M-H, Random, 95% CI)	-0.07 [-0.25, 0.11]
8.7 Calcipotriol vs. tacrolimus ointment	1	124	Risk Difference (M-H, Random, 95% CI)	-0.02 [-0.07, 0.03]
8.8 Calcipotriol vs. tazarotene	1	208	Risk Difference (M-H, Random, 95% CI)	0.0 [-0.02, 0.02]
8.9 Calcipotriol vs. tazarotene gel plus mometasone furoate cream	1	120	Risk Difference (M-H, Random, 95% CI)	0.0 [-0.05, 0.05]
8.10 Calcipotriol vs. vitamin B12 cream	1	26	Risk Difference (M-H, Random, 95% CI)	0.0 [-0.14, 0.14]
8.11 Head-to-head vitamin D alone or in combination: twice daily vs OD	3	998	Risk Difference (M-H, Random, 95% CI)	0.00 [-0.01, 0.01]
8.12 Head-to-head vitamin D alone or in combination: no occlusion vs. occlusion	0	0	Risk Difference (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
9 Adverse events (local)	11		Risk Difference (M-H, Random, 95% CI)	Subtotals only

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
9.1 Calcipotriol vs. coal tar	2	120	Risk Difference (M-H, Random, 95% CI)	0.02 [-0.06, 0.10]
9.2 Calcipotriol vs. coal tar polytherapy	1	122	Risk Difference (M-H, Random, 95% CI)	0.06 [-0.09, 0.20]
9.3 Calcipotriol vs. nicotinamide 1.4%, twice daily	1	96	Risk Difference (M-H, Random, 95% CI)	-0.15 [-0.32, 0.03]
9.4 Calcipotriol vs. calcipotriol + nicotinamide (0.05%, 0.1%, 0.7%, or 1.4%), twice daily	1	192	Risk Difference (M-H, Random, 95% CI)	-0.17 [-0.30, -0.03]
9.5 Calcipotriol vs. corticosteroid + salicylic acid	1	160	Risk Difference (M-H, Random, 95% CI)	0.09 [0.02, 0.15]
9.6 Calcipotriol vs. propylthiouracil cream	1	28	Risk Difference (M-H, Random, 95% CI)	-0.07 [-0.25, 0.11]
9.7 Calcipotriol vs. tacrolimus ointment	1	124	Risk Difference (M-H, Random, 95% CI)	-0.19 [-0.37, -0.01]
9.8 Calcipotriol vs. tazarotene	1	204	Risk Difference (M-H, Random, 95% CI)	-0.03 [-0.11, 0.06]
9.9 Calcipotriol vs. tazarotene gel plus mometasone furoate cream	0	0	Risk Difference (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
9.10 Calcipotriol vs. vitamin B12 cream	1	26	Risk Difference (M-H, Random, 95% CI)	0.23 [-0.06, 0.52]
9.11 Head-to-head vitamin D alone or in combination: twice daily vs OD	2	731	Risk Difference (M-H, Random, 95% CI)	-0.00 [-0.06, 0.05]
9.12 Head-to-head vitamin D alone or in combination: no occlusion vs. occlusion	0	0	Risk Difference (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
10 Adverse events (systemic)	8		Risk Difference (M-H, Random, 95% CI)	Subtotals only
10.1 Calcipotriol vs. coal tar	1	60	Risk Difference (M-H, Random, 95% CI)	0.0 [-0.09, 0.09]
10.2 Calcipotriol vs. coal tar polytherapy	1	88	Risk Difference (M-H, Random, 95% CI)	0.0 [-0.04, 0.04]
10.3 Calcipotriol vs. nicotinamide 1.4%, twice daily	0	0	Risk Difference (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
10.4 Calcipotriol vs. calcipotriol + nicotinamide 1.4%, twice daily	0	0	Risk Difference (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
10.5 Calcipotriol vs. corticosteroid + salicylic acid	1	160	Risk Difference (M-H, Random, 95% CI)	0.0 [-0.02, 0.02]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
10.6 Calcipotriol vs. propylthiouracil cream	1	28	Risk Difference (M-H, Random, 95% CI)	0.0 [-0.13, 0.13]
10.7 Calcipotriol vs. tacrolimus ointment	1	124	Risk Difference (M-H, Random, 95% CI)	0.0 [-0.04, 0.04]
10.8 Calcipotriol vs. tazarotene	1	183	Risk Difference (M-H, Random, 95% CI)	-0.01 [-0.05, 0.03]
10.9 Calcipotriol vs. tazarotene gel plus mometasone furoate cream	0	0	Risk Difference (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
10.10 Calcipotriol vs. vitamin B12 cream	0	0	Risk Difference (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
10.11 Head-to-head vitamin D alone or in combination: twice daily vs OD	1	264	Risk Difference (M-H, Random, 95% CI)	0.0 [-0.01, 0.01]
10.12 Head-to-head vitamin D alone or in combination: no occlusion vs. occlusion	1	38	Risk Difference (M-H, Random, 95% CI)	0.0 [-0.10, 0.10]

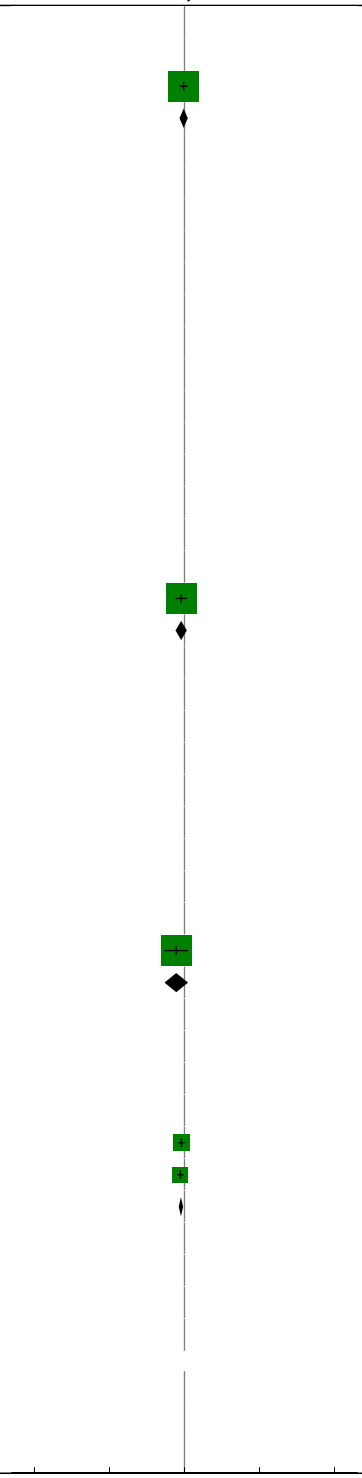
Analysis 15.1. Comparison 15 Vitamin D analogues versus other treatment, Outcome 1 IAGI.

Study or subgroup	Vitamin D analogue N	Vitamin D analogue Mean(SD)	Other treatment N	Other treatment Mean(SD)	Std. Mean Difference Random, 95% CI	Weight	Std. Mean Difference Random, 95% CI
15.1.1 Calcipotriol vs. coal tar							
Alora-Palli 2010	28	2.2 (1)	27	1.6 (1)		34.2%	0.59[0.04,1.13]
De Simone 1993	15	-2.7 (0.9)	15	-1.8 (0.9)		31.99%	-1.01[-1.77,-0.24]
Tham 1994	27	-2.3 (0.8)	27	-1.2 (1)		33.82%	-1.21[-1.79,-0.62]
Subtotal ***	**70**		**69**			**100%**	**-0.53[-1.74,0.68]**
Heterogeneity: Tau^2=1.03; Chi^2=22.54, df=2(P<0.0001); I^2=91.13%							
Test for overall effect: Z=0.86(P=0.39)							
15.1.2 Calcipotriol vs. coal tar polytherapy							
Pinheiro 1997	65	-2.7 (0.7)	57	-2.3 (0.9)		59.39%	-0.47[-0.83,-0.11]
Van de Kerkhof 2002a	41	-3.4 (1.2)	46	-2.5 (1.2)		40.61%	-0.75[-1.19,-0.32]
Subtotal ***	**106**		**103**			**100%**	**-0.59[-0.87,-0.31]**
Heterogeneity: Tau^2=0; Chi^2=0.94, df=1(P=0.33); I^2=0%							
Test for overall effect: Z=4.15(P<0.0001)							
15.1.3 Calcipotriol vs. nicotinamide 1.4%, twice daily							
Subtotal ***	**0**		**0**				**Not estimable**
Heterogeneity: Not applicable							
Test for overall effect: Not applicable							
15.1.4 Calcipotriol vs. calcipotriol + nicotinamide 1.4%, twice daily							
Subtotal ***	**0**		**0**				**Not estimable**
Heterogeneity: Not applicable							
Test for overall effect: Not applicable							

Favours vitamin D analogue

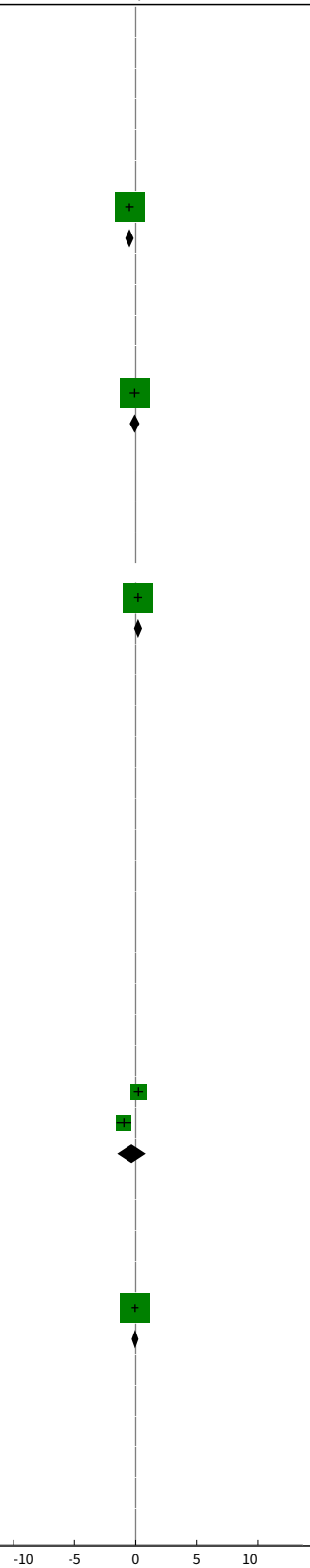
Favours other treatment

Study or subgroup	Vitamin D analogue N	Vitamin D analogue Mean(SD)	Other treatment N	Other treatment Mean(SD)	Std. Mean Difference Random, 95% CI	Weight	Std. Mean Difference Random, 95% CI
15.1.5 Calcipotriol vs. corticosteroid + salicylic acid							
Scarpa 1994	100	-2.7 (1.3)	100	-2.6 (1.2)		100%	-0.06[-0.33,0.22]
Subtotal ***	**100**		**100**			**100%**	**-0.06[-0.33,0.22]**
Heterogeneity: Not applicable							
Test for overall effect: Z=0.4(P=0.69)							
15.1.6 Calcipotriol vs. propylthiouracil cream							
Subtotal ***	**0**		**0**				**Not estimable**
Heterogeneity: Not applicable							
Test for overall effect: Not applicable							
15.1.7 Calcipotriol vs. tazarotene							
Subtotal ***	**0**		**0**				**Not estimable**
Heterogeneity: Not applicable							
Test for overall effect: Not applicable							
15.1.8 Calcipotriol vs. tacrolimus ointment							
Ortonne 2006	40	-3.2 (1)	84	-3 (1.1)		100%	-0.22[-0.6,0.16]
Subtotal ***	**40**		**84**			**100%**	**-0.22[-0.6,0.16]**
Heterogeneity: Not applicable							
Test for overall effect: Z=1.15(P=0.25)							
15.1.9 Calcipotriol vs. tazarotene gel plus mometasone furoate cream							
Subtotal ***	**0**		**0**				**Not estimable**
Heterogeneity: Not applicable							
Test for overall effect: Not applicable							
15.1.10 Calcipotriol vs. vitamin B12 cream							
Stuecker 2001	13	-2.1 (0.5)	13	-1.8 (0.6)		100%	-0.55[-1.33,0.24]
Subtotal ***	**13**		**13**			**100%**	**-0.55[-1.33,0.24]**
Heterogeneity: Not applicable							
Test for overall effect: Z=1.37(P=0.17)							
15.1.11 Head-to-head vitamin D alone or in combination: twice daily vs OD							
Guenther 2002 (H)	234	-3.8 (1)	150	-3.6 (1)		51.63%	-0.2[-0.41,0]
Kragballe 1998b	172	-3 (1.2)	172	-2.6 (1.3)		48.37%	-0.27[-0.48,-0.06]
Subtotal ***	**406**		**322**			**100%**	**-0.24[-0.38,-0.09]**
Heterogeneity: Tau^2=0; Chi^2=0.2, df=1(P=0.65); I^2=0%							
Test for overall effect: Z=3.14(P=0)							
15.1.12 Head-to-head vitamin D alone or in combination: no occlusion vs. occlusion							
Subtotal ***	**0**		**0**				**Not estimable**
Heterogeneity: Not applicable							
Test for overall effect: Not applicable							

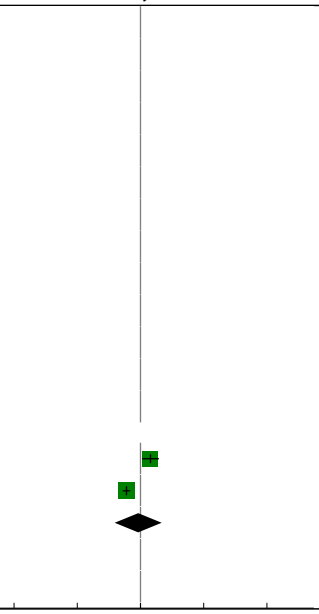


Analysis 15.2. Comparison 15 Vitamin D analogues versus other treatment, Outcome 2 TSS.

Study or subgroup	Vitamin D analogue N	Vitamin D analogue Mean(SD)	Other treatment N	Other treatment Mean(SD)	Std. Mean Difference Random, 95% CI	Weight	Std. Mean Difference Random, 95% CI
15.2.1 Calcipotriol vs. coal tar							
Subtotal ***	**0**		**0**				**Not estimable**
Heterogeneity: Not applicable							
Test for overall effect: Not applicable							
15.2.2 Calcipotriol vs. coal tar polytherapy							
Pinheiro 1997	69	2.7 (2.1)	63	3.8 (2.1)		100%	-0.51[-0.86,-0.16]
Subtotal ***	**69**		**63**			**100%**	**-0.51[-0.86,-0.16]**
Heterogeneity: Not applicable							
Test for overall effect: Z=2.88(P=0)							
15.2.3 Calcipotriol vs. nicotinamide 1.4%, twice daily							
Levine 2010 (H)	48	3.5 (2)	48	3.7 (1.9)		100%	-0.09[-0.49,0.31]
Subtotal ***	**48**		**48**			**100%**	**-0.09[-0.49,0.31]**
Heterogeneity: Not applicable							
Test for overall effect: Z=0.43(P=0.67)							
15.2.4 Calcipotriol vs. calcipotriol+nicotinamide (0.05%, 0.1%, 0.7%, or 1.4%), twice daily							
Levine 2010 (H)	48	3.5 (2)	144	3.2 (1.9)		100%	0.19[-0.14,0.52]
Subtotal ***	**48**		**144**			**100%**	**0.19[-0.14,0.52]**
Heterogeneity: Not applicable							
Test for overall effect: Z=1.14(P=0.26)							
15.2.5 Calcipotriol vs. corticosteroid + salicylic acid							
Subtotal ***	**0**		**0**				**Not estimable**
Heterogeneity: Not applicable							
Test for overall effect: Not applicable							
15.2.6 Calcipotriol vs. propylthiouracil cream							
Subtotal ***	**0**		**0**				**Not estimable**
Heterogeneity: Not applicable							
Test for overall effect: Not applicable							
15.2.7 Calcipotriol vs. tacrolimus ointment							
Ortonne 2006	40	3.3 (1)	84	3 (1.1)		52.09%	0.22[-0.16,0.6]
Zonneveld 1998 (H)	23	2.6 (2.1)	24	4.7 (2.1)		47.91%	-0.96[-1.57,-0.36]
Subtotal ***	**63**		**108**			**100%**	**-0.35[-1.51,0.81]**
Heterogeneity: Tau^2=0.64; Chi^2=10.58, df=1(P=0); I^2=90.54%							
Test for overall effect: Z=0.59(P=0.56)							
15.2.8 Calcipotriol vs. tazarotene							
Han 2001	101	3.9 (6.1)	98	4.2 (4.4)		100%	-0.05[-0.33,0.23]
Subtotal ***	**101**		**98**			**100%**	**-0.05[-0.33,0.23]**
Heterogeneity: Tau^2=0; Chi^2=0, df=0(P<0.0001); I^2=100%							
Test for overall effect: Z=0.36(P=0.72)							
15.2.9 Calcipotriol vs. tazarotene gel plus mometasone furoate cream							
Subtotal ***	**0**		**0**				**Not estimable**
Heterogeneity: Not applicable							

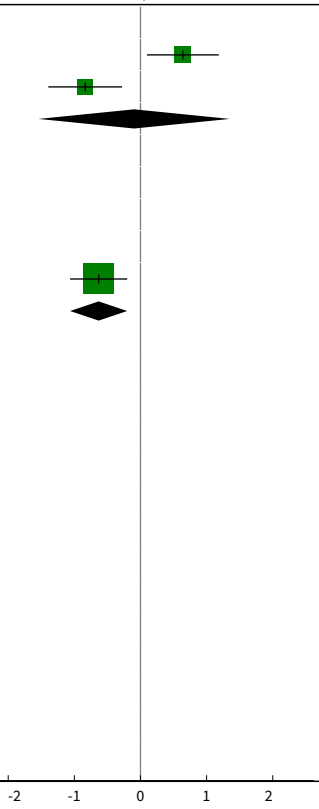


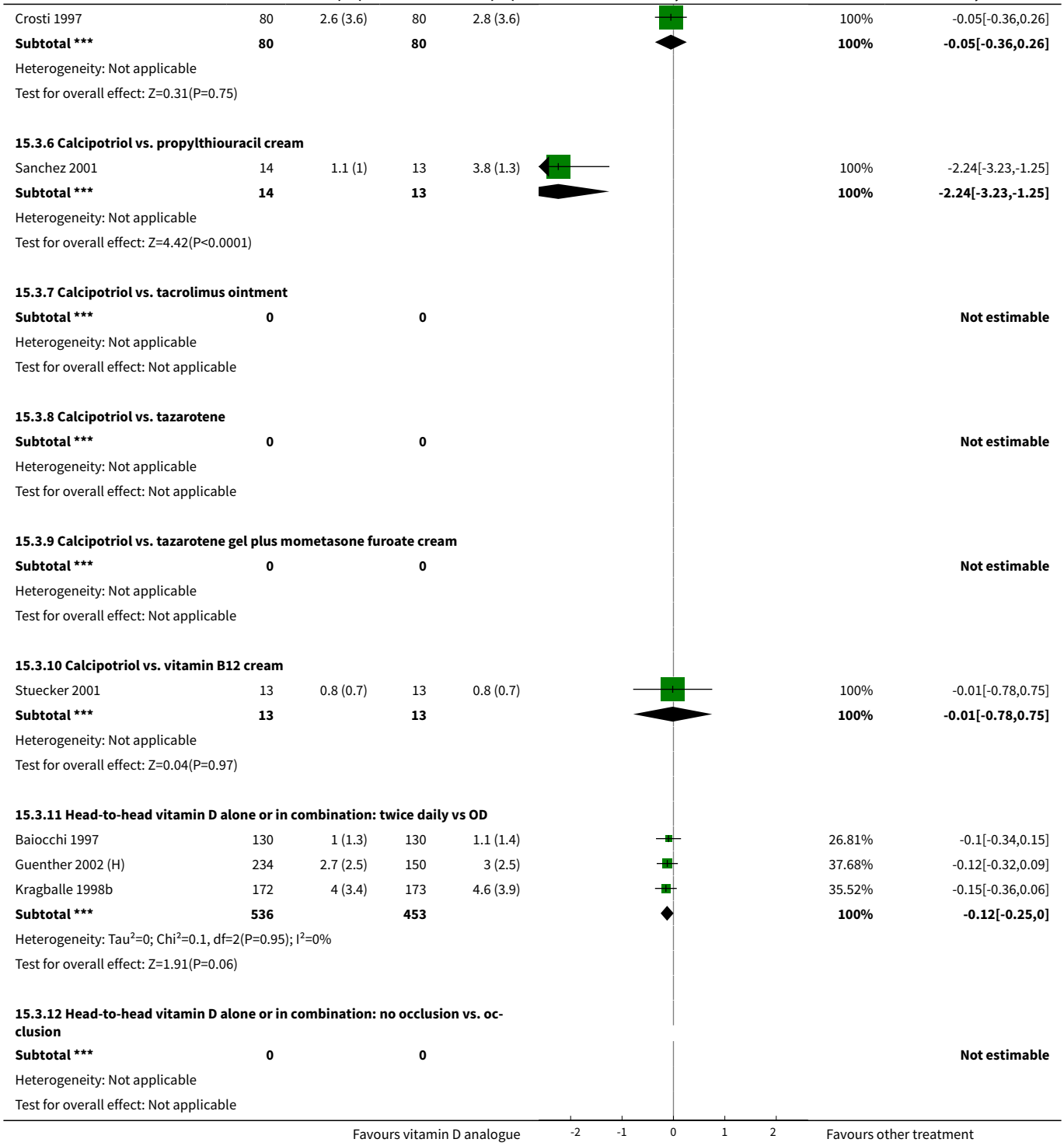
Study or subgroup	Vitamin D analogue N	Vitamin D analogue Mean(SD)	Other treatment N	Other treatment Mean(SD)	Std. Mean Difference Random, 95% CI	Weight	Std. Mean Difference Random, 95% CI
Test for overall effect: Not applicable							
15.2.10 Calcipotriol vs. vitamin B12 cream							
Subtotal ***	**0**		**0**				**Not estimable**
Heterogeneity: Not applicable							
Test for overall effect: Not applicable							
15.2.11 Head-to-head vitamin D alone or in combination: twice daily vs OD							
Subtotal ***	**0**		**0**				**Not estimable**
Heterogeneity: Not applicable							
Test for overall effect: Not applicable							
15.2.12 Head-to-head vitamin D alone or in combination: no occlusion vs. occlusion							
Bourke 1993b	19	-3.1 (2.6)	19	-5.2 (2.6)		48.72%	0.79[0.13,1.45]
Hindsén 2006 (H)	114	5.2 (3.3)	95	9.7 (4.8)		51.28%	-1.11[-1.4,-0.81]
Subtotal ***	**133**		**114**			**100%**	**-0.18[-2.04,1.68]**
Heterogeneity: Tau^2=1.73; Chi^2=26.34, df=1(P<0.0001); I^2=96.2%							
Test for overall effect: Z=0.19(P=0.85)							



Analysis 15.3. Comparison 15 Vitamin D analogues versus other treatment, Outcome 3 PASI.

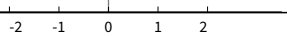
Study or subgroup	Vitamin D analogue N	Vitamin D analogue Mean(SD)	Other treatment N	Other treatment Mean(SD)	Std. Mean Difference Random, 95% CI	Weight	Std. Mean Difference Random, 95% CI
15.3.1 Calcipotriol vs. coal tar							
Alora-Palli 2010	28	-0.4 (0.3)	27	-0.6 (0.4)		50.1%	0.64[0.1,1.18]
Tham 1994	27	2 (2.1)	27	4.5 (3.6)		49.9%	-0.84[-1.39,-0.28]
Subtotal ***	**55**		**54**			**100%**	**-0.1[-1.54,1.35]**
Heterogeneity: Tau^2=1.01; Chi^2=13.82, df=1(P=0); I^2=92.77%							
Test for overall effect: Z=0.13(P=0.9)							
15.3.2 Calcipotriol vs. coal tar polytherapy							
Van de Kerkhof 2002a	41	-0.6 (0.3)	46	-0.4 (0.4)		100%	-0.63[-1.06,-0.2]
Subtotal ***	**41**		**46**			**100%**	**-0.63[-1.06,-0.2]**
Heterogeneity: Not applicable							
Test for overall effect: Z=2.87(P=0)							
15.3.3 Calcipotriol vs. nicotinamide 1.4%, twice daily							
Subtotal ***	**0**		**0**				**Not estimable**
Heterogeneity: Not applicable							
Test for overall effect: Not applicable							
15.3.4 Calcipotriol vs. calcipotriol + nicotinamide 1.4%, twice daily							
Subtotal ***	**0**		**0**				**Not estimable**
Heterogeneity: Not applicable							
Test for overall effect: Not applicable							
15.3.5 Calcipotriol vs. corticosteroid + salicylic acid							





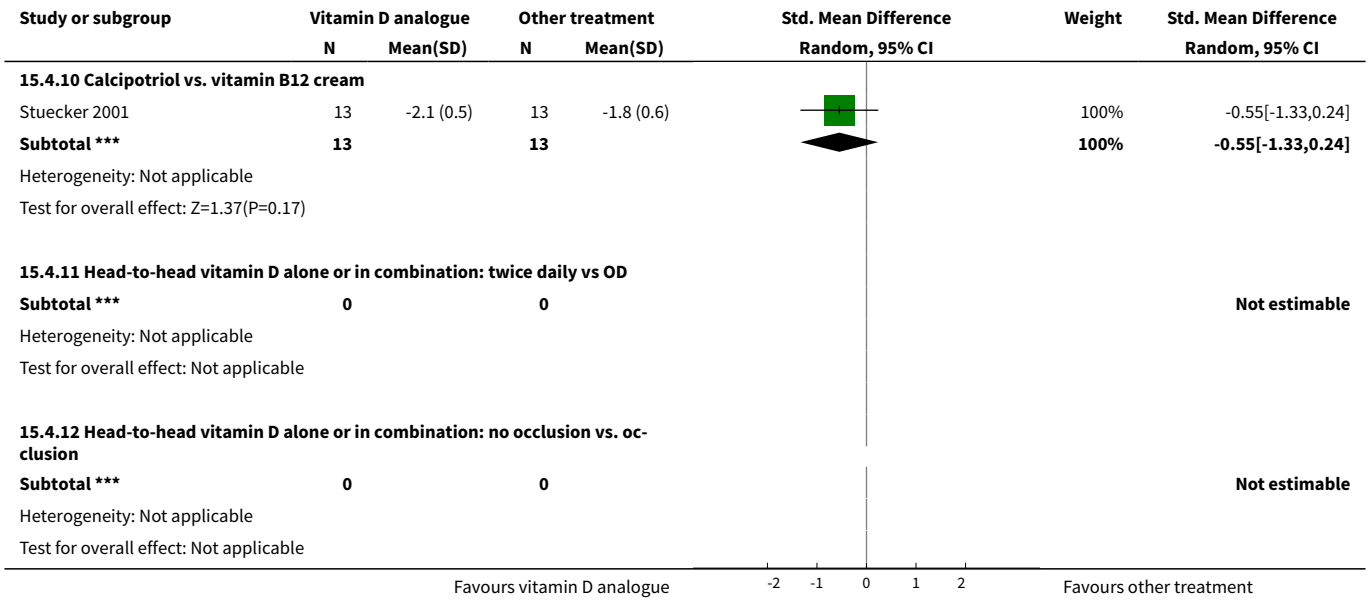
Analysis 15.4. Comparison 15 Vitamin D analogues versus other treatment, Outcome 4 PAGI.

Study or subgroup	Vitamin D analogue N	Vitamin D analogue Mean(SD)	Other treatment N	Other treatment Mean(SD)	Std. Mean Difference Random, 95% CI	Weight	Std. Mean Difference Random, 95% CI
15.4.1 Calcipotriol vs. coal tar							
Tham 1994	27	-2.4 (0.9)	27	-1.1 (0.9)		100%	-1.51[-2.12,-0.9]
Subtotal ***	**27**		**27**			**100%**	**-1.51[-2.12,-0.9]**
Heterogeneity: Not applicable							
Test for overall effect: Z=4.84(P<0.0001)							
15.4.2 Calcipotriol vs. coal tar polytherapy							
Van de Kerkhof 2002a	41	-3.3 (1.2)	46	-2.6 (1.4)		100%	-0.56[-0.99,-0.13]
Subtotal ***	**41**		**46**			**100%**	**-0.56[-0.99,-0.13]**
Heterogeneity: Not applicable							
Test for overall effect: Z=2.54(P=0.01)							
15.4.3 Calcipotriol vs. nicotinamide 1.4%, twice daily							
Subtotal ***	**0**		**0**				**Not estimable**
Heterogeneity: Not applicable							
Test for overall effect: Not applicable							
15.4.4 Calcipotriol vs. calcipotriol + nicotinamide 1.4%, twice daily							
Subtotal ***	**0**		**0**				**Not estimable**
Heterogeneity: Not applicable							
Test for overall effect: Not applicable							
15.4.5 Calcipotriol vs. corticosteroid + salicylic acid							
Scarpa 1994	89	-3.3 (0.7)	97	-2.9 (0.9)		100%	-0.49[-0.79,-0.2]
Subtotal ***	**89**		**97**			**100%**	**-0.49[-0.79,-0.2]**
Heterogeneity: Tau^2=0; Chi^2=0, df=0(P<0.0001); I^2=100%							
Test for overall effect: Z=3.32(P=0)							
15.4.6 Calcipotriol vs. propylthiouracil cream							
Subtotal ***	**0**		**0**				**Not estimable**
Heterogeneity: Not applicable							
Test for overall effect: Not applicable							
15.4.7 Calcipotriol vs. tacrolimus ointment							
Ortonne 2006	40	-3.2 (1.1)	84	-3.1 (1.1)		100%	-0.13[-0.51,0.24]
Subtotal ***	**40**		**84**			**100%**	**-0.13[-0.51,0.24]**
Heterogeneity: Not applicable							
Test for overall effect: Z=0.7(P=0.48)							
15.4.8 Calcipotriol vs. tazarotene							
Tzung 2005	19	-3.2 (0.7)	19	-2.9 (0.8)		100%	-0.35[-0.99,0.29]
Subtotal ***	**19**		**19**			**100%**	**-0.35[-0.99,0.29]**
Heterogeneity: Not applicable							
Test for overall effect: Z=1.07(P=0.28)							
15.4.9 Calcipotriol vs. tazarotene gel plus mometasone furoate cream							
Subtotal ***	**0**		**0**				**Not estimable**
Heterogeneity: Not applicable							
Test for overall effect: Not applicable							

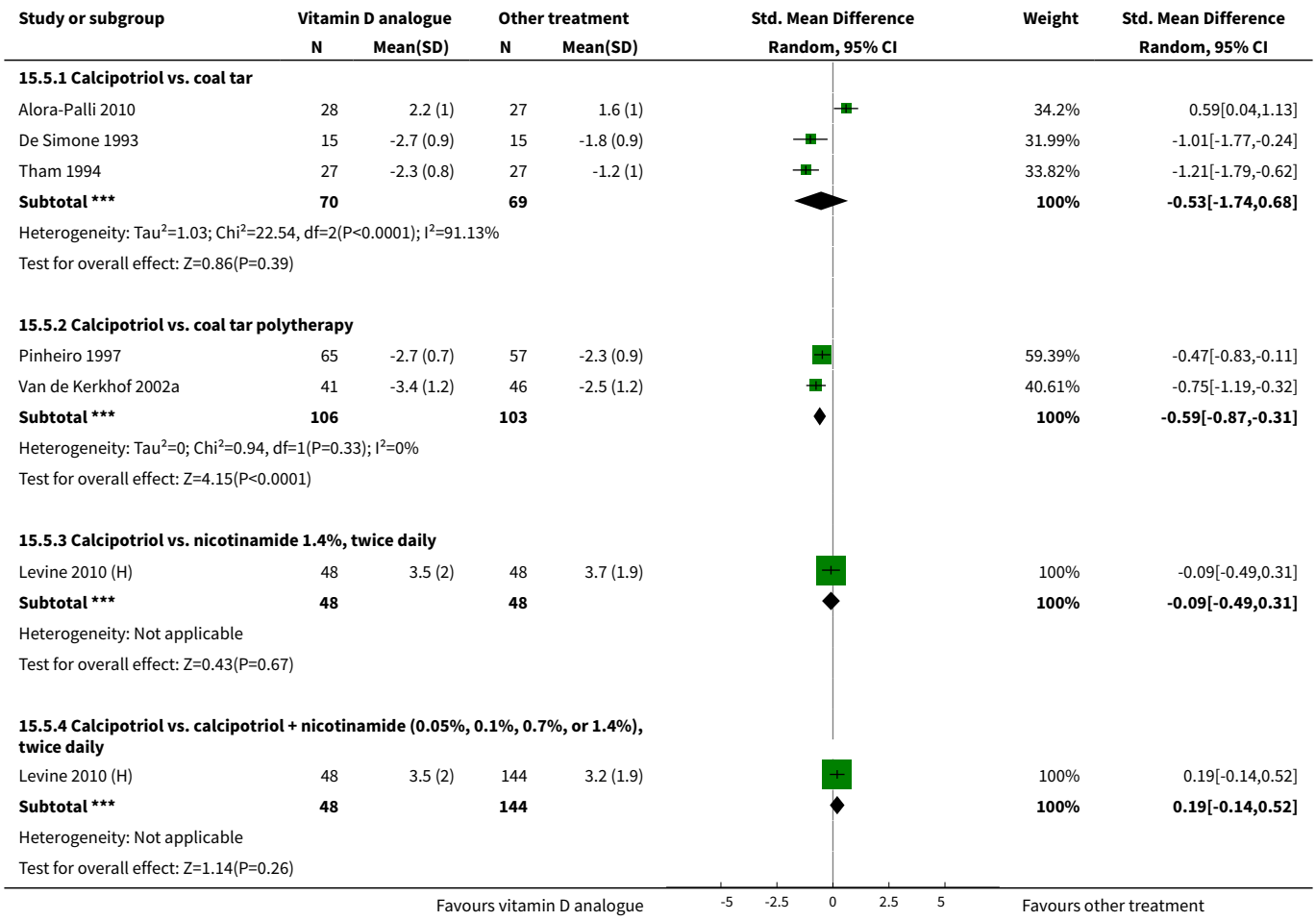


Favours vitamin D analogue

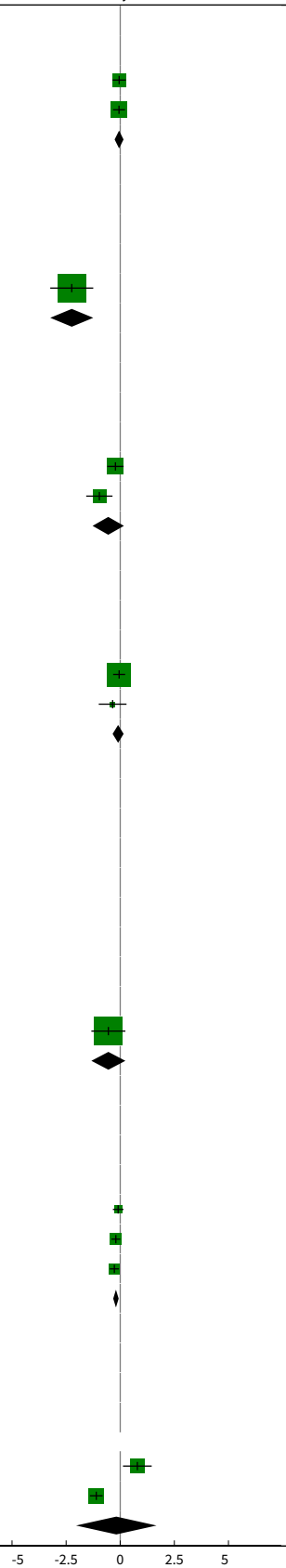
Favours other treatment

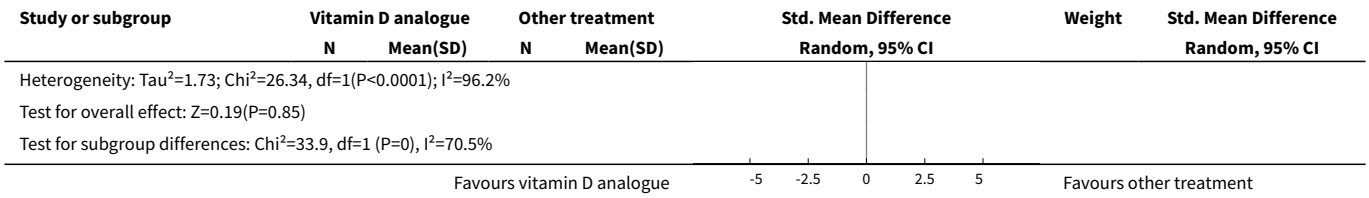


Analysis 15.5. Comparison 15 Vitamin D analogues versus other treatment, Outcome 5 Combined end point (IAGI/TSS/PASI/PAGI).

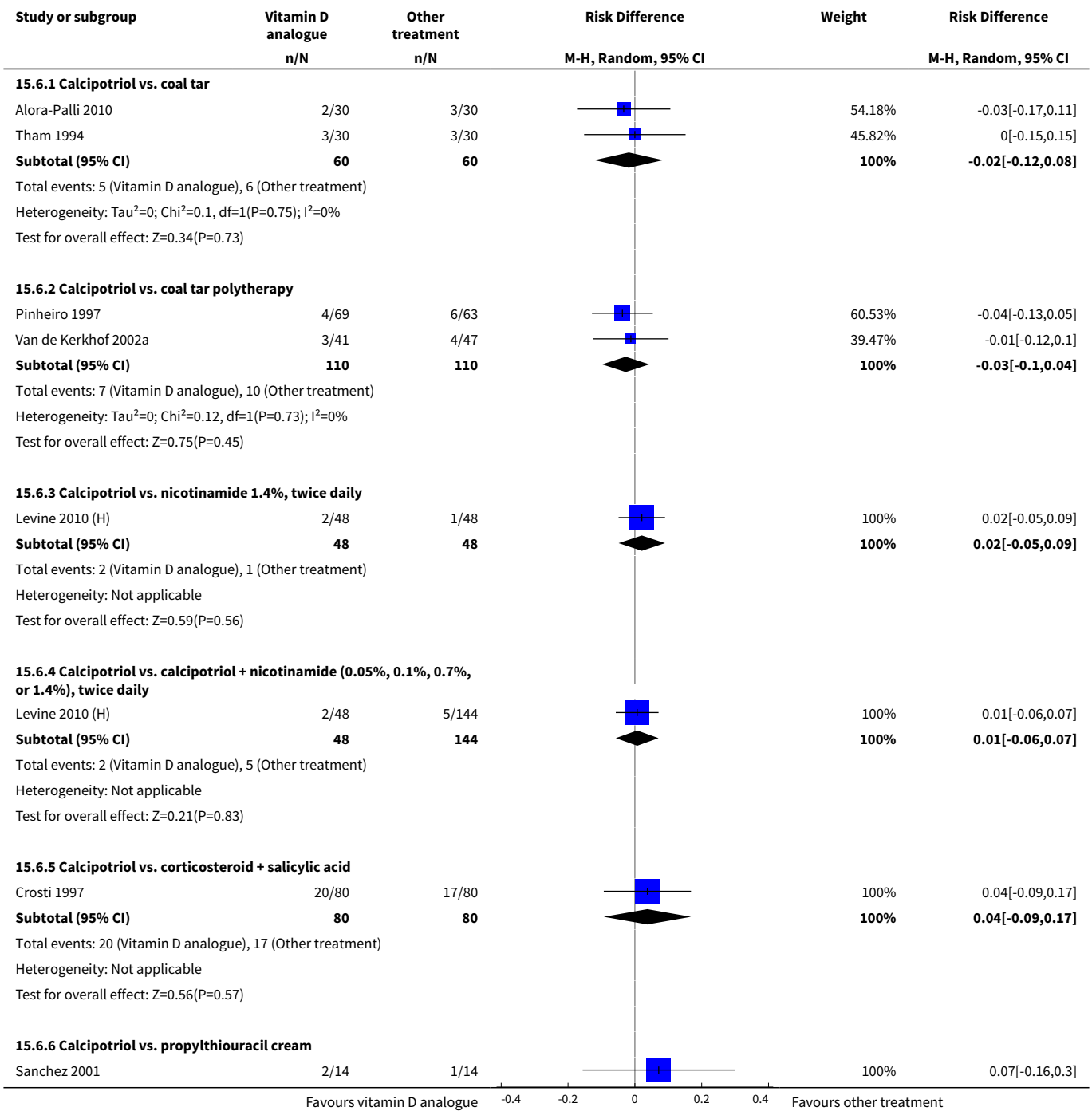


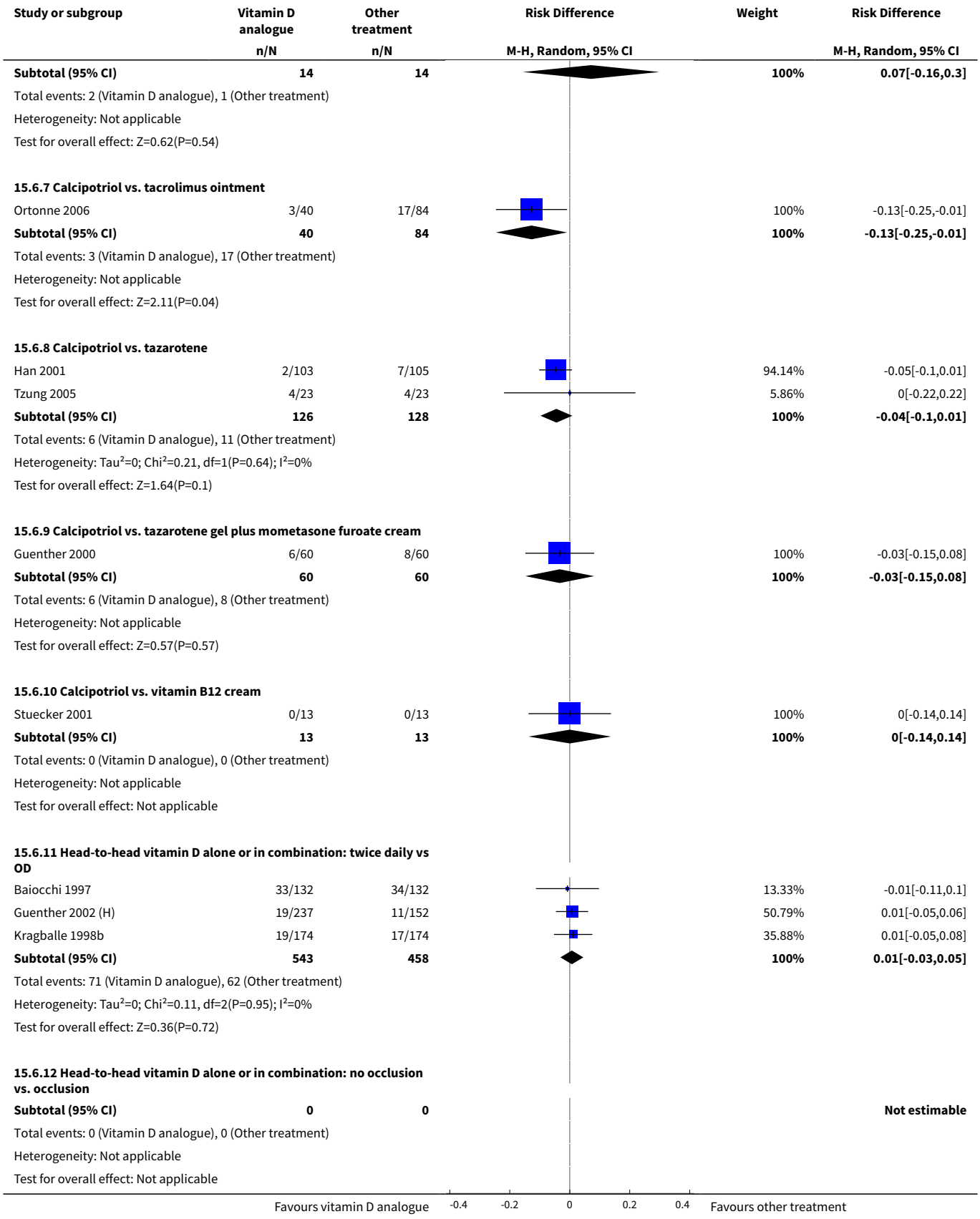
Study or subgroup	Vitamin D analogue N	Vitamin D analogue Mean(SD)	Other treatment N	Other treatment Mean(SD)	Std. Mean Difference Random, 95% CI	Weight	Std. Mean Difference Random, 95% CI
15.5.5 Calcipotriol vs. corticosteroid + salicylic acid							
Crosti 1997	80	2.6 (3.6)	80	2.8 (3.6)		44.45%	-0.05[-0.36,0.26]
Scarpa 1994	100	-2.7 (1.3)	100	-2.6 (1.2)		55.55%	-0.06[-0.33,0.22]
Subtotal ***	**180**		**180**			**100%**	**-0.05[-0.26,0.15]**
Heterogeneity: Tau^2=0; Chi^2=0, df=1(P=0.97); I^2=0%							
Test for overall effect: Z=0.51(P=0.61)							
15.5.6 Calcipotriol vs. propylthiouracil cream							
Sanchez 2001	14	1.1 (1)	13	3.8 (1.3)		100%	-2.24[-3.23,-1.25]
Subtotal ***	**14**		**13**			**100%**	**-2.24[-3.23,-1.25]**
Heterogeneity: Not applicable							
Test for overall effect: Z=4.42(P<0.0001)							
15.5.7 Calcipotriol vs. tacrolimus ointment							
Ortonne 2006	40	-3.2 (1)	84	-3 (1.1)		55.32%	-0.22[-0.6,0.16]
Zonneveld 1998 (H)	23	2.6 (2.1)	24	4.7 (2.1)		44.68%	-0.96[-1.57,-0.36]
Subtotal ***	**63**		**108**			**100%**	**-0.55[-1.28,0.17]**
Heterogeneity: Tau^2=0.21; Chi^2=4.15, df=1(P=0.04); I^2=75.92%							
Test for overall effect: Z=1.5(P=0.13)							
15.5.8 Calcipotriol vs. tazarotene							
Han 2001	101	3.9 (6.1)	98	4.2 (4.4)		84.19%	-0.05[-0.33,0.23]
Tzung 2005	19	-3.2 (0.7)	19	-2.9 (0.8)		15.81%	-0.35[-0.99,0.29]
Subtotal ***	**120**		**117**			**100%**	**-0.1[-0.35,0.16]**
Heterogeneity: Tau^2=0; Chi^2=0.71, df=1(P=0.4); I^2=0%							
Test for overall effect: Z=0.75(P=0.45)							
15.5.9 Calcipotriol vs. tazarotene gel plus mometasone furoate cream							
Subtotal ***	**0**		**0**				**Not estimable**
Heterogeneity: Not applicable							
Test for overall effect: Not applicable							
15.5.10 Calcipotriol vs. vitamin B12 cream							
Stuecker 2001	13	-2.1 (0.5)	13	-1.8 (0.6)		100%	-0.55[-1.33,0.24]
Subtotal ***	**13**		**13**			**100%**	**-0.55[-1.33,0.24]**
Heterogeneity: Not applicable							
Test for overall effect: Z=1.37(P=0.17)							
15.5.11 Head-to-head vitamin D alone or in combination: twice daily vs OD							
Baiocchi 1997	130	1 (1.3)	130	1.1 (1.4)		26.93%	-0.1[-0.34,0.15]
Guenther 2002 (H)	234	-3.8 (1)	150	-3.6 (1)		37.73%	-0.2[-0.41,0]
Kragballe 1998b	172	-3 (1.2)	172	-2.6 (1.3)		35.34%	-0.27[-0.48,-0.06]
Subtotal ***	**536**		**452**			**100%**	**-0.2[-0.32,-0.07]**
Heterogeneity: Tau^2=0; Chi^2=1.14, df=2(P=0.57); I^2=0%							
Test for overall effect: Z=3.08(P=0)							
15.5.12 Head-to-head vitamin D alone or in combination: no occlusion vs. occlusion							
Bourke 1993b	19	-3.1 (2.6)	19	-5.2 (2.6)		48.72%	0.79[0.13,1.45]
Hindsén 2006 (H)	114	5.2 (3.3)	95	9.7 (4.8)		51.28%	-1.11[-1.4,-0.81]
Subtotal ***	**133**		**114**			**100%**	**-0.18[-2.04,1.68]**





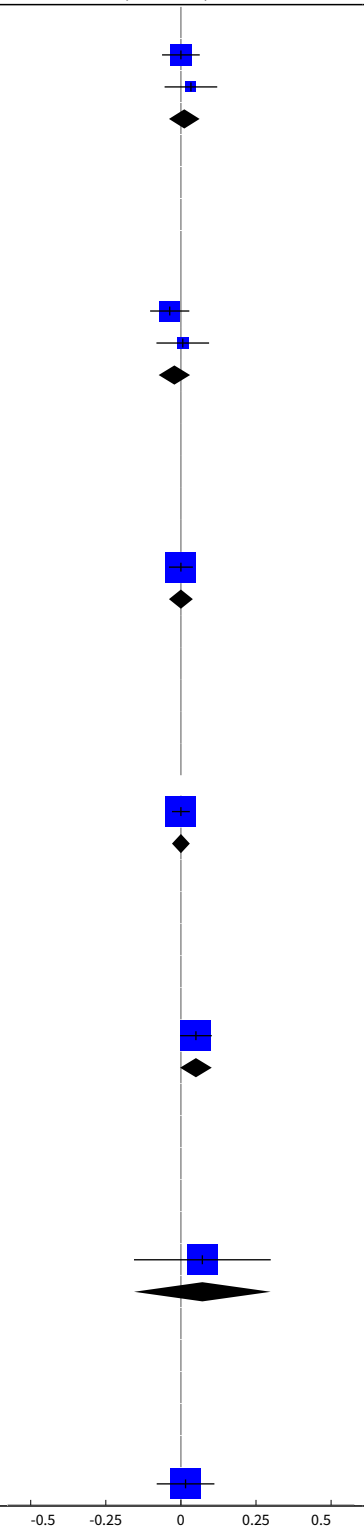
Analysis 15.6. Comparison 15 Vitamin D analogues versus other treatment, Outcome 6 Total withdrawals.

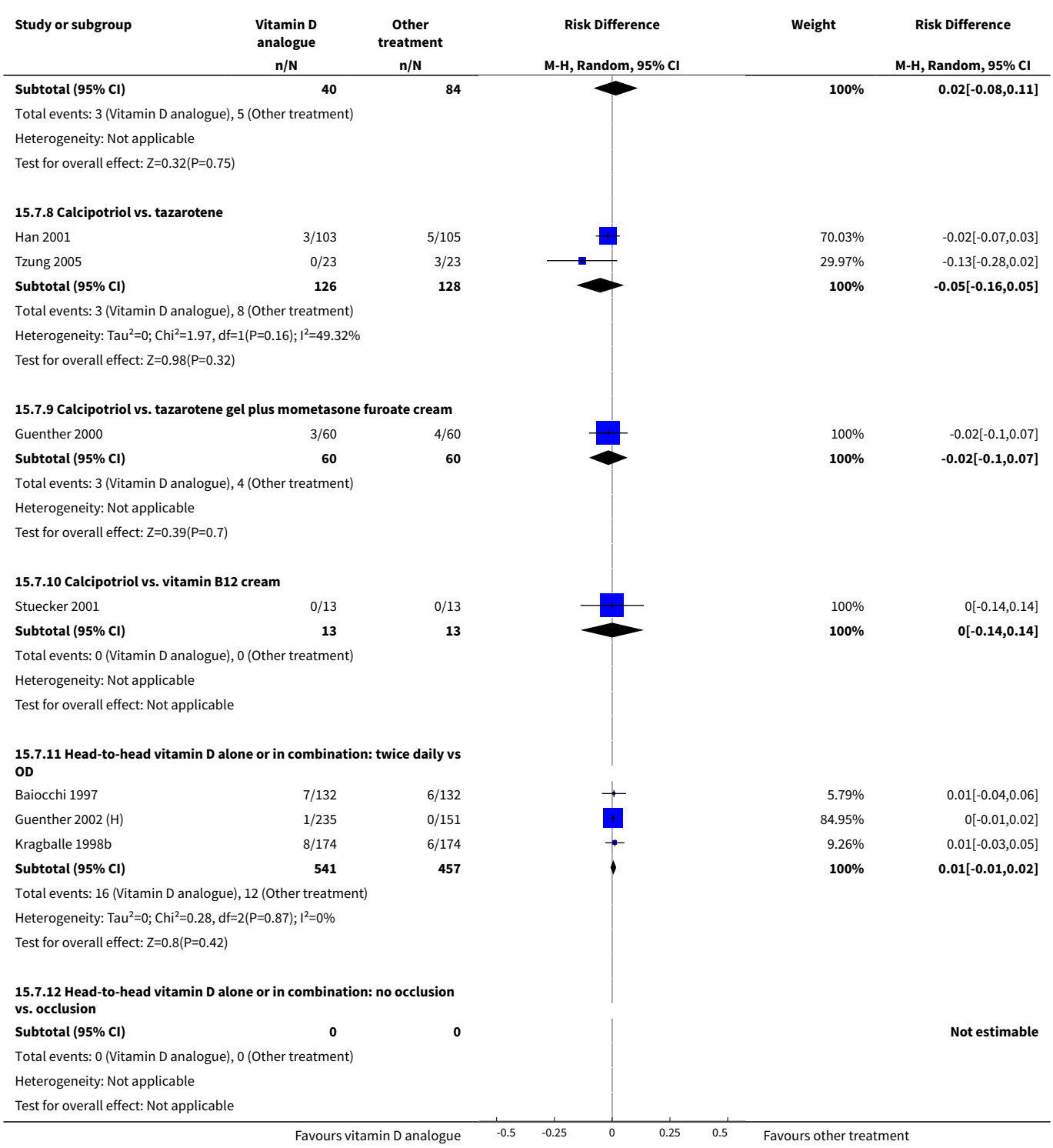




Analysis 15.7. Comparison 15 Vitamin D analogues versus other treatment, Outcome 7 Withdrawals due to adverse events.

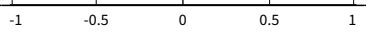
Study or subgroup	Vitamin D analogue n/N	Other treatment n/N	Risk Difference M-H, Random, 95% CI	Weight	Risk Difference M-H, Random, 95% CI
15.7.1 Calcipotriol vs. coal tar					
Alora-Palli 2010	0/30	0/30		66.11%	0[-0.06,0.06]
Tham 1994	1/30	0/30		33.89%	0.03[-0.05,0.12]
Subtotal (95% CI)	**60**	**60**		**100%**	**0.01[-0.04,0.06]**
Total events: 1 (Vitamin D analogue), 0 (Other treatment)					
Heterogeneity: Tau^2=0; Chi^2=0.41, df=1(P=0.52); I^2=0%					
Test for overall effect: Z=0.43(P=0.66)					
15.7.2 Calcipotriol vs. coal tar polytherapy					
Pinheiro 1997	1/65	3/57		64.34%	-0.04[-0.1,0.03]
Van de Kerkhof 2002a	2/41	2/47		35.66%	0.01[-0.08,0.09]
Subtotal (95% CI)	**106**	**104**		**100%**	**-0.02[-0.07,0.03]**
Total events: 3 (Vitamin D analogue), 5 (Other treatment)					
Heterogeneity: Tau^2=0; Chi^2=0.62, df=1(P=0.43); I^2=0%					
Test for overall effect: Z=0.81(P=0.42)					
15.7.3 Calcipotriol vs. nicotinamide 1.4%, twice daily					
Levine 2010 (H)	0/48	0/48		100%	0[-0.04,0.04]
Subtotal (95% CI)	**48**	**48**		**100%**	**0[-0.04,0.04]**
Total events: 0 (Vitamin D analogue), 0 (Other treatment)					
Heterogeneity: Not applicable					
Test for overall effect: Not applicable					
15.7.4 Calcipotriol vs. calcipotriol + nicotinamide (0.05%, 0.1%, 0.7%, or 1.4%), twice daily					
Levine 2010 (H)	0/48	0/144		100%	0[-0.03,0.03]
Subtotal (95% CI)	**48**	**144**		**100%**	**0[-0.03,0.03]**
Total events: 0 (Vitamin D analogue), 0 (Other treatment)					
Heterogeneity: Not applicable					
Test for overall effect: Not applicable					
15.7.5 Calcipotriol vs. corticosteroid + salicylic acid					
Crosti 1997	4/80	0/80		100%	0.05[-0,0.1]
Subtotal (95% CI)	**80**	**80**		**100%**	**0.05[-0,0.1]**
Total events: 4 (Vitamin D analogue), 0 (Other treatment)					
Heterogeneity: Not applicable					
Test for overall effect: Z=1.86(P=0.06)					
15.7.6 Calcipotriol vs. propylthiouracil cream					
Sanchez 2001	2/14	1/14		100%	0.07[-0.16,0.3]
Subtotal (95% CI)	**14**	**14**		**100%**	**0.07[-0.16,0.3]**
Total events: 2 (Vitamin D analogue), 1 (Other treatment)					
Heterogeneity: Not applicable					
Test for overall effect: Z=0.62(P=0.54)					
15.7.7 Calcipotriol vs. tacrolimus ointment					
Ortonne 2006	3/40	5/84		100%	0.02[-0.08,0.11]



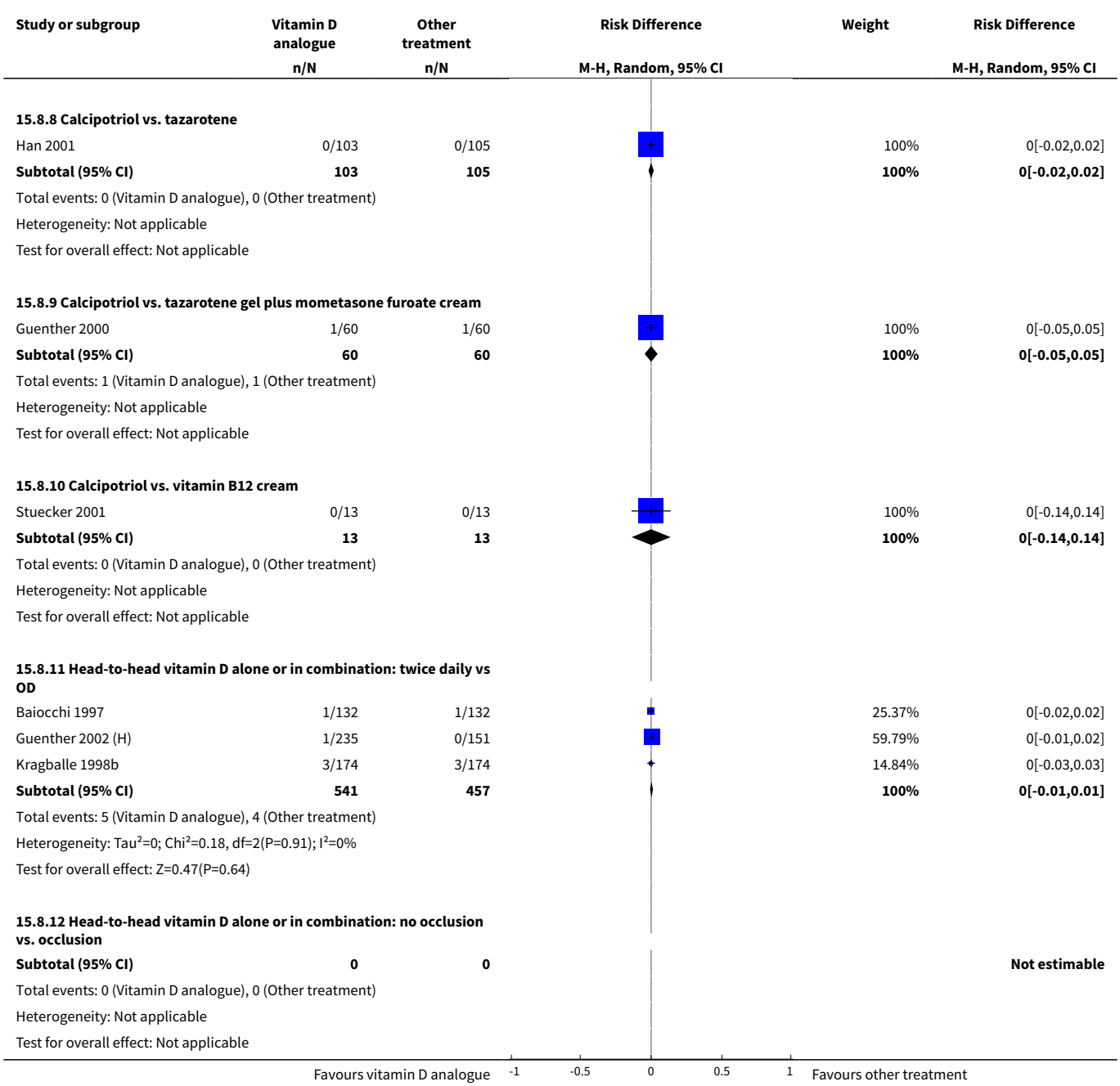


Analysis 15.8. Comparison 15 Vitamin D analogues versus other treatment, Outcome 8 Withdrawals due to treatment failure.

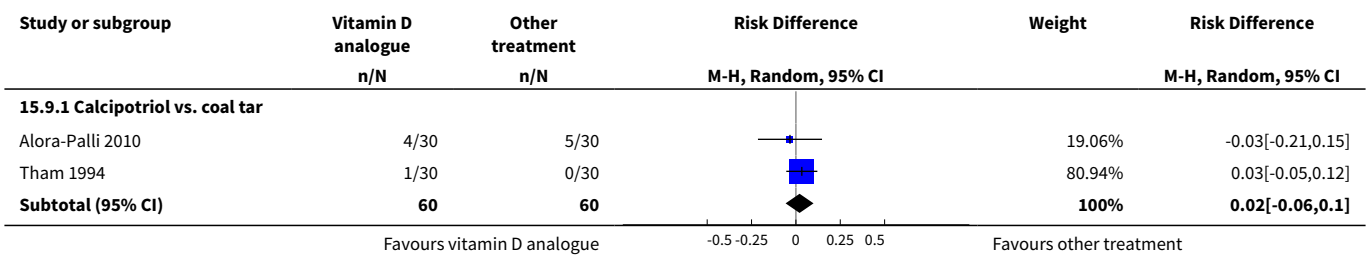
Study or subgroup	Vitamin D analogue n/N	Other treatment n/N	Risk Difference M-H, Random, 95% CI	Weight	Risk Difference M-H, Random, 95% CI
15.8.1 Calcipotriol vs. coal tar					
Tham 1994	0/30	0/30		100%	0[-0.06,0.06]
Subtotal (95% CI)	**30**	**30**		**100%**	**0[-0.06,0.06]**
Total events: 0 (Vitamin D analogue), 0 (Other treatment)					
Heterogeneity: Not applicable					
Test for overall effect: Not applicable					
15.8.2 Calcipotriol vs. coal tar polytherapy					
Van de Kerkhof 2002a	1/41	1/47		100%	0[-0.06,0.07]
Subtotal (95% CI)	**41**	**47**		**100%**	**0[-0.06,0.07]**
Total events: 1 (Vitamin D analogue), 1 (Other treatment)					
Heterogeneity: Not applicable					
Test for overall effect: Z=0.1(P=0.92)					
15.8.3 Calcipotriol vs. nicotinamide 1.4%, twice daily					
Levine 2010 (H)	0/48	0/48		100%	0[-0.04,0.04]
Subtotal (95% CI)	**48**	**48**		**100%**	**0[-0.04,0.04]**
Total events: 0 (Vitamin D analogue), 0 (Other treatment)					
Heterogeneity: Not applicable					
Test for overall effect: Not applicable					
15.8.4 Calcipotriol vs. calcipotriol + nicotinamide (0.05%, 0.1%, 0.7%, or 1.4%), twice daily					
Levine 2010 (H)	0/48	0/144		100%	0[-0.03,0.03]
Subtotal (95% CI)	**48**	**144**		**100%**	**0[-0.03,0.03]**
Total events: 0 (Vitamin D analogue), 0 (Other treatment)					
Heterogeneity: Not applicable					
Test for overall effect: Not applicable					
15.8.5 Calcipotriol vs. corticosteroid + salicylic acid					
Crosti 1997	1/80	3/80		100%	-0.02[-0.07,0.02]
Subtotal (95% CI)	**80**	**80**		**100%**	**-0.02[-0.07,0.02]**
Total events: 1 (Vitamin D analogue), 3 (Other treatment)					
Heterogeneity: Not applicable					
Test for overall effect: Z=1.02(P=0.31)					
15.8.6 Calcipotriol vs. propylthiouracil cream					
Sanchez 2001	0/14	1/14		100%	-0.07[-0.25,0.11]
Subtotal (95% CI)	**14**	**14**		**100%**	**-0.07[-0.25,0.11]**
Total events: 0 (Vitamin D analogue), 1 (Other treatment)					
Heterogeneity: Not applicable					
Test for overall effect: Z=0.79(P=0.43)					
15.8.7 Calcipotriol vs. tacrolimus ointment					
Ortonne 2006	0/40	2/84		100%	-0.02[-0.07,0.03]
Subtotal (95% CI)	**40**	**84**		**100%**	**-0.02[-0.07,0.03]**
Total events: 0 (Vitamin D analogue), 2 (Other treatment)					
Heterogeneity: Not applicable					
Test for overall effect: Z=0.95(P=0.34)					

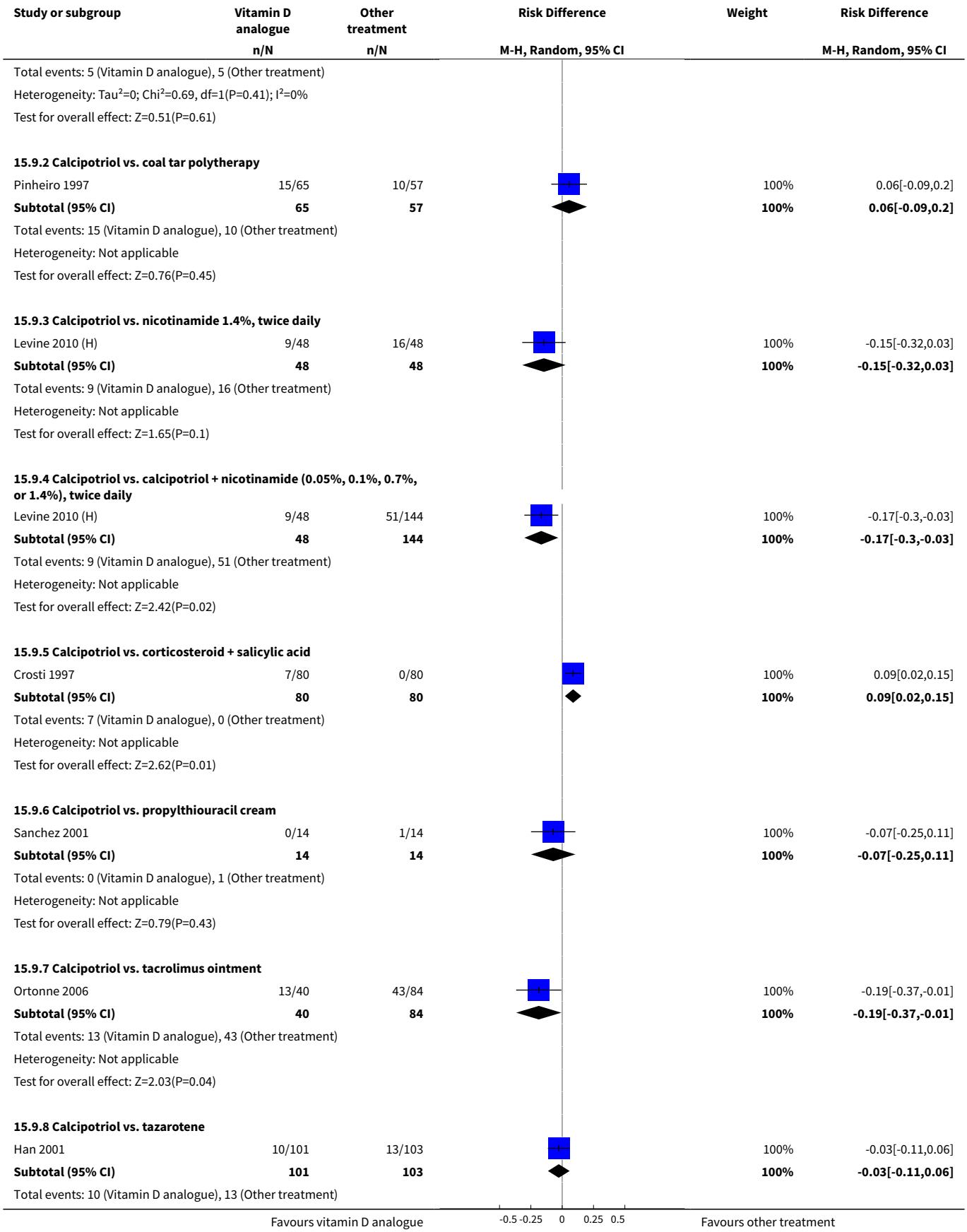


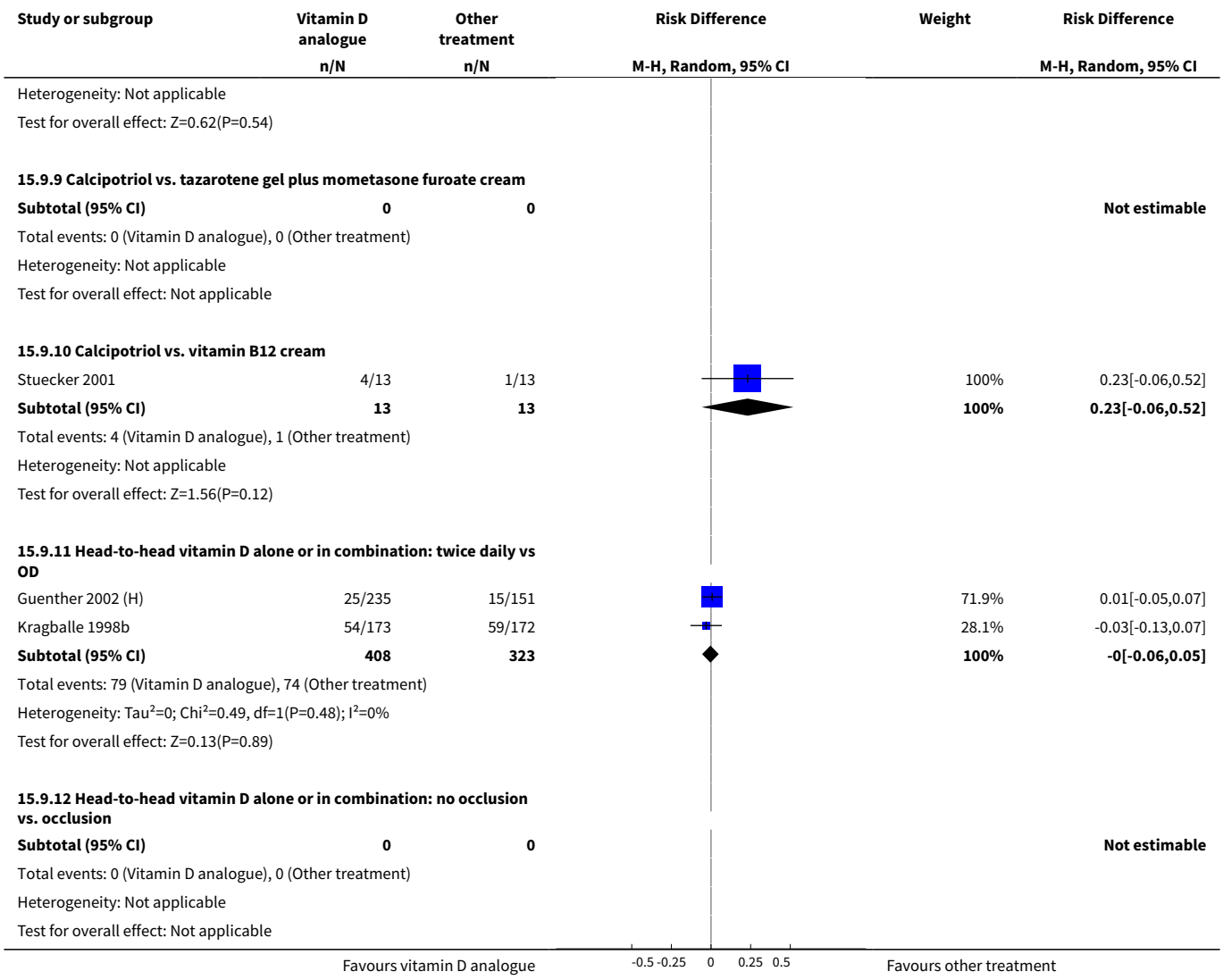
Favours vitamin D analogue Favours other treatment



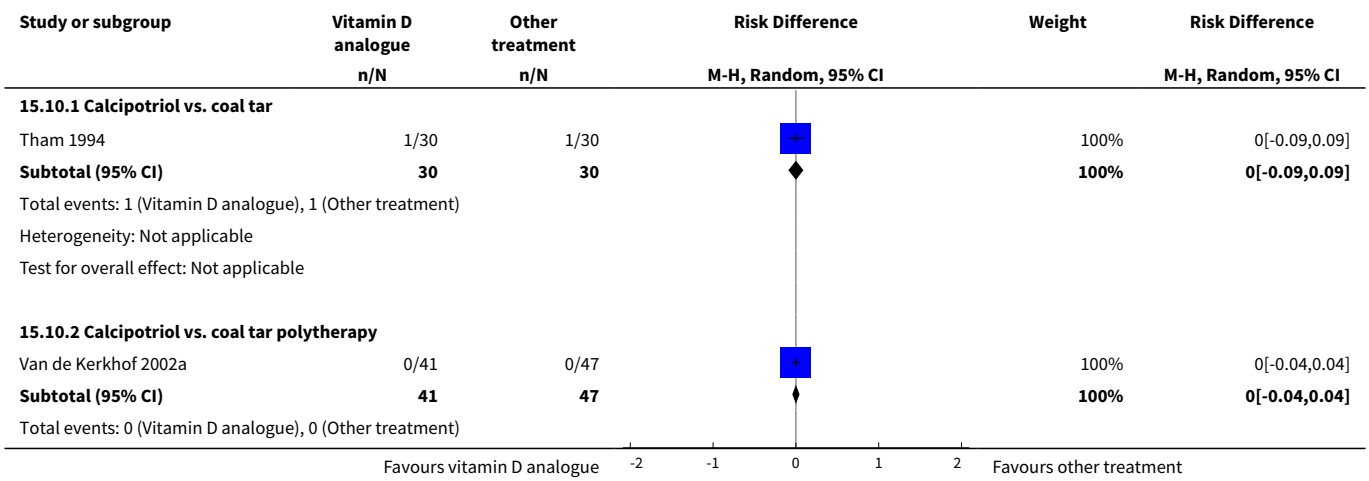
Analysis 15.9. Comparison 15 Vitamin D analogues versus other treatment, Outcome 9 Adverse events (local).



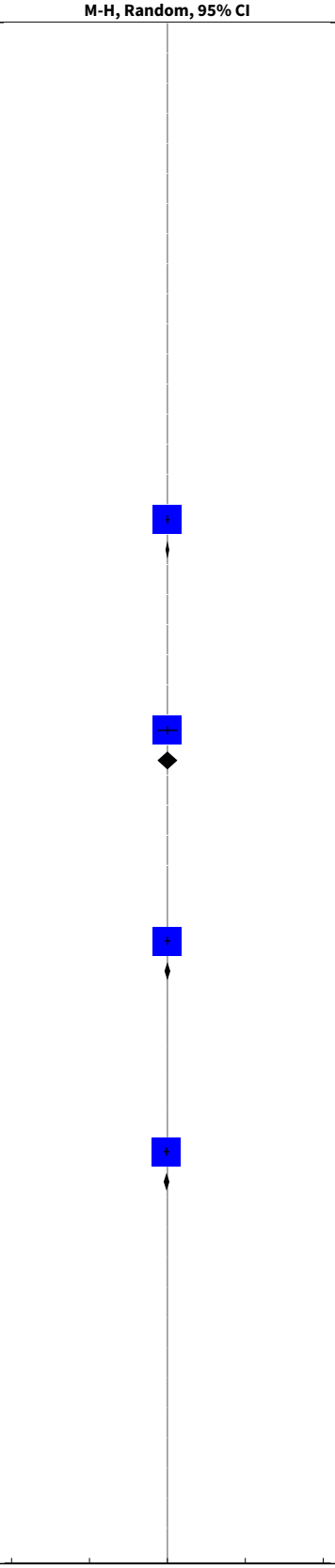


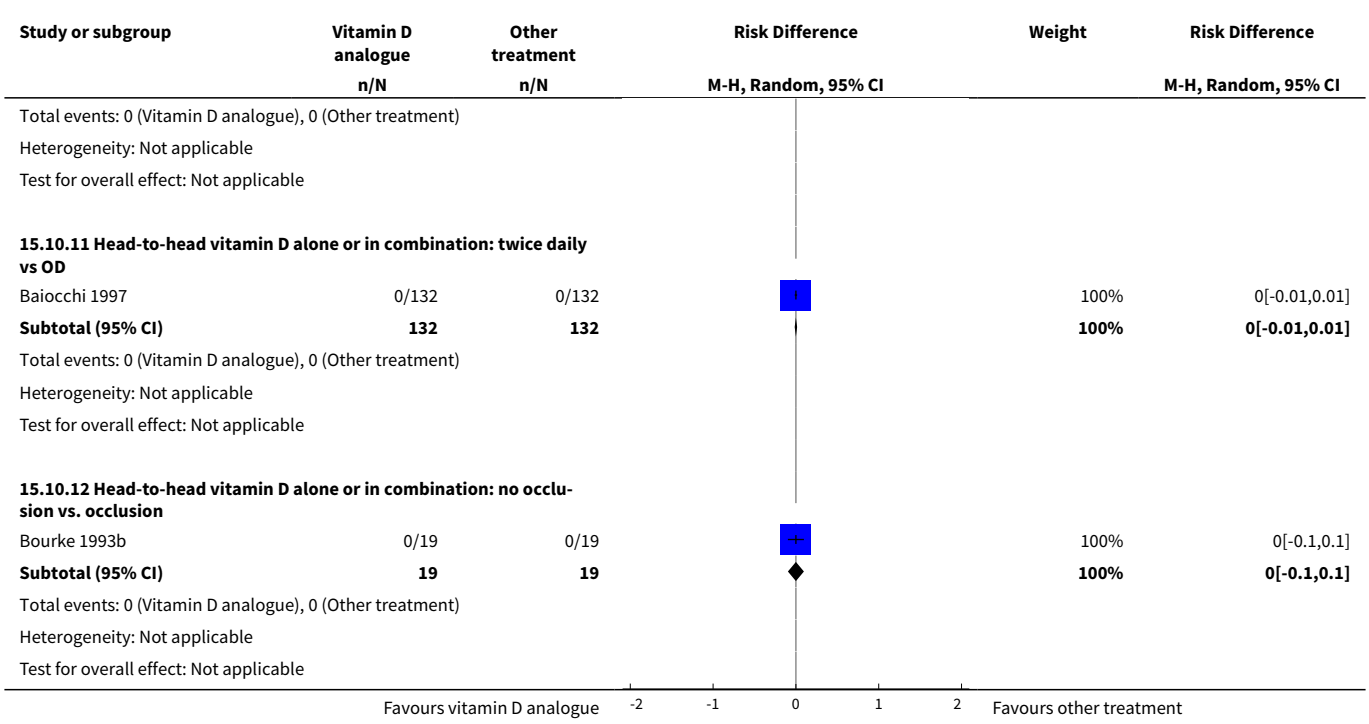


Analysis 15.10. Comparison 15 Vitamin D analogues versus other treatment, Outcome 10 Adverse events (systemic).



Study or subgroup	Vitamin D analogue n/N	Other treatment n/N	Risk Difference M-H, Random, 95% CI	Weight	Risk Difference M-H, Random, 95% CI
Heterogeneity: Not applicable					
Test for overall effect: Not applicable					
15.10.3 Calcipotriol vs. nicotinamide 1.4%, twice daily					
Subtotal (95% CI)	**0**	**0**			**Not estimable**
Total events: 0 (Vitamin D analogue), 0 (Other treatment)					
Heterogeneity: Not applicable					
Test for overall effect: Not applicable					
15.10.4 Calcipotriol vs. calcipotriol + nicotinamide 1.4%, twice daily					
Subtotal (95% CI)	**0**	**0**			**Not estimable**
Total events: 0 (Vitamin D analogue), 0 (Other treatment)					
Heterogeneity: Not applicable					
Test for overall effect: Not applicable					
15.10.5 Calcipotriol vs. corticosteroid + salicylic acid					
Crosti 1997	0/80	0/80		100%	0[-0.02,0.02]
Subtotal (95% CI)	**80**	**80**		**100%**	**0[-0.02,0.02]**
Total events: 0 (Vitamin D analogue), 0 (Other treatment)					
Heterogeneity: Not applicable					
Test for overall effect: Not applicable					
15.10.6 Calcipotriol vs. propylthiouracil cream					
Sanchez 2001	0/14	0/14		100%	0[-0.13,0.13]
Subtotal (95% CI)	**14**	**14**		**100%**	**0[-0.13,0.13]**
Total events: 0 (Vitamin D analogue), 0 (Other treatment)					
Heterogeneity: Not applicable					
Test for overall effect: Not applicable					
15.10.7 Calcipotriol vs. tacrolimus ointment					
Ortonne 2006	0/40	0/84		100%	0[-0.04,0.04]
Subtotal (95% CI)	**40**	**84**		**100%**	**0[-0.04,0.04]**
Total events: 0 (Vitamin D analogue), 0 (Other treatment)					
Heterogeneity: Not applicable					
Test for overall effect: Not applicable					
15.10.8 Calcipotriol vs. tazarotene					
Han 2001	1/92	2/91		100%	-0.01[-0.05,0.03]
Subtotal (95% CI)	**92**	**91**		**100%**	**-0.01[-0.05,0.03]**
Total events: 1 (Vitamin D analogue), 2 (Other treatment)					
Heterogeneity: Not applicable					
Test for overall effect: Z=0.59(P=0.55)					
15.10.9 Calcipotriol vs. tazarotene gel plus mometasone furoate cream					
Subtotal (95% CI)	**0**	**0**			**Not estimable**
Total events: 0 (Vitamin D analogue), 0 (Other treatment)					
Heterogeneity: Not applicable					
Test for overall effect: Not applicable					
15.10.10 Calcipotriol vs. vitamin B12 cream					
Subtotal (95% CI)	**0**	**0**			**Not estimable**





Comparison 16. Flexural/facial psoriasis: placebo-controlled trials

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 IAGI	1		Std. Mean Difference (IV, Random, 95% CI)	Totals not selected
1.1 Betamethasone valerate 0.1%, OD	0		Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
1.2 Calcipotriol ointment, OD	0		Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
1.3 Pimecrolimus cream, 1% OD/twice daily	1		Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
1.4 Tacrolimus ointment 0.1%, twice daily	0		Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
2 TSS	1		Std. Mean Difference (IV, Random, 95% CI)	Totals not selected
2.1 Betamethasone valerate 0.1%, OD	0		Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
2.2 Calcipotriol ointment, OD	0		Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
2.3 Pimecrolimus cream, 1% OD/twice daily	1		Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]

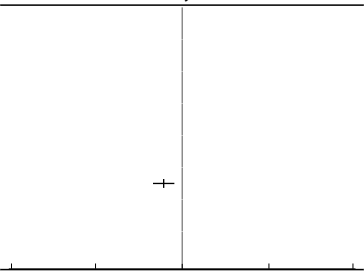
Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
2.4 Tacrolimus ointment 0.1%, twice daily	0		Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
3 PASI	1		Std. Mean Difference (IV, Random, 95% CI)	Totals not selected
3.1 Betamethasone valerate 0.1%, OD	1		Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
3.2 Calcipotriol ointment, OD	1		Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
3.3 Pimecrolimus cream, 1% OD/twice daily	1		Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
3.4 Tacrolimus ointment 0.1%, twice daily	0		Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
4 PAGI	1		Std. Mean Difference (IV, Random, 95% CI)	Subtotals only
4.1 Betamethasone valerate 0.1%, OD	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
4.2 Calcipotriol ointment, OD	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
4.3 Pimecrolimus cream, 1% OD/twice daily	1	47	Std. Mean Difference (IV, Random, 95% CI)	-0.65 [-1.24, -0.06]
4.4 Tacrolimus ointment 0.1%, twice daily	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
5 Combined end point (IAGI/TSS/PASI/PAGI)	2		Std. Mean Difference (IV, Random, 95% CI)	Subtotals only
5.1 Betamethasone valerate 0.1%, OD	1	36	Std. Mean Difference (IV, Random, 95% CI)	-2.83 [-3.79, -1.88]
5.2 Calcipotriol ointment, OD	1	38	Std. Mean Difference (IV, Random, 95% CI)	-1.08 [-1.77, -0.40]
5.3 Pimecrolimus cream, 1% OD/twice daily	2	86	Std. Mean Difference (IV, Random, 95% CI)	-0.86 [-1.30, -0.41]
5.4 Tacrolimus ointment 0.1%, twice daily	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
6 Total withdrawals	3		Risk Difference (M-H, Random, 95% CI)	Subtotals only
6.1 Betamethasone valerate 0.1%, OD	1	40	Risk Difference (M-H, Random, 95% CI)	0.10 [-0.08, 0.28]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
6.2 Calcipotriol ointment, OD	1	40	Risk Difference (M-H, Random, 95% CI)	0.0 [-0.14, 0.14]
6.3 Pimecrolimus cream, 1% OD/twice daily	2	97	Risk Difference (M-H, Random, 95% CI)	-0.06 [-0.16, 0.04]
6.4 Tacrolimus ointment 0.1%, twice daily	1	167	Risk Difference (M-H, Random, 95% CI)	-0.17 [-0.30, -0.03]
7 Withdrawals due to adverse events	3		Risk Difference (M-H, Random, 95% CI)	Subtotals only
7.1 Betamethasone valerate 0.1%, OD	1	40	Risk Difference (M-H, Random, 95% CI)	0.0 [-0.09, 0.09]
7.2 Calcipotriol ointment, OD	1	40	Risk Difference (M-H, Random, 95% CI)	0.0 [-0.09, 0.09]
7.3 Pimecrolimus cream, 1% OD/twice daily	2	97	Risk Difference (M-H, Random, 95% CI)	0.0 [-0.05, 0.05]
7.4 Tacrolimus ointment 0.1%, twice daily	1	167	Risk Difference (M-H, Random, 95% CI)	-0.02 [-0.06, 0.03]
8 Withdrawals due to treatment failure	3		Risk Difference (M-H, Random, 95% CI)	Subtotals only
8.1 Betamethasone valerate 0.1%, OD	1	40	Risk Difference (M-H, Random, 95% CI)	-0.05 [-0.18, 0.08]
8.2 Calcipotriol ointment, OD	1	40	Risk Difference (M-H, Random, 95% CI)	-0.05 [-0.18, 0.08]
8.3 Pimecrolimus cream, 1% OD/twice daily	2	97	Risk Difference (M-H, Random, 95% CI)	-0.04 [-0.13, 0.04]
8.4 Tacrolimus ointment 0.1%, twice daily	1	167	Risk Difference (M-H, Random, 95% CI)	-0.11 [-0.19, -0.02]
9 Adverse events (local)	3		Risk Difference (M-H, Random, 95% CI)	Subtotals only
9.1 Betamethasone valerate 0.1%, OD	1	40	Risk Difference (M-H, Random, 95% CI)	-0.05 [-0.18, 0.08]
9.2 Calcipotriol ointment, OD	1	40	Risk Difference (M-H, Random, 95% CI)	0.05 [-0.11, 0.21]
9.3 Pimecrolimus cream 1%, OD/twice daily	2	97	Risk Difference (M-H, Random, 95% CI)	0.08 [-0.15, 0.31]
9.4 Tacrolimus ointment 0.1%, twice daily	1	167	Risk Difference (M-H, Random, 95% CI)	-0.17 [-0.30, -0.03]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
10 Adverse events (systemic)	1		Risk Difference (M-H, Random, 95% CI)	Totals not selected
10.1 Betamethasone valerate 0.1%, OD	0		Risk Difference (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
10.2 Calcipotriol ointment, OD	0		Risk Difference (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
10.3 Pimecrolimus cream 1%, OD/twice daily	0		Risk Difference (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
10.4 Tacrolimus ointment 0.1%, twice daily	1		Risk Difference (M-H, Random, 95% CI)	0.0 [0.0, 0.0]

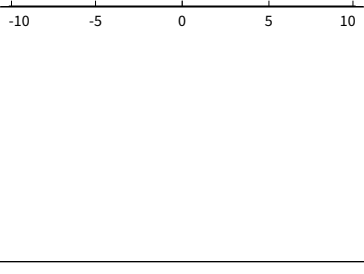
Analysis 16.1. Comparison 16 Flexural/facial psoriasis: placebo-controlled trials, Outcome 1 IAGI.

Study or subgroup	Active treatment N	Mean(SD)	Placebo N	Mean(SD)	Std. Mean Difference Random, 95% CI	Std. Mean Difference Random, 95% CI
16.1.1 Betamethasone valerate 0.1%, OD						
16.1.2 Calcipotriol ointment, OD						
16.1.3 Pimecrolimus cream, 1% OD/twice daily						
Gribetz 2004	22	-2.9 (1.3)	25	-1.6 (1.2)		-1.07[-1.69,-0.45]
16.1.4 Tacrolimus ointment 0.1%, twice daily						



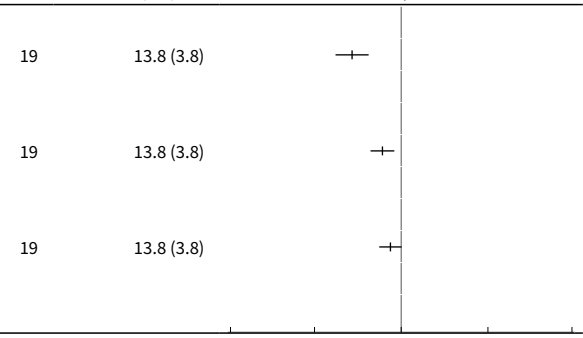
Analysis 16.2. Comparison 16 Flexural/facial psoriasis: placebo-controlled trials, Outcome 2 TSS.

Study or subgroup	Active treatment N	Mean(SD)	Placebo N	Mean(SD)	Std. Mean Difference Random, 95% CI	Std. Mean Difference Random, 95% CI
16.2.1 Betamethasone valerate 0.1%, OD						
16.2.2 Calcipotriol ointment, OD						
16.2.3 Pimecrolimus cream, 1% OD/twice daily						
Gribetz 2004	28	-4.1 (1)	29	-2.7 (1)		-1.37[-1.95,-0.79]
16.2.4 Tacrolimus ointment 0.1%, twice daily						



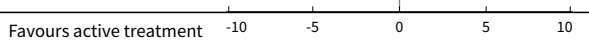
Analysis 16.3. Comparison 16 Flexural/facial psoriasis: placebo-controlled trials, Outcome 3 PASI.

Study or subgroup	Active treatment N	Mean(SD)	Placebo N	Mean(SD)	Std. Mean Difference Random, 95% CI	Std. Mean Difference Random, 95% CI
16.3.1 Betamethasone valerate 0.1%, OD						
Kreuter 2006 (P)	17	2.9 (3.8)	19	13.8 (3.8)		-2.83[-3.79,-1.88]
16.3.2 Calcipotriol ointment, OD						
Kreuter 2006 (P)	19	9.7 (3.8)	19	13.8 (3.8)		-1.08[-1.77,-0.4]
16.3.3 Pimecrolimus cream, 1% OD/twice daily						
Kreuter 2006 (P)	20	11.5 (3.8)	19	13.8 (3.8)		-0.62[-1.27,0.02]
16.3.4 Tacrolimus ointment 0.1%, twice daily						



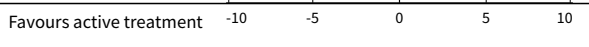
Analysis 16.4. Comparison 16 Flexural/facial psoriasis: placebo-controlled trials, Outcome 4 PAGI.

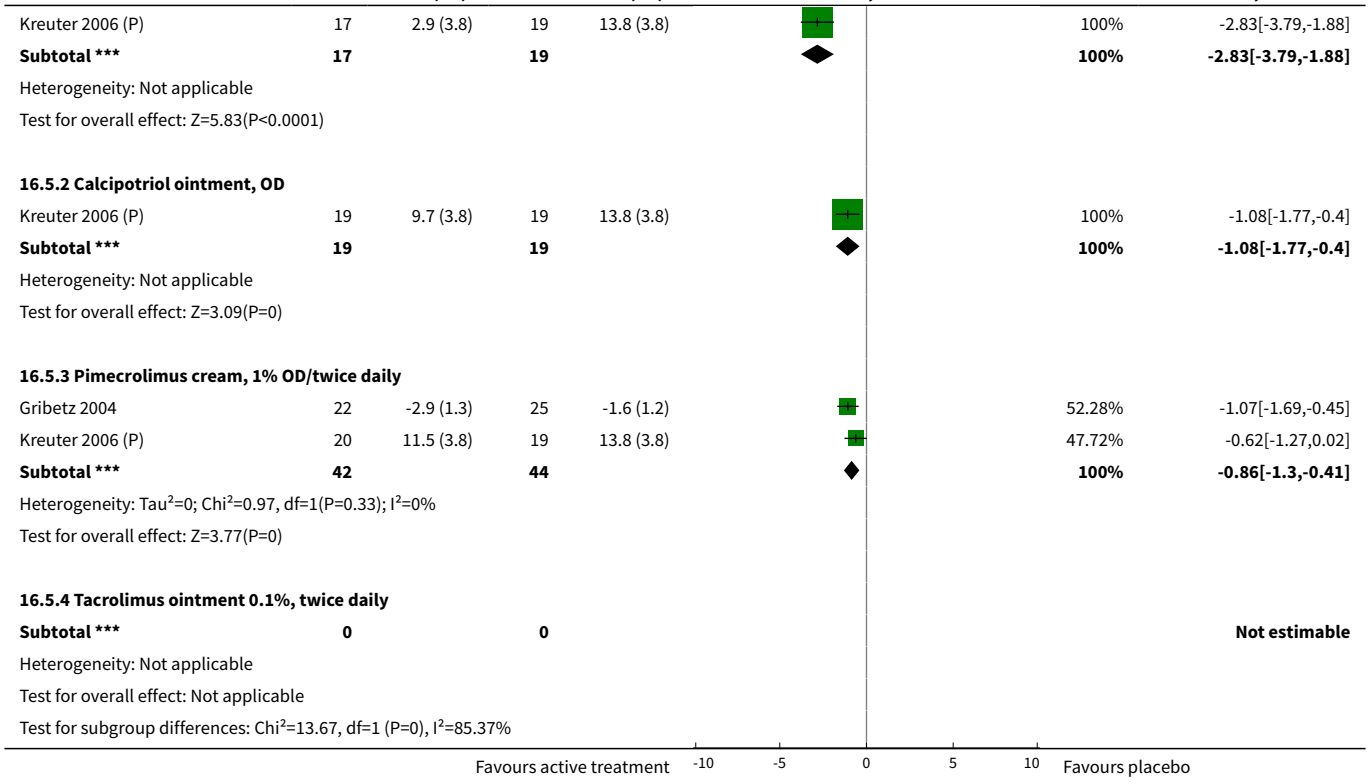
Study or subgroup	Active treatment N	Mean(SD)	Placebo N	Mean(SD)	Std. Mean Difference Random, 95% CI	Weight	Std. Mean Difference Random, 95% CI
16.4.1 Betamethasone valerate 0.1%, OD							
Subtotal ***	**0**		**0**				**Not estimable**
Heterogeneity: Not applicable							
Test for overall effect: Not applicable							
16.4.2 Calcipotriol ointment, OD							
Subtotal ***	**0**		**0**				**Not estimable**
Heterogeneity: Not applicable							
Test for overall effect: Not applicable							
16.4.3 Pimecrolimus cream, 1% OD/twice daily							
Gribetz 2004	22	-2.4 (0.9)	25	-1.7 (1.1)		100%	-0.65[-1.24,-0.06]
Subtotal ***	**22**		**25**			**100%**	**-0.65[-1.24,-0.06]**
Heterogeneity: Not applicable							
Test for overall effect: Z=2.16(P=0.03)							
16.4.4 Tacrolimus ointment 0.1%, twice daily							
Subtotal ***	**0**		**0**				**Not estimable**
Heterogeneity: Not applicable							
Test for overall effect: Not applicable							
Test for subgroup differences: Not applicable							



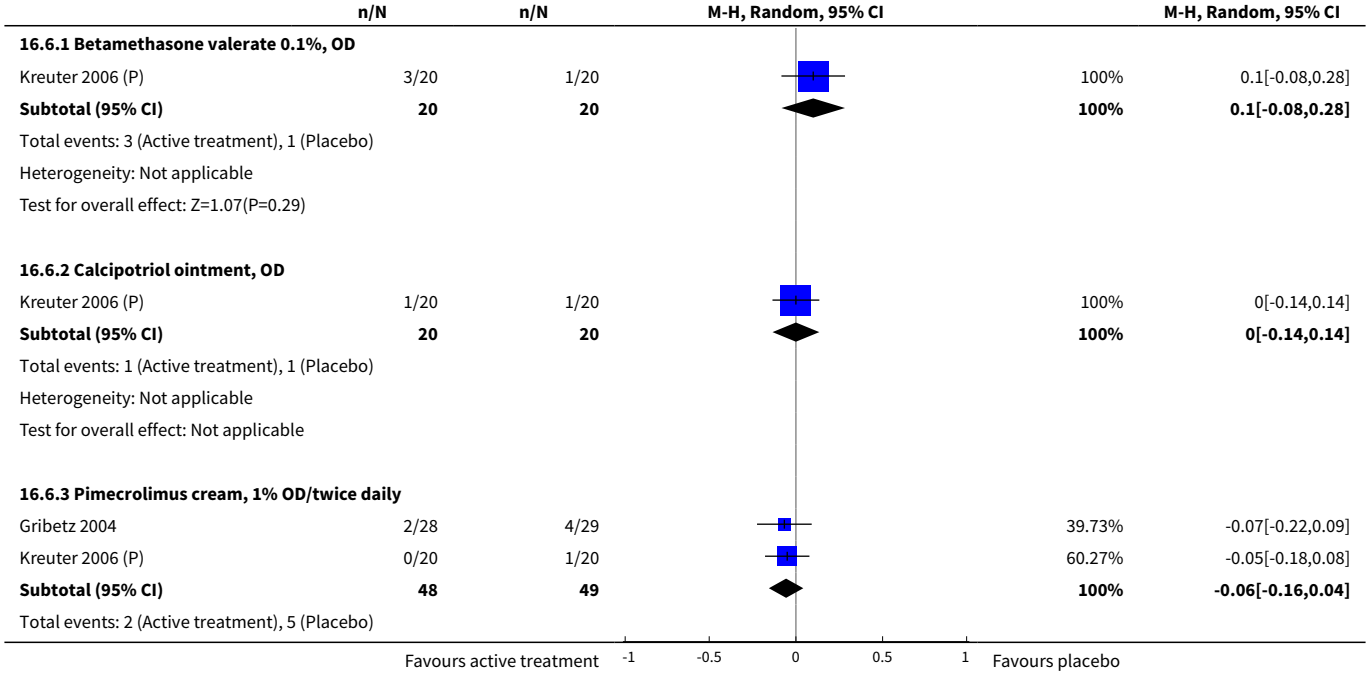
Analysis 16.5. Comparison 16 Flexural/facial psoriasis: placebo-controlled trials, Outcome 5 Combined end point (IAGI/TSS/PASI/PAGI).

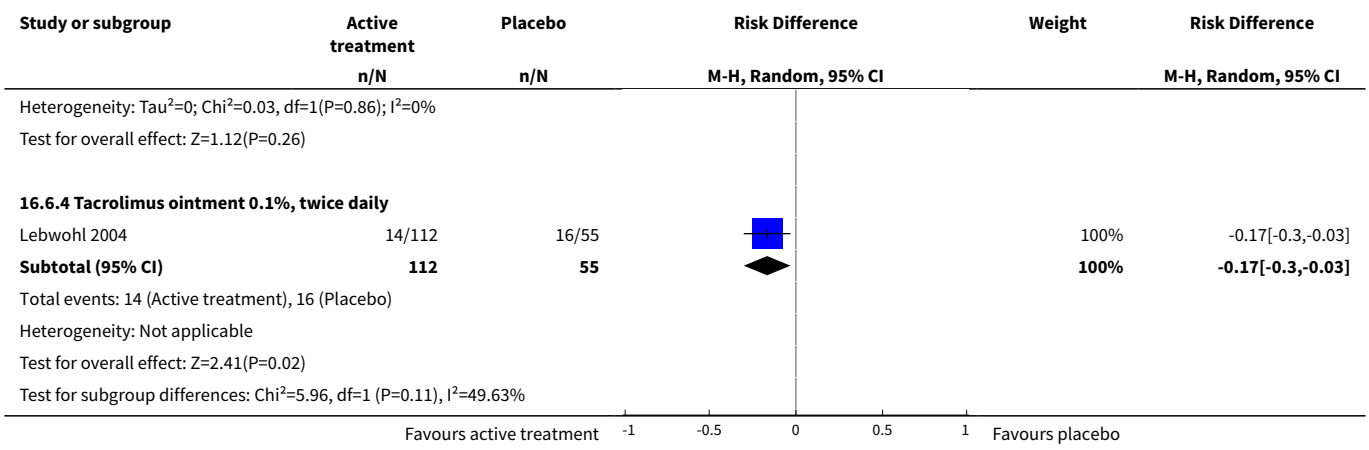
Study or subgroup	Active treatment N	Mean(SD)	Placebo N	Mean(SD)	Std. Mean Difference Random, 95% CI	Weight	Std. Mean Difference Random, 95% CI
16.5.1 Betamethasone valerate 0.1%, OD							



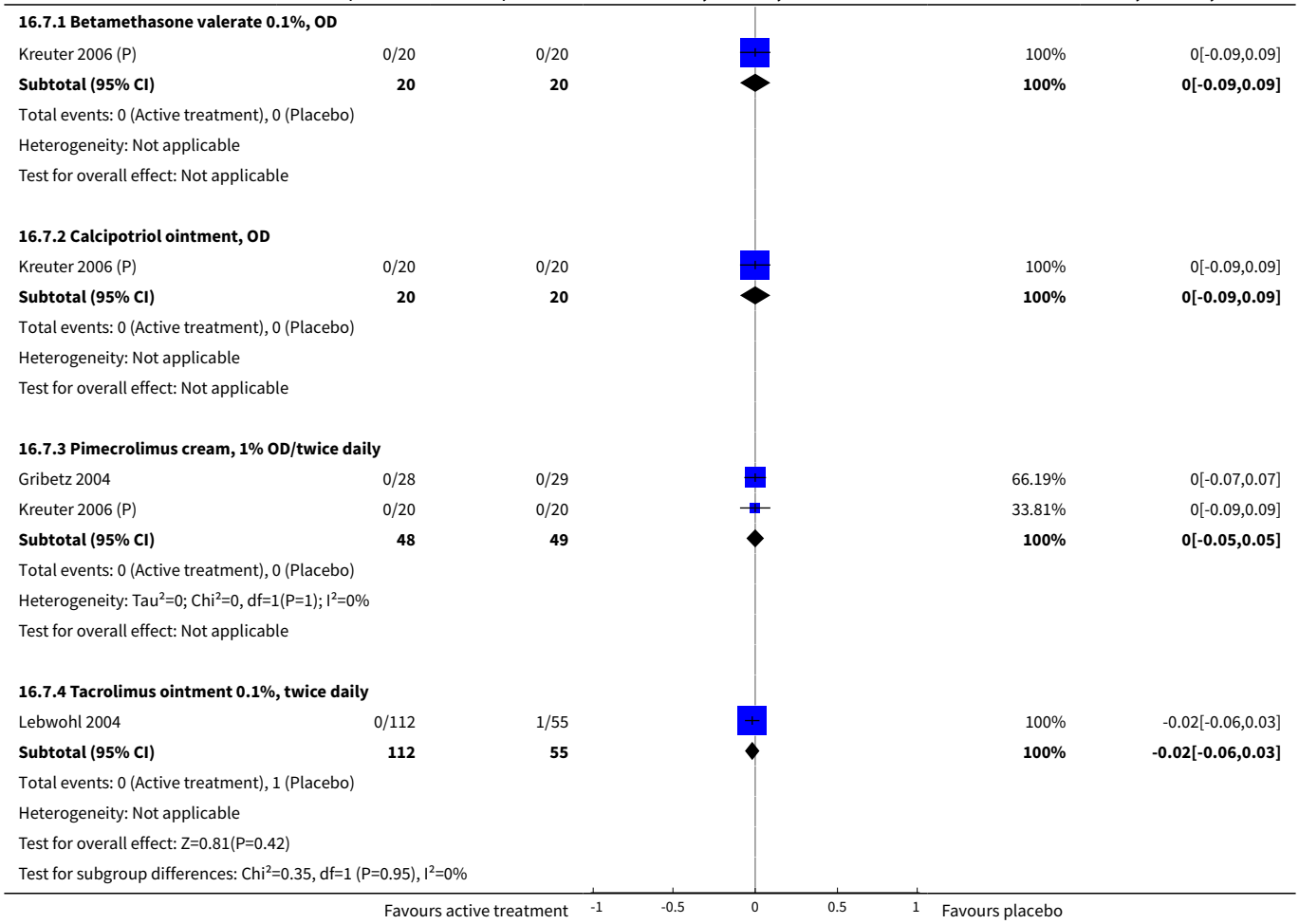


Analysis 16.6. Comparison 16 Flexural/facial psoriasis: placebo-controlled trials, Outcome 6 Total withdrawals.



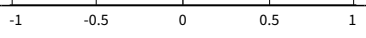


Analysis 16.7. Comparison 16 Flexural/facial psoriasis: placebo-controlled trials, Outcome 7 Withdrawals due to adverse events.



Analysis 16.8. Comparison 16 Flexural/facial psoriasis: placebo-controlled trials, Outcome 8 Withdrawals due to treatment failure.

Study or subgroup	Active treatment n/N	Placebo n/N	Risk Difference M-H, Random, 95% CI	Weight	Risk Difference M-H, Random, 95% CI
16.8.1 Betamethasone valerate 0.1%, OD					
Kreuter 2006 (P)	0/20	1/20		100%	-0.05[-0.18,0.08]
Subtotal (95% CI)	**20**	**20**		**100%**	**-0.05[-0.18,0.08]**
Total events: 0 (Active treatment), 1 (Placebo)					
Heterogeneity: Not applicable					
Test for overall effect: Z=0.77(P=0.44)					
16.8.2 Calcipotriol ointment, OD					
Kreuter 2006 (P)	0/20	1/20		100%	-0.05[-0.18,0.08]
Subtotal (95% CI)	**20**	**20**		**100%**	**-0.05[-0.18,0.08]**
Total events: 0 (Active treatment), 1 (Placebo)					
Heterogeneity: Not applicable					
Test for overall effect: Z=0.77(P=0.44)					
16.8.3 Pimecrolimus cream, 1% OD/twice daily					
Gribetz 2004	1/28	2/29		55.33%	-0.03[-0.15,0.08]
Kreuter 2006 (P)	0/20	1/20		44.67%	-0.05[-0.18,0.08]
Subtotal (95% CI)	**48**	**49**		**100%**	**-0.04[-0.13,0.04]**
Total events: 1 (Active treatment), 3 (Placebo)					
Heterogeneity: Tau^2=0; Chi^2=0.04, df=1(P=0.85); I^2=0%					
Test for overall effect: Z=0.93(P=0.35)					
16.8.4 Tacrolimus ointment 0.1%, twice daily					
Lebwohl 2004	0/112	6/55		100%	-0.11[-0.19,-0.02]
Subtotal (95% CI)	**112**	**55**		**100%**	**-0.11[-0.19,-0.02]**
Total events: 0 (Active treatment), 6 (Placebo)					
Heterogeneity: Not applicable					
Test for overall effect: Z=2.52(P=0.01)					
Test for subgroup differences: Chi^2=1.44, df=1 (P=0.7), I^2=0%					

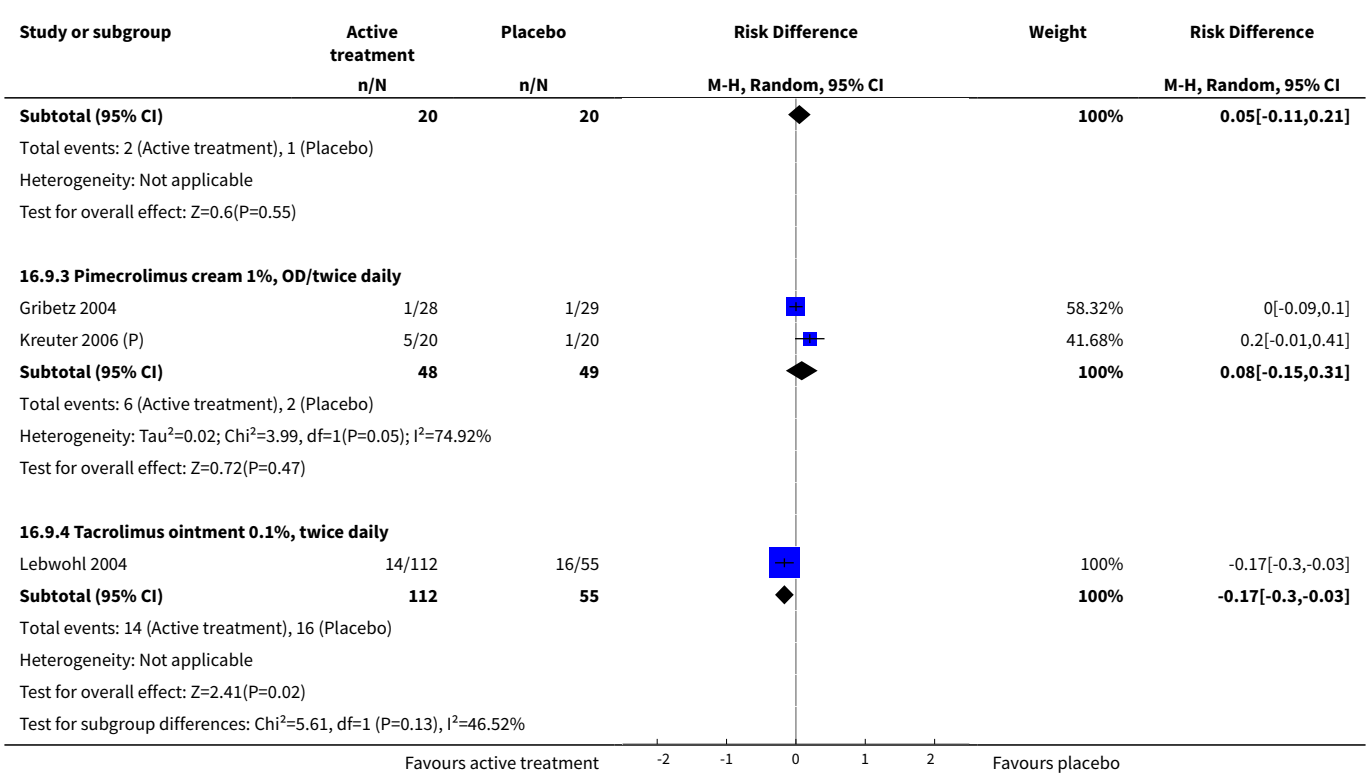


Favours active treatment — Favours placebo

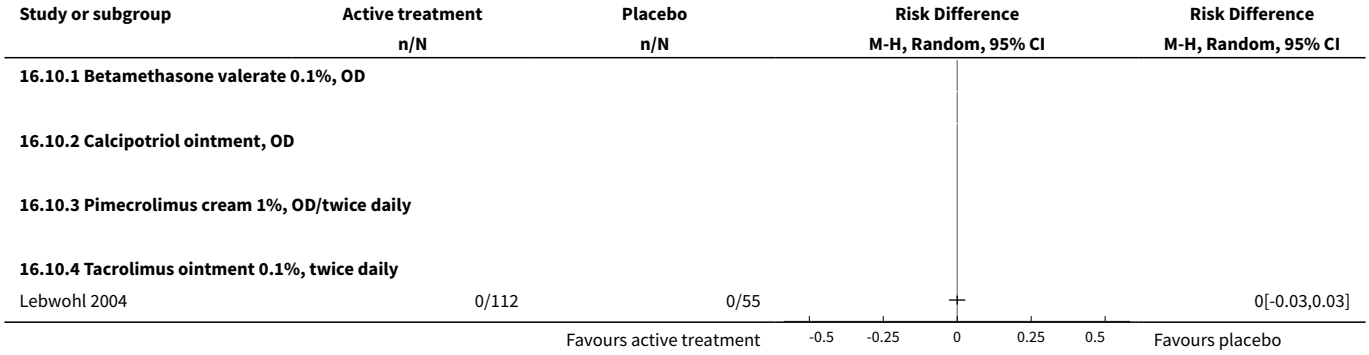
Analysis 16.9. Comparison 16 Flexural/facial psoriasis: placebo-controlled trials, Outcome 9 Adverse events (local).

Study or subgroup	Active treatment n/N	Placebo n/N	Risk Difference M-H, Random, 95% CI	Weight	Risk Difference M-H, Random, 95% CI
16.9.1 Betamethasone valerate 0.1%, OD					
Kreuter 2006 (P)	0/20	1/20		100%	-0.05[-0.18,0.08]
Subtotal (95% CI)	**20**	**20**		**100%**	**-0.05[-0.18,0.08]**
Total events: 0 (Active treatment), 1 (Placebo)					
Heterogeneity: Not applicable					
Test for overall effect: Z=0.77(P=0.44)					
16.9.2 Calcipotriol ointment, OD					
Kreuter 2006 (P)	2/20	1/20		100%	0.05[-0.11,0.21]

Favours active treatment — Favours placebo



Analysis 16.10. Comparison 16 Flexural/facial psoriasis: placebo-controlled trials, Outcome 10 Adverse events (systemic).



Comparison 17. Flexural/facial psoriasis: vitamin D alone or in combination versus other treatment

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 IAGI	2		Std. Mean Difference (IV, Random, 95% CI)	Subtotals only
1.1 Calcipotriol vs. BMV	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1.2 Calcipotriol vs. calcipotriol + hydrocortisone	1	408	Std. Mean Difference (IV, Random, 95% CI)	0.30 [0.11, 0.50]
1.3 Calcipotriol vs. calcitriol	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
1.4 Calcipotriol vs. pimecrolimus	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
1.5 Calcitriol vs. tacrolimus	1	49	Std. Mean Difference (IV, Random, 95% CI)	0.42 [-0.15, 0.98]
2 TSS	2		Std. Mean Difference (IV, Random, 95% CI)	Subtotals only
2.1 Calcipotriol vs. BMV	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
2.2 Calcipotriol vs. calcipotriol + hydrocortisone	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
2.3 Calcipotriol vs. calcitriol	1	150	Std. Mean Difference (IV, Random, 95% CI)	0.61 [0.28, 0.94]
2.4 Calcipotriol vs. pimecrolimus	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
2.5 Calcitriol vs. tacrolimus	1	49	Std. Mean Difference (IV, Random, 95% CI)	0.29 [-0.27, 0.85]
3 PASI	2		Std. Mean Difference (IV, Random, 95% CI)	Subtotals only
3.1 Calcipotriol vs. BMV	1	36	Std. Mean Difference (IV, Random, 95% CI)	2.02 [1.20, 2.84]
3.2 Calcipotriol vs. calcipotriol + hydrocortisone	1	408	Std. Mean Difference (IV, Random, 95% CI)	0.32 [0.12, 0.51]
3.3 Calcipotriol vs. calcitriol	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
3.4 Calcipotriol vs. pimecrolimus	1	39	Std. Mean Difference (IV, Random, 95% CI)	-0.53 [-1.17, 0.11]
3.5 Calcitriol vs. tacrolimus	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
4 PAGI	0		Std. Mean Difference (IV, Random, 95% CI)	Subtotals only
4.1 Calcipotriol vs. BMV	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]

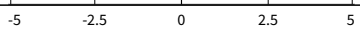
Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
4.2 Calcipotriol vs. calcipotriol + hydrocortisone	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
4.3 Calcipotriol vs. calcitriol	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
4.4 Calcipotriol vs. pimecrolimus	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
4.5 Calcitriol vs. tacrolimus	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
5 Combined end point (IAGI/TSS/PASI/PAGI)	4		Std. Mean Difference (IV, Random, 95% CI)	Subtotals only
5.1 Calcipotriol vs. BMV	1	36	Std. Mean Difference (IV, Random, 95% CI)	2.02 [1.20, 2.84]
5.2 Calcipotriol vs. calcipotriol + hydrocortisone	1	408	Std. Mean Difference (IV, Random, 95% CI)	0.30 [0.11, 0.50]
5.3 Calcipotriol vs. calcitriol	1	150	Std. Mean Difference (IV, Random, 95% CI)	0.61 [0.28, 0.94]
5.4 Calcipotriol vs. pimecrolimus	1	39	Std. Mean Difference (IV, Random, 95% CI)	-0.53 [-1.17, 0.11]
5.5 Calcitriol vs. tacrolimus	1	49	Std. Mean Difference (IV, Random, 95% CI)	0.42 [-0.15, 0.98]
6 Total withdrawals	4		Risk Difference (M-H, Random, 95% CI)	Subtotals only
6.1 Calcipotriol vs. BMV	1	40	Risk Difference (M-H, Random, 95% CI)	-0.10 [-0.28, 0.08]
6.2 Calcipotriol vs. calcipotriol + hydrocortisone	1	408	Risk Difference (M-H, Random, 95% CI)	0.04 [-0.03, 0.11]
6.3 Calcipotriol vs. calcitriol	1	150	Risk Difference (M-H, Random, 95% CI)	0.0 [-0.11, 0.11]
6.4 Calcipotriol vs. pimecrolimus	1	40	Risk Difference (M-H, Random, 95% CI)	0.05 [-0.08, 0.18]
6.5 Calcitriol vs. tacrolimus	1	50	Risk Difference (M-H, Random, 95% CI)	0.12 [-0.02, 0.26]
7 Withdrawals due to adverse events	4		Risk Difference (M-H, Random, 95% CI)	Subtotals only
7.1 Calcipotriol vs. BMV	1	40	Risk Difference (M-H, Random, 95% CI)	0.0 [-0.09, 0.09]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
7.2 Calcipotriol vs. calcipotriol + hydrocortisone	1	408	Risk Difference (M-H, Random, 95% CI)	0.06 [0.02, 0.11]
7.3 Calcipotriol vs. calcitriol	1	150	Risk Difference (M-H, Random, 95% CI)	0.09 [0.01, 0.18]
7.4 Calcipotriol vs. pimecrolimus	1	40	Risk Difference (M-H, Random, 95% CI)	0.0 [-0.09, 0.09]
7.5 Calcitriol vs. tacrolimus	1	50	Risk Difference (M-H, Random, 95% CI)	0.0 [-0.07, 0.07]
8 Withdrawals due to treatment failure	4		Risk Difference (M-H, Random, 95% CI)	Subtotals only
8.1 Calcipotriol vs. BMV	1	40	Risk Difference (M-H, Random, 95% CI)	0.0 [-0.09, 0.09]
8.2 Calcipotriol vs. calcipotriol + hydrocortisone	1	408	Risk Difference (M-H, Random, 95% CI)	0.02 [-0.01, 0.05]
8.3 Calcipotriol vs. calcitriol	1	150	Risk Difference (M-H, Random, 95% CI)	0.0 [-0.03, 0.03]
8.4 Calcipotriol vs. pimecrolimus	1	40	Risk Difference (M-H, Random, 95% CI)	0.0 [-0.09, 0.09]
8.5 Calcitriol vs. tacrolimus	1	50	Risk Difference (M-H, Random, 95% CI)	0.0 [-0.07, 0.07]
9 Adverse events (local)	3		Risk Difference (M-H, Random, 95% CI)	Subtotals only
9.1 calcipotriol vs. BMV	1	40	Risk Difference (M-H, Random, 95% CI)	0.10 [-0.05, 0.25]
9.2 Calcipotriol vs. calcipotriol + hydrocortisone	1	404	Risk Difference (M-H, Random, 95% CI)	0.15 [0.08, 0.23]
9.3 Calcipotriol vs. calcitriol	1	150	Risk Difference (M-H, Random, 95% CI)	0.09 [0.02, 0.17]
9.4 Calcipotriol vs. pimecrolimus	1	40	Risk Difference (M-H, Random, 95% CI)	-0.15 [-0.38, 0.08]
9.5 Calcitriol vs. tacrolimus	0	0	Risk Difference (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
10 Adverse events (systemic)	0		Risk Difference (M-H, Random, 95% CI)	Subtotals only
10.1 Calcipotriol vs. BMV	0	0	Risk Difference (M-H, Random, 95% CI)	0.0 [0.0, 0.0]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
10.2 Calcipotriol vs. calcipotriol + hydrocortisone	0	0	Risk Difference (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
10.3 Calcipotriol vs. calcitriol	0	0	Risk Difference (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
10.4 Calcipotriol vs. pimecrolimus	0	0	Risk Difference (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
10.5 Calcitriol vs. tacrolimus	0	0	Risk Difference (M-H, Random, 95% CI)	0.0 [0.0, 0.0]

Analysis 17.1. Comparison 17 Flexural/facial psoriasis: vitamin D alone or in combination versus other treatment, Outcome 1 IAGI.

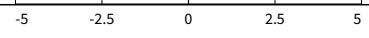
Study or subgroup	Vitamin D alone or in combination N	Mean(SD)	Other treatment N	Mean(SD)	Std. Mean Difference Random, 95% CI	Weight	Std. Mean Difference Random, 95% CI
17.1.1 Calcipotriol vs. BMV							
Subtotal ***	**0**		**0**				**Not estimable**
Heterogeneity: Not applicable							
Test for overall effect: Not applicable							
17.1.2 Calcipotriol vs. calcipotriol + hydrocortisone							
Ortonne 2010	202	1.4 (1.2)	206	1 (1)		100%	0.3[0.11,0.5]
Subtotal ***	**202**		**206**			**100%**	**0.3[0.11,0.5]**
Heterogeneity: Not applicable							
Test for overall effect: Z=3.03(P=0)							
17.1.3 Calcipotriol vs. calcitriol							
Subtotal ***	**0**		**0**				**Not estimable**
Heterogeneity: Not applicable							
Test for overall effect: Not applicable							
17.1.4 Calcipotriol vs. pimecrolimus							
Subtotal ***	**0**		**0**				**Not estimable**
Heterogeneity: Not applicable							
Test for overall effect: Not applicable							
17.1.5 Calcitriol vs. tacrolimus							
Liao 2007	24	-3.7 (1.8)	25	-4.5 (2)		100%	0.42[-0.15,0.98]
Subtotal ***	**24**		**25**			**100%**	**0.42[-0.15,0.98]**
Heterogeneity: Not applicable							
Test for overall effect: Z=1.45(P=0.15)							
Test for subgroup differences: Chi^2=0.14, df=1 (P=0.7), I^2=0%							



Favours vitamin D alone or in combination — Favours other treatment

Analysis 17.2. Comparison 17 Flexural/facial psoriasis: vitamin D alone or in combination versus other treatment, Outcome 2 TSS.

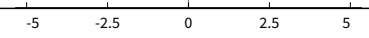
Study or subgroup	Vitamin D alone or in combination N	Mean(SD)	Other treatment N	Mean(SD)	Std. Mean Difference Random, 95% CI	Weight	Std. Mean Difference Random, 95% CI
17.2.1 Calcipotriol vs. BMV							
Subtotal * **	**0**		**0**				**Not estimable**
Heterogeneity: Not applicable							
Test for overall effect: Not applicable							
17.2.2 Calcipotriol vs. calcipotriol + hydrocortisone							
Subtotal * **	**0**		**0**				**Not estimable**
Heterogeneity: Not applicable							
Test for overall effect: Not applicable							
17.2.3 Calcipotriol vs. calcitriol							
Ortonne 2003	75	1.8 (1.5)	75	0.9 (1.5)		100%	0.61[0.28,0.94]
Subtotal * **	**75**		**75**			**100%**	**0.61[0.28,0.94]**
Heterogeneity: Not applicable							
Test for overall effect: Z=3.65(P=0)							
17.2.4 Calcipotriol vs. pimecrolimus							
Subtotal * **	**0**		**0**				**Not estimable**
Heterogeneity: Not applicable							
Test for overall effect: Not applicable							
17.2.5 Calcitriol vs. tacrolimus							
Liao 2007	24	-0.5 (0.4)	25	-0.6 (0.5)		100%	0.29[-0.27,0.85]
Subtotal * **	**24**		**25**			**100%**	**0.29[-0.27,0.85]**
Heterogeneity: Not applicable							
Test for overall effect: Z=1.01(P=0.31)							
Test for subgroup differences: Chi^2=0.92, df=1 (P=0.34), I^2=0%							



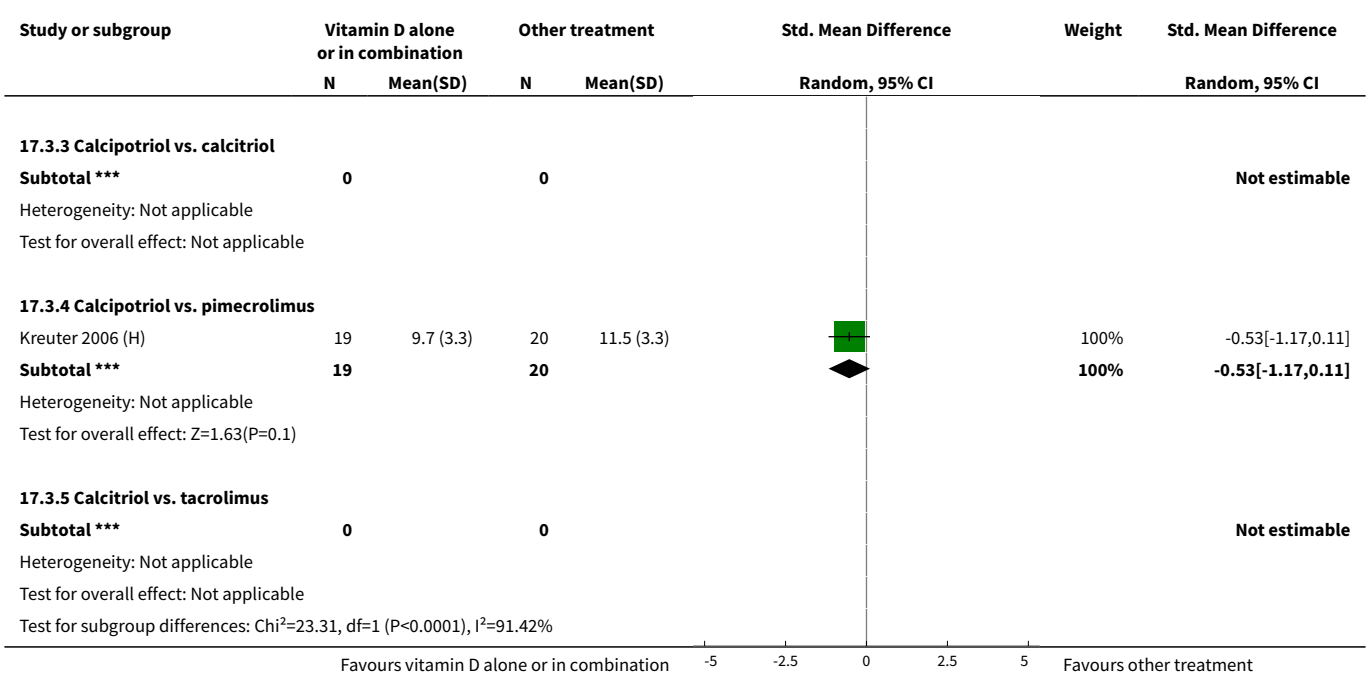
Favours vitamin D alone or in combination — Favours other treatment

Analysis 17.3. Comparison 17 Flexural/facial psoriasis: vitamin D alone or in combination versus other treatment, Outcome 3 PASI.

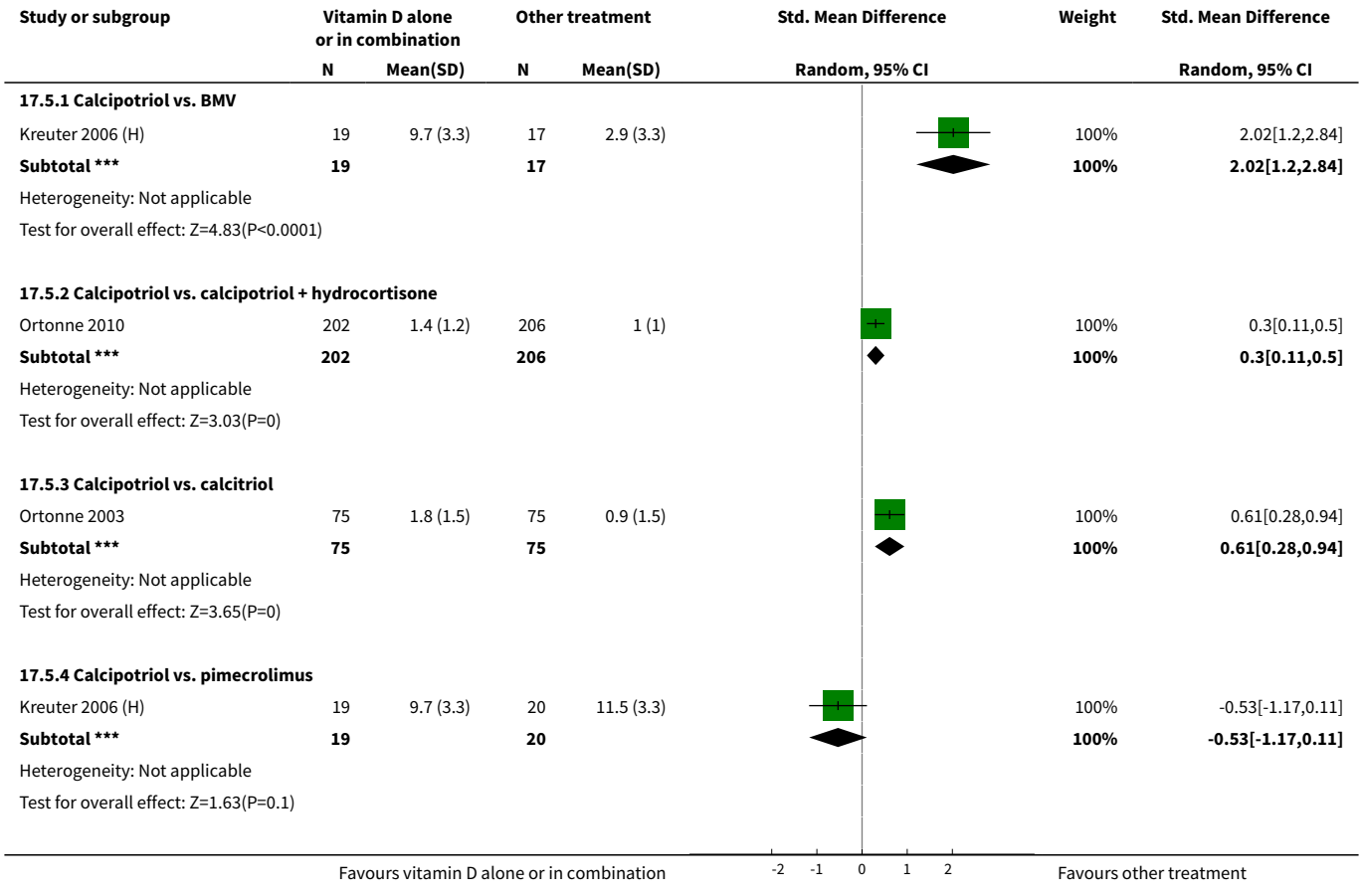
Study or subgroup	Vitamin D alone or in combination N	Mean(SD)	Other treatment N	Mean(SD)	Std. Mean Difference Random, 95% CI	Weight	Std. Mean Difference Random, 95% CI
17.3.1 Calcipotriol vs. BMV							
Kreuter 2006 (H)	19	9.7 (3.3)	17	2.9 (3.3)		100%	2.02[1.2,2.84]
Subtotal * **	**19**		**17**			**100%**	**2.02[1.2,2.84]**
Heterogeneity: Not applicable							
Test for overall effect: Z=4.83(P<0.0001)							
17.3.2 Calcipotriol vs. calcipotriol + hydrocortisone							
Ortonne 2010	202	0.2 (0.3)	206	0.1 (0.2)		100%	0.32[0.12,0.51]
Subtotal * **	**202**		**206**			**100%**	**0.32[0.12,0.51]**
Heterogeneity: Not applicable							
Test for overall effect: Z=3.2(P=0)							

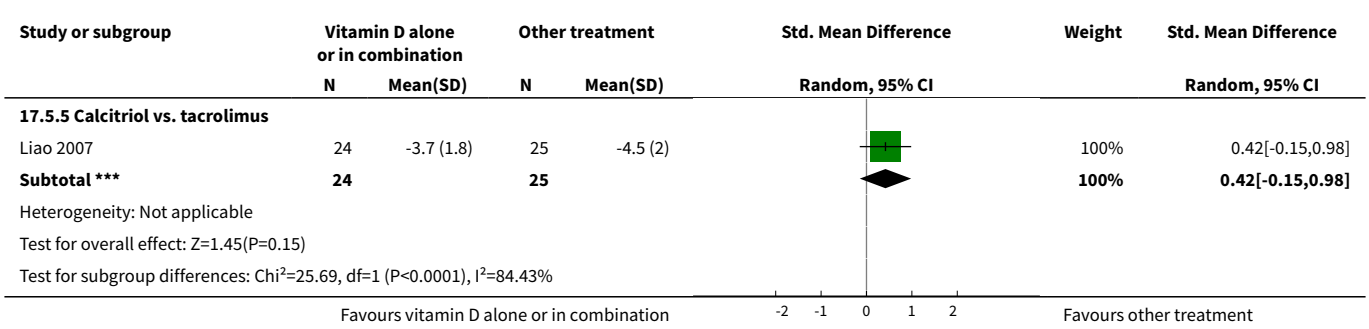


Favours vitamin D alone or in combination — Favours other treatment

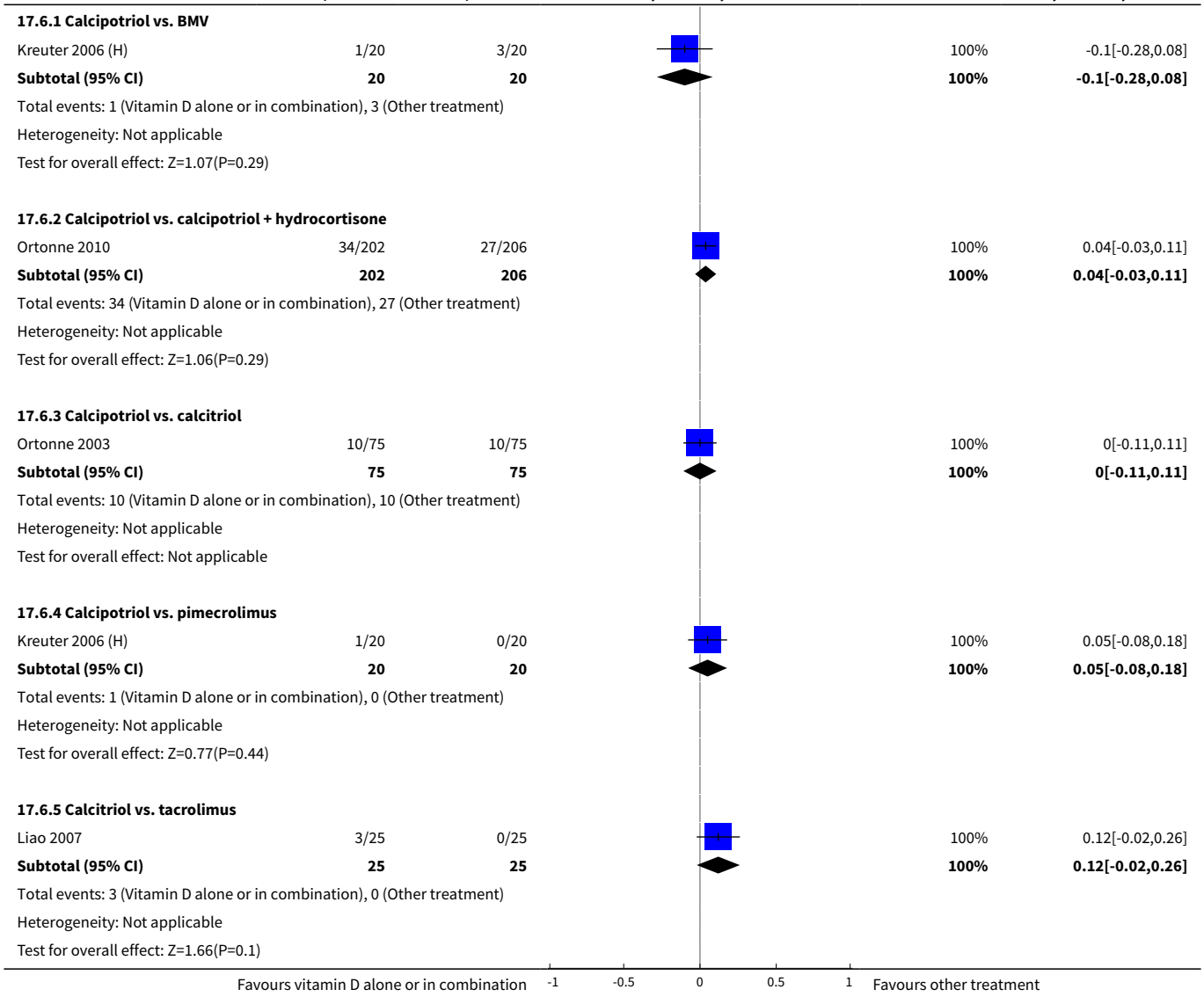


Analysis 17.5. Comparison 17 Flexural/facial psoriasis: vitamin D alone or in combination versus other treatment, Outcome 5 Combined end point (IAGI/TSS/PASI/PAGI).

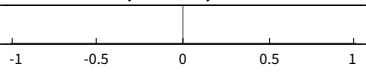




Analysis 17.6. Comparison 17 Flexural/facial psoriasis: vitamin D alone or in combination versus other treatment, Outcome 6 Total withdrawals.

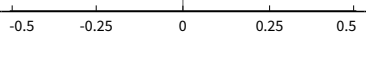


Study or subgroup	Vitamin D alone or in combination	Other treatment	Risk Difference	Weight	Risk Difference
	n/N	n/N	M-H, Random, 95% CI		M-H, Random, 95% CI
Test for subgroup differences: Chi²=3.91, df=1 (P=0.42), I²=0%					

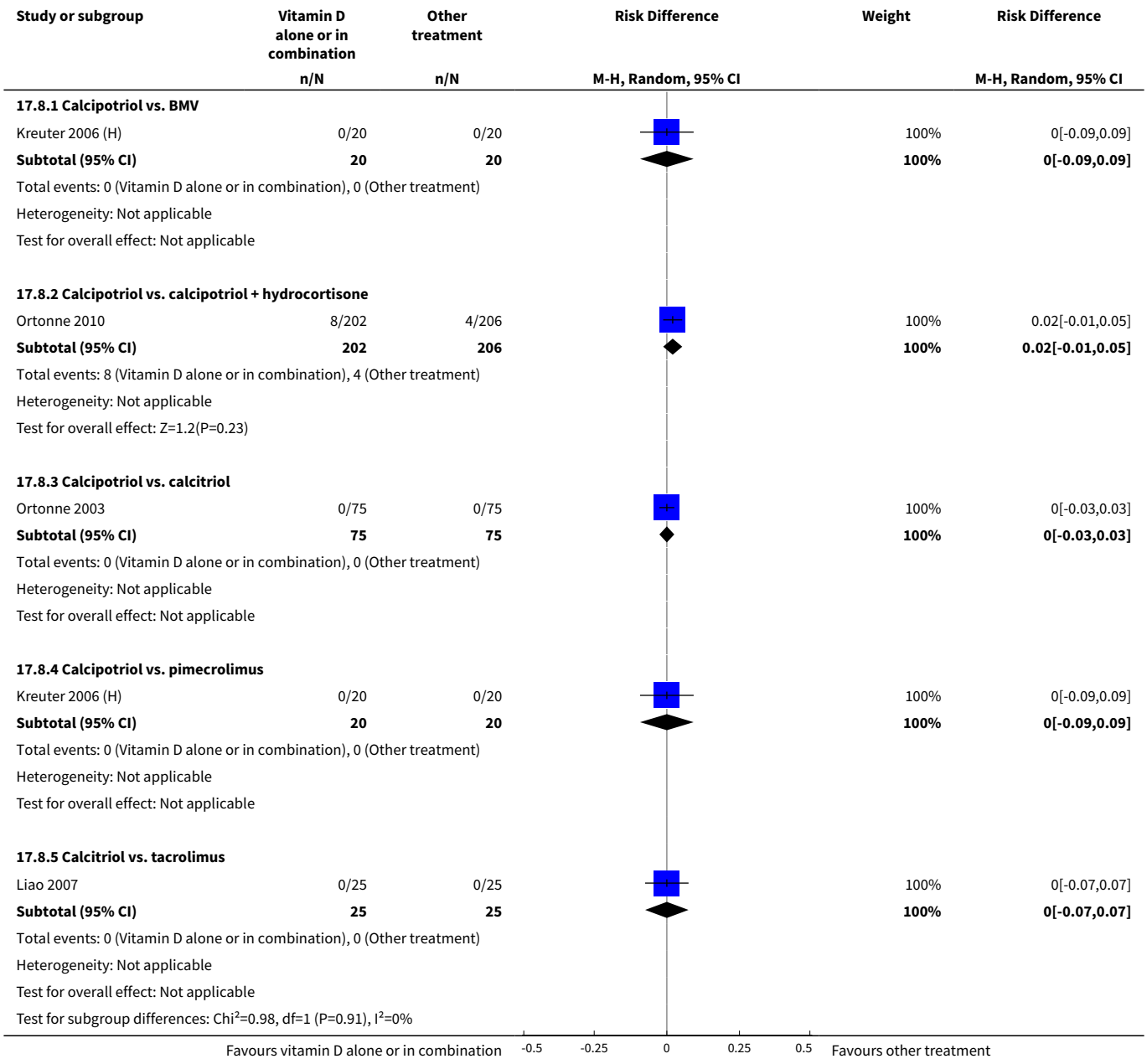


Analysis 17.7. Comparison 17 Flexural/facial psoriasis: vitamin D alone or in combination versus other treatment, Outcome 7 Withdrawals due to adverse events.

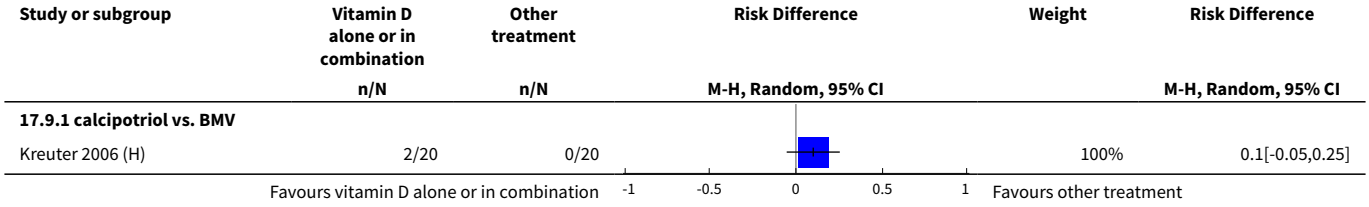
Study or subgroup	Vitamin D alone or in combination	Other treatment	Risk Difference	Weight	Risk Difference
	n/N	n/N	M-H, Random, 95% CI		M-H, Random, 95% CI
17.7.1 Calcipotriol vs. BMV					
Kreuter 2006 (H)	0/20	0/20		100%	0[-0.09,0.09]
Subtotal (95% CI)	**20**	**20**		**100%**	**0[-0.09,0.09]**
Total events: 0 (Vitamin D alone or in combination), 0 (Other treatment)					
Heterogeneity: Not applicable					
Test for overall effect: Not applicable					
17.7.2 Calcipotriol vs. calcipotriol + hydrocortisone					
Ortonne 2010	19/202	6/206		100%	0.06[0.02,0.11]
Subtotal (95% CI)	**202**	**206**		**100%**	**0.06[0.02,0.11]**
Total events: 19 (Vitamin D alone or in combination), 6 (Other treatment)					
Heterogeneity: Not applicable					
Test for overall effect: Z=2.75(P=0.01)					
17.7.3 Calcipotriol vs. calcitriol					
Ortonne 2003	9/75	2/75		100%	0.09[0.01,0.18]
Subtotal (95% CI)	**75**	**75**		**100%**	**0.09[0.01,0.18]**
Total events: 9 (Vitamin D alone or in combination), 2 (Other treatment)					
Heterogeneity: Not applicable					
Test for overall effect: Z=2.23(P=0.03)					
17.7.4 Calcipotriol vs. pimecrolimus					
Kreuter 2006 (H)	0/20	0/20		100%	0[-0.09,0.09]
Subtotal (95% CI)	**20**	**20**		**100%**	**0[-0.09,0.09]**
Total events: 0 (Vitamin D alone or in combination), 0 (Other treatment)					
Heterogeneity: Not applicable					
Test for overall effect: Not applicable					
17.7.5 Calcitriol vs. tacrolimus					
Liao 2007	0/25	0/25		100%	0[-0.07,0.07]
Subtotal (95% CI)	**25**	**25**		**100%**	**0[-0.07,0.07]**
Total events: 0 (Vitamin D alone or in combination), 0 (Other treatment)					
Heterogeneity: Not applicable					
Test for overall effect: Not applicable					
Test for subgroup differences: Chi²=5.25, df=1 (P=0.26), I²=23.8%					

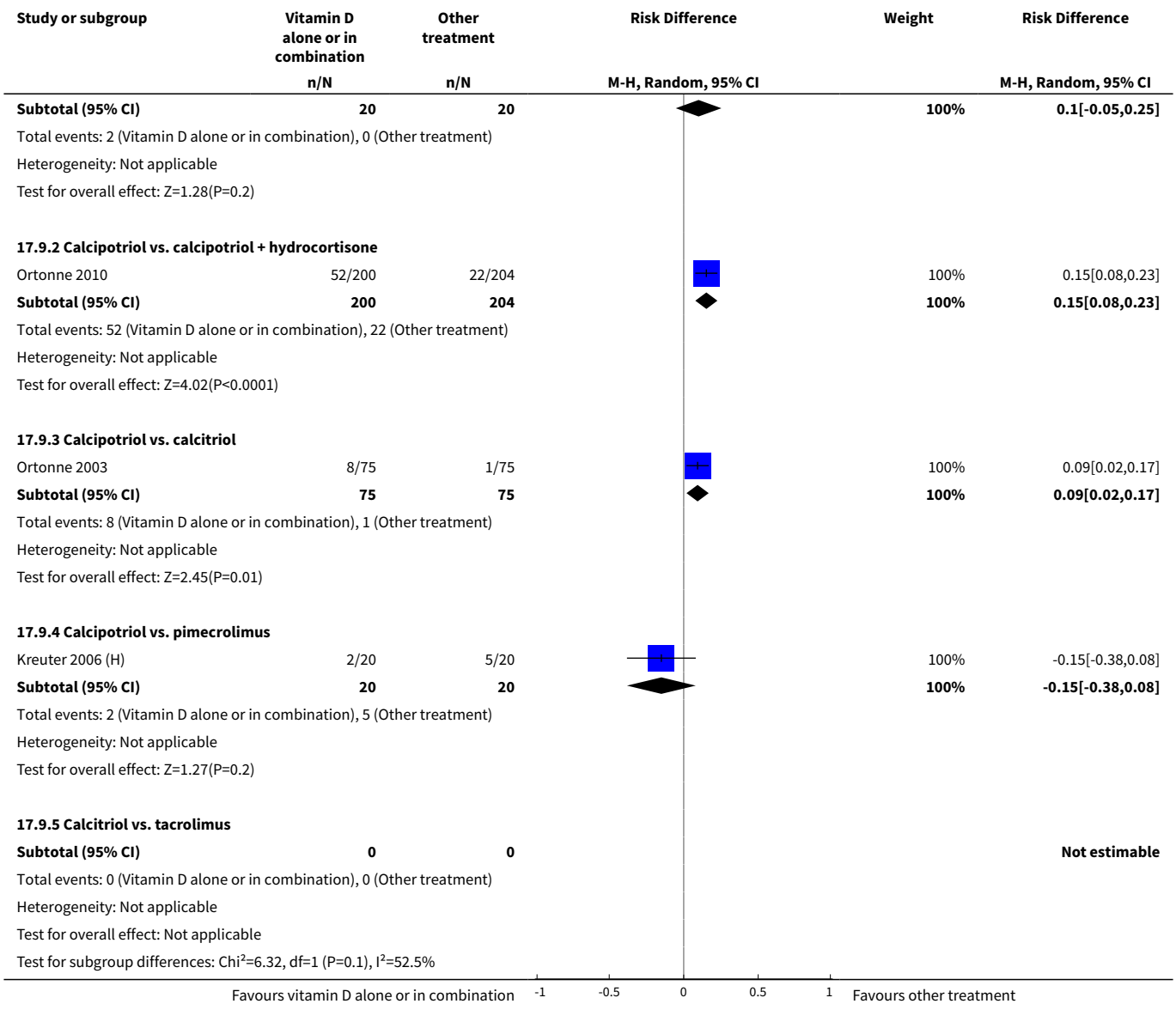


Analysis 17.8. Comparison 17 Flexural/facial psoriasis: vitamin D alone or in combination versus other treatment, Outcome 8 Withdrawals due to treatment failure.



Analysis 17.9. Comparison 17 Flexural/facial psoriasis: vitamin D alone or in combination versus other treatment, Outcome 9 Adverse events (local).





Comparison 18. Scalp psoriasis: placebo-controlled trials

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 IAGI	9		Std. Mean Difference (IV, Random, 95% CI)	Subtotals only
1.1 Vitamin D: calcipotriol	2	457	Std. Mean Difference (IV, Random, 95% CI)	-0.72 [-1.28, -0.16]
1.2 Potent steroid: betamethasone dipropionate	2	712	Std. Mean Difference (IV, Random, 95% CI)	-1.09 [-1.29, -0.90]
1.3 Potent steroid: betamethasone valerate	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1.4 Very potent steroid: amcinonide	1	132	Std. Mean Difference (IV, Random, 95% CI)	-1.42 [-1.80, -1.04]
1.5 Very potent steroid: clobetasol propionate	2	458	Std. Mean Difference (IV, Random, 95% CI)	-1.73 [-1.99, -1.48]
1.6 Very potent steroid: halcinonide	1	54	Std. Mean Difference (IV, Random, 95% CI)	-1.11 [-1.69, -0.53]
1.7 Vitamin D in combination: calcipotriol + BMD	2	854	Std. Mean Difference (IV, Random, 95% CI)	-0.97 [-1.61, -0.32]
1.8 Other treatment: betamethasone-17,21-dipropionate plus salicylic acid	1	20	Std. Mean Difference (IV, Random, 95% CI)	-1.48 [-2.50, -0.47]
1.9 Other treatment: ciclopirox olamine shampoo	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
1.10 Other treatment: fluocinolone acetonide, plus occlusion	1	84	Std. Mean Difference (IV, Random, 95% CI)	-1.22 [-1.69, -0.76]
1.11 Other treatment: salicylic acid	1	20	Std. Mean Difference (IV, Random, 95% CI)	-0.86 [-1.79, 0.06]
2 TSS	11		Std. Mean Difference (IV, Random, 95% CI)	Subtotals only
2.1 Vitamin D: calcipotriol	2	457	Std. Mean Difference (IV, Random, 95% CI)	-0.44 [-0.64, -0.25]
2.2 Potent steroid: betamethasone dipropionate	2	712	Std. Mean Difference (IV, Random, 95% CI)	-1.00 [-1.19, -0.81]
2.3 Potent steroid: betamethasone valerate	1	172	Std. Mean Difference (IV, Random, 95% CI)	-1.40 [-1.75, -1.05]
2.4 Very potent steroid: amcinonide	1	126	Std. Mean Difference (IV, Random, 95% CI)	-1.58 [-1.98, -1.18]
2.5 Very potent steroid: clobetasol propionate	3	707	Std. Mean Difference (IV, Random, 95% CI)	-1.53 [-1.77, -1.28]
2.6 Very potent steroid: halcinonide	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
2.7 Vitamin D in combination: calcipotriol + BMD	2	854	Std. Mean Difference (IV, Random, 95% CI)	-0.92 [-1.42, -0.43]
2.8 Other treatment: betamethasone-17,21-dipropionate plus salicylic acid	1	20	Std. Mean Difference (IV, Random, 95% CI)	-1.15 [-2.11, -0.19]
2.9 Other treatment: ciclopirox olamine shampoo	1	37	Std. Mean Difference (IV, Random, 95% CI)	-0.07 [-0.82, 0.68]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
2.10 Other treatment: fluocinolone acetonide, plus occlusion	1	84	Std. Mean Difference (IV, Random, 95% CI)	-0.89 [-1.34, -0.44]
2.11 Other treatment: salicylic acid	1	20	Std. Mean Difference (IV, Random, 95% CI)	-0.57 [-1.47, 0.32]
3 PASI	0		Std. Mean Difference (IV, Random, 95% CI)	Subtotals only
3.1 Vitamin D: calcipotriol	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
3.2 Potent steroid: betamethasone dipropionate	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
3.3 Potent steroid: betamethasone valerate	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
3.4 Very potent steroid: amcinonide	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
3.5 Very potent steroid: clobetasol propionate	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
3.6 Very potent steroid: halcinonide	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
3.7 Vitamin D in combination: calcipotriol + BMD	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
3.8 Other treatment: betamethasone-17,21-dipropionate plus salicylic acid	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
3.9 Other treatment: ciclopirox olamine shampoo	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
3.10 Other treatment: fluocinolone acetonide, plus occlusion	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
3.11 Other treatment: salicylic acid	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
4 PAGI	5		Std. Mean Difference (IV, Random, 95% CI)	Subtotals only
4.1 Vitamin D: calcipotriol	2	450	Std. Mean Difference (IV, Random, 95% CI)	-0.66 [-1.28, -0.05]
4.2 Potent steroid: betamethasone dipropionate	1	685	Std. Mean Difference (IV, Random, 95% CI)	-1.23 [-1.43, -1.03]
4.3 Potent steroid: betamethasone valerate	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
4.4 Very potent steroid: amcinonide	1	132	Std. Mean Difference (IV, Random, 95% CI)	-0.97 [-1.33, -0.61]
4.5 Very potent steroid: clobetasol propionate	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
4.6 Very potent steroid: halcinonide	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
4.7 Vitamin D in combination: calcipotriol + BMD	2	841	Std. Mean Difference (IV, Random, 95% CI)	-1.00 [-1.79, -0.22]
4.8 Other treatment: betamethasone-17,21-dipropionate plus salicylic acid	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
4.9 Other treatment: ciclopirox olamine shampoo	1	37	Std. Mean Difference (IV, Random, 95% CI)	-0.11 [-0.86, 0.64]
4.10 Other treatment: fluocinolone acetonide, plus occlusion	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
4.11 Other treatment: salicylic acid	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
5 Combined end point (IAGI/TSS/PASI/PAGI)	13		Std. Mean Difference (IV, Random, 95% CI)	Subtotals only
5.1 Vitamin D: calcipotriol	2	457	Std. Mean Difference (IV, Random, 95% CI)	-0.72 [-1.28, -0.16]
5.2 Potent steroid: betamethasone dipropionate	2	712	Std. Mean Difference (IV, Random, 95% CI)	-1.09 [-1.29, -0.90]
5.3 Potent steroid: betamethasone valerate	1	172	Std. Mean Difference (IV, Random, 95% CI)	-1.40 [-1.75, -1.05]
5.4 Very potent steroid: amcinonide	1	132	Std. Mean Difference (IV, Random, 95% CI)	-1.42 [-1.80, -1.04]
5.5 Very potent steroid: clobetasol propionate	4	788	Std. Mean Difference (IV, Random, 95% CI)	-1.57 [-1.81, -1.34]
5.6 Very potent steroid: halcinonide	1	54	Std. Mean Difference (IV, Random, 95% CI)	-1.11 [-1.69, -0.53]
5.7 Vitamin D in combination: calcipotriol + BMD	2	854	Std. Mean Difference (IV, Random, 95% CI)	-0.97 [-1.61, -0.32]
5.8 Other treatment: betamethasone-17,21-dipropionate plus salicylic acid	1	20	Std. Mean Difference (IV, Random, 95% CI)	-1.48 [-2.50, -0.47]
5.9 Other treatment: ciclopirox olamine shampoo	1	37	Std. Mean Difference (IV, Random, 95% CI)	-0.07 [-0.82, 0.68]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
5.10 Other treatment: fluocinolone acetonide, plus occlusion	1	84	Std. Mean Difference (IV, Random, 95% CI)	-1.22 [-1.69, -0.76]
5.11 Other treatment: salicylic acid	1	20	Std. Mean Difference (IV, Random, 95% CI)	-0.86 [-1.79, 0.06]
6 Total withdrawals	13		Risk Difference (M-H, Random, 95% CI)	Subtotals only
6.1 Vitamin D: calcipotriol	3	517	Risk Difference (M-H, Random, 95% CI)	-0.02 [-0.08, 0.05]
6.2 Potent steroid: betamethasone dipropionate	1	692	Risk Difference (M-H, Random, 95% CI)	-0.14 [-0.21, -0.06]
6.3 Potent steroid: betamethasone valerate	0	0	Risk Difference (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
6.4 Very potent steroid: amcinonide	1	165	Risk Difference (M-H, Random, 95% CI)	-0.00 [-0.11, 0.11]
6.5 Very potent steroid: clobetasol propionate	5	1006	Risk Difference (M-H, Random, 95% CI)	-0.03 [-0.10, 0.04]
6.6 Very potent steroid: halcinonide	1	58	Risk Difference (M-H, Random, 95% CI)	0.0 [-0.13, 0.13]
6.7 Vitamin D in combination: calcipotriol + BMD	2	854	Risk Difference (M-H, Random, 95% CI)	-0.09 [-0.16, -0.03]
6.8 Other treatment: betamethasone-17,21-dipropionate plus salicylic acid	0	0	Risk Difference (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
6.9 Other treatment: ciclopirox olamine shampoo	1	40	Risk Difference (M-H, Random, 95% CI)	-0.15 [-0.38, 0.09]
6.10 Other treatment: fluocinolone acetonide, plus occlusion	1	89	Risk Difference (M-H, Random, 95% CI)	-0.04 [-0.13, 0.04]
6.11 Other treatment: salicylic acid	0	0	Risk Difference (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
7 Withdrawals due to adverse events	13		Risk Difference (M-H, Random, 95% CI)	Subtotals only
7.1 Vitamin D: calcipotriol	3	517	Risk Difference (M-H, Random, 95% CI)	0.02 [-0.02, 0.05]
7.2 Potent steroid: betamethasone dipropionate	2	712	Risk Difference (M-H, Random, 95% CI)	-0.04 [-0.08, -0.00]
7.3 Potent steroid: betamethasone valerate	1	172	Risk Difference (M-H, Random, 95% CI)	0.0 [-0.03, 0.03]

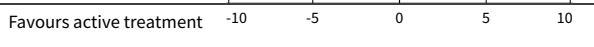
Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
7.4 Very potent steroid: amcinonide	1	165	Risk Difference (M-H, Random, 95% CI)	0.01 [-0.02, 0.04]
7.5 Very potent steroid: clobetasol propionate	5	1006	Risk Difference (M-H, Random, 95% CI)	-0.00 [-0.02, 0.01]
7.6 Very potent steroid: halcinonide	1	58	Risk Difference (M-H, Random, 95% CI)	0.0 [-0.06, 0.06]
7.7 Vitamin D in combination: calcipotriol + BMD	1	677	Risk Difference (M-H, Random, 95% CI)	-0.04 [-0.08, 0.00]
7.8 Other treatment: betamethasone-17,21-dipropionate plus salicylic acid	1	20	Risk Difference (M-H, Random, 95% CI)	0.0 [-0.17, 0.17]
7.9 Other treatment: ciclopirox olamine shampoo	1	40	Risk Difference (M-H, Random, 95% CI)	-0.18 [-0.42, 0.05]
7.10 Other treatment: fluocinolone acetonide, plus occlusion	0	0	Risk Difference (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
7.11 Other treatment: salicylic acid	1	20	Risk Difference (M-H, Random, 95% CI)	0.0 [-0.17, 0.17]
8 Withdrawals due to treatment failure	9		Risk Difference (M-H, Random, 95% CI)	Subtotals only
8.1 Vitamin D: calcipotriol	2	457	Risk Difference (M-H, Random, 95% CI)	-0.05 [-0.11, 0.00]
8.2 Potent steroid: betamethasone dipropionate	1	692	Risk Difference (M-H, Random, 95% CI)	-0.10 [-0.16, -0.05]
8.3 Potent steroid: betamethasone valerate	0	0	Risk Difference (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
8.4 Very potent steroid: amcinonide	1	165	Risk Difference (M-H, Random, 95% CI)	-0.01 [-0.05, 0.02]
8.5 Very potent steroid: clobetasol propionate	5	1006	Risk Difference (M-H, Random, 95% CI)	-0.01 [-0.05, 0.02]
8.6 Very potent steroid: halcinonide	0	0	Risk Difference (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
8.7 Vitamin D in combination: calcipotriol + BMD	1	677	Risk Difference (M-H, Random, 95% CI)	-0.11 [-0.17, -0.06]
8.8 Other treatment: betamethasone-17,21-dipropionate plus salicylic acid	0	0	Risk Difference (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
8.9 Other treatment: ciclopirox olamine shampoo	1	40	Risk Difference (M-H, Random, 95% CI)	-0.09 [-0.28, 0.10]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
8.10 Other treatment: fluocinolone acetonide, plus occlusion	0	0	Risk Difference (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
8.11 Other treatment: salicylic acid	0	0	Risk Difference (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
9 Adverse events (local)	12		Risk Difference (M-H, Random, 95% CI)	Subtotals only
9.1 Vitamin D: calcipotriol	3	510	Risk Difference (M-H, Random, 95% CI)	-0.00 [-0.05, 0.04]
9.2 Potent steroid: betamethasone dipropionate	2	703	Risk Difference (M-H, Random, 95% CI)	-0.07 [-0.13, -0.01]
9.3 Potent steroid: betamethasone valerate	0	0	Risk Difference (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
9.4 Very potent steroid: amcinonide	0	0	Risk Difference (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
9.5 Very potent steroid: clobetasol propionate	4	817	Risk Difference (M-H, Random, 95% CI)	0.00 [-0.03, 0.04]
9.6 Very potent steroid: halcinonide	1	58	Risk Difference (M-H, Random, 95% CI)	-0.03 [-0.12, 0.06]
9.7 Vitamin D in combination: calcipotriol + BMD	2	831	Risk Difference (M-H, Random, 95% CI)	-0.06 [-0.13, 0.02]
9.8 Other treatment: betamethasone-17,21-dipropionate plus salicylic acid	1	20	Risk Difference (M-H, Random, 95% CI)	0.0 [-0.17, 0.17]
9.9 Other treatment: ciclopirox olamine shampoo	1	40	Risk Difference (M-H, Random, 95% CI)	-0.06 [-0.24, 0.13]
9.10 Other treatment: fluocinolone acetonide, plus occlusion	1	89	Risk Difference (M-H, Random, 95% CI)	0.02 [-0.04, 0.08]
9.11 Other treatment: salicylic acid	1	20	Risk Difference (M-H, Random, 95% CI)	0.0 [-0.17, 0.17]
10 Adverse events (systemic)	4		Risk Difference (M-H, Random, 95% CI)	Subtotals only
10.1 Vitamin D: calcipotriol	1	408	Risk Difference (M-H, Random, 95% CI)	0.0 [-0.01, 0.01]
10.2 Potent steroid: betamethasone dipropionate	1	692	Risk Difference (M-H, Random, 95% CI)	0.0 [-0.01, 0.01]
10.3 Potent steroid: betamethasone valerate	0	0	Risk Difference (M-H, Random, 95% CI)	0.0 [0.0, 0.0]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
10.4 Very potent steroid: amcinonide	0	0	Risk Difference (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
10.5 Very potent steroid: clobetasol propionate	2	385	Risk Difference (M-H, Random, 95% CI)	-0.01 [-0.03, 0.02]
10.6 Very potent steroid: halcinonide	0	0	Risk Difference (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
10.7 Vitamin D in combination: calcipotriol + BMD	2	843	Risk Difference (M-H, Random, 95% CI)	0.0 [-0.01, 0.01]
10.8 Other treatment: betamethasone-17,21-dipropionate plus salicylic acid	0	0	Risk Difference (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
10.9 Other treatment: ciclopirox olamine shampoo	0	0	Risk Difference (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
10.10 Other treatment: fluocinolone acetonide, plus occlusion	0	0	Risk Difference (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
10.11 Other treatment: salicylic acid	0	0	Risk Difference (M-H, Random, 95% CI)	0.0 [0.0, 0.0]

Analysis 18.1. Comparison 18 Scalp psoriasis: placebo-controlled trials, Outcome 1 IAGI.

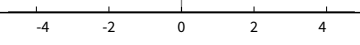
Study or subgroup	Active treatment N	Active treatment Mean(SD)	Placebo N	Placebo Mean(SD)	Std. Mean Difference Random, 95% CI	Weight	Std. Mean Difference Random, 95% CI
18.1.1 Vitamin D: calcipotriol							
Green 1994	25	-2.5 (1.1)	24	-1.2 (1.2)		37.91%	-1.09[-1.69,-0.48]
Jemec 2008 (P)	272	1.9 (1.2)	136	2.4 (1.1)		62.09%	-0.5[-0.71,-0.29]
Subtotal ***	**297**		**160**			**100%**	**-0.72[-1.28,-0.16]**
Heterogeneity: Tau^2=0.12; Chi^2=3.25, df=1(P=0.07); I^2=69.25%							
Test for overall effect: Z=2.53(P=0.01)							
18.1.2 Potent steroid: betamethasone dipropionate							
Elie 1983	10	-1.8 (1)	10	-0.9 (1)		4.3%	-0.86[-1.79,0.06]
Jemec 2008 (P)	556	1.2 (1.1)	136	2.4 (1.1)		95.7%	-1.1[-1.3,-0.91]
Subtotal ***	**566**		**146**			**100%**	**-1.09[-1.29,-0.9]**
Heterogeneity: Tau^2=0; Chi^2=0.25, df=1(P=0.62); I^2=0%							
Test for overall effect: Z=11.15(P<0.0001)							
18.1.3 Potent steroid: betamethasone valerate							
Subtotal ***	**0**		**0**				**Not estimable**
Heterogeneity: Not applicable							
Test for overall effect: Not applicable							
18.1.4 Very potent steroid: amcinonide							
Ellis 1988	65	-4.6 (1.3)	67	-2.8 (1.2)		100%	-1.42[-1.8,-1.04]

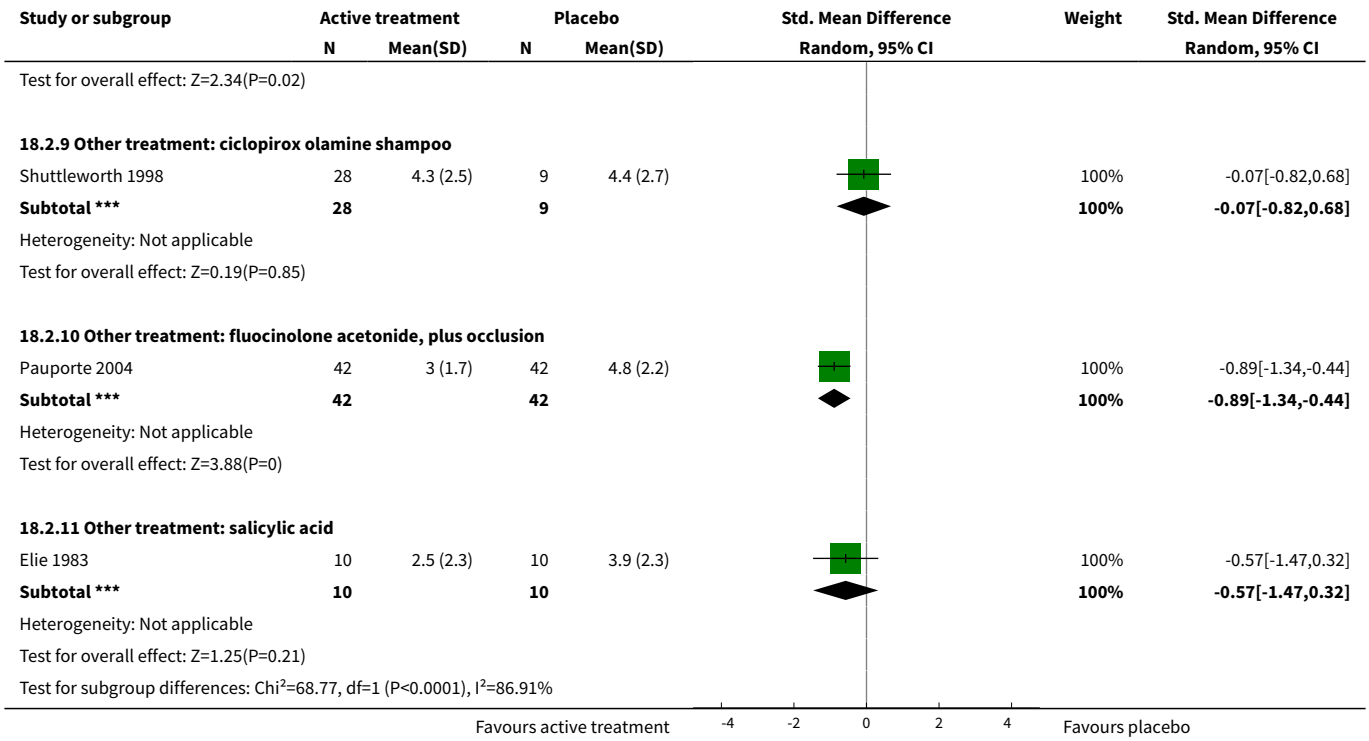


Study or subgroup	Active treatment N	Mean(SD)	Placebo N	Mean(SD)	Std. Mean Difference Random, 95% CI	Weight	Std. Mean Difference Random, 95% CI
Subtotal ***	**65**		**67**			**100%**	**-1.42[-1.8,-1.04]**
Heterogeneity: Tau²=0; Chi²=0, df=0(P<0.0001); I²=100%							
Test for overall effect: Z=7.27(P<0.0001)							
18.1.5 Very potent steroid: clobetasol propionate							
Cook-Bolden 2010	41	0.7 (0.9)	40	2.6 (1)		20.88%	-1.99[-2.53,-1.45]
Olsen 1991	188	-3.6 (1.2)	189	-1.7 (1.1)		79.12%	-1.67[-1.9,-1.43]
Subtotal ***	**229**		**229**			**100%**	**-1.73[-1.99,-1.48]**
Heterogeneity: Tau²=0.01; Chi²=1.17, df=1(P=0.28); I²=14.27%							
Test for overall effect: Z=13.22(P<0.0001)							
18.1.6 Very potent steroid: halcinonide							
Lepaw 1978	27	-2.3 (1)	27	-1.3 (0.8)		100%	-1.11[-1.69,-0.53]
Subtotal ***	**27**		**27**			**100%**	**-1.11[-1.69,-0.53]**
Heterogeneity: Not applicable							
Test for overall effect: Z=3.78(P=0)							
18.1.7 Vitamin D in combination: calcipotriol + BMD							
Jemec 2008 (P)	541	1.1 (1)	136	2.4 (1.1)		52.52%	-1.28[-1.48,-1.08]
Tyring 2010	135	1.1 (1.2)	42	1.8 (1.3)		47.48%	-0.62[-0.98,-0.27]
Subtotal ***	**676**		**178**			**100%**	**-0.97[-1.61,-0.32]**
Heterogeneity: Tau²=0.2; Chi²=10.15, df=1(P=0); I²=90.15%							
Test for overall effect: Z=2.95(P=0)							
18.1.8 Other treatment: betamethasone-17,21-dipropionate plus salicylic acid							
Elie 1983	10	-2.4 (1)	10	-0.9 (1)		100%	-1.48[-2.5,-0.47]
Subtotal ***	**10**		**10**			**100%**	**-1.48[-2.5,-0.47]**
Heterogeneity: Not applicable							
Test for overall effect: Z=2.86(P=0)							
18.1.9 Other treatment: ciclopirox olamine shampoo							
Subtotal ***	**0**		**0**				**Not estimable**
Heterogeneity: Not applicable							
Test for overall effect: Not applicable							
18.1.10 Other treatment: fluocinolone acetonide, plus occlusion							
Pauporte 2004	42	-4.4 (1)	42	-2.8 (1.6)		100%	-1.22[-1.69,-0.76]
Subtotal ***	**42**		**42**			**100%**	**-1.22[-1.69,-0.76]**
Heterogeneity: Not applicable							
Test for overall effect: Z=5.12(P<0.0001)							
18.1.11 Other treatment: salicylic acid							
Elie 1983	10	-1.8 (1)	10	-0.9 (1)		100%	-0.86[-1.79,0.06]
Subtotal ***	**10**		**10**			**100%**	**-0.86[-1.79,0.06]**
Heterogeneity: Not applicable							
Test for overall effect: Z=1.82(P=0.07)							
Test for subgroup differences: Chi²=22.17, df=1 (P=0), I²=63.91%							

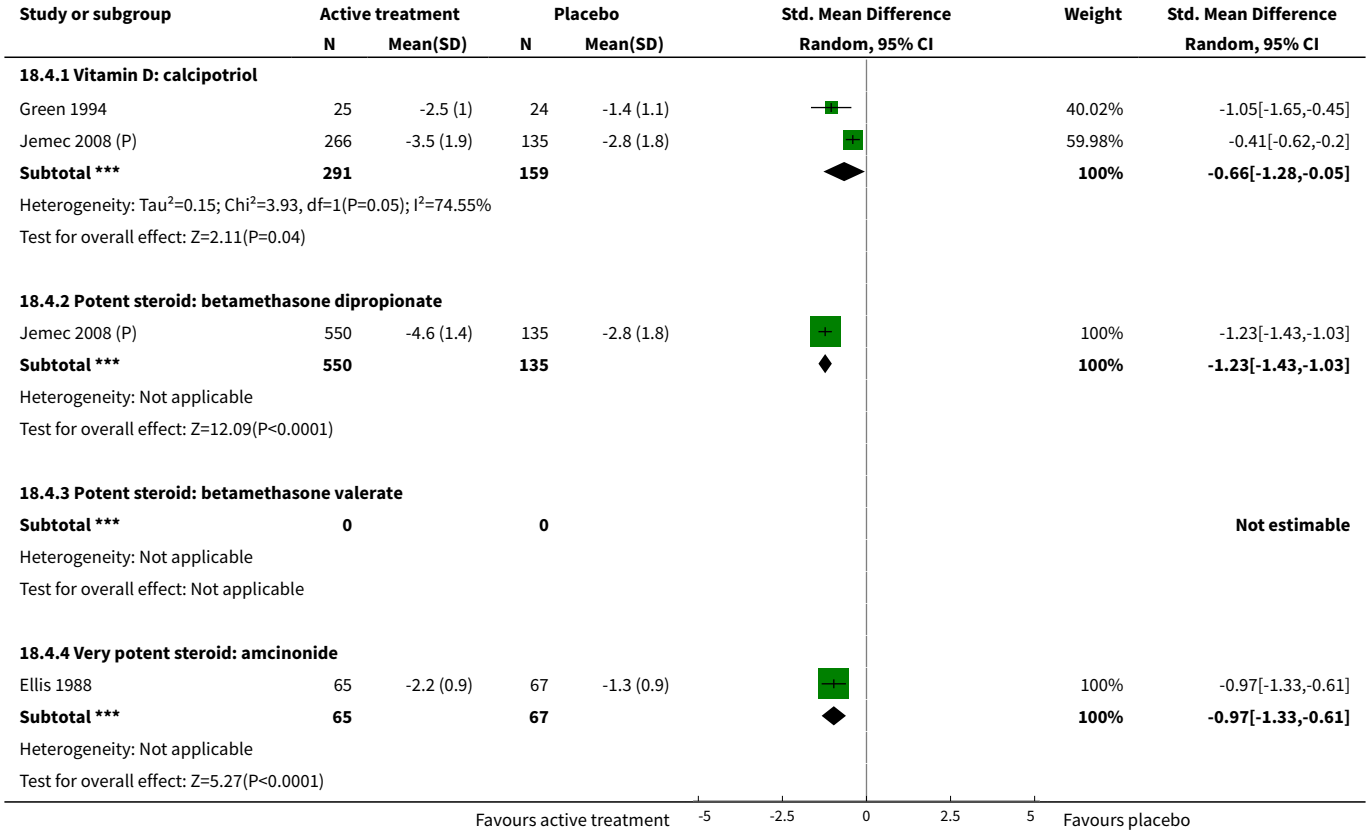
Analysis 18.2. Comparison 18 Scalp psoriasis: placebo-controlled trials, Outcome 2 TSS.

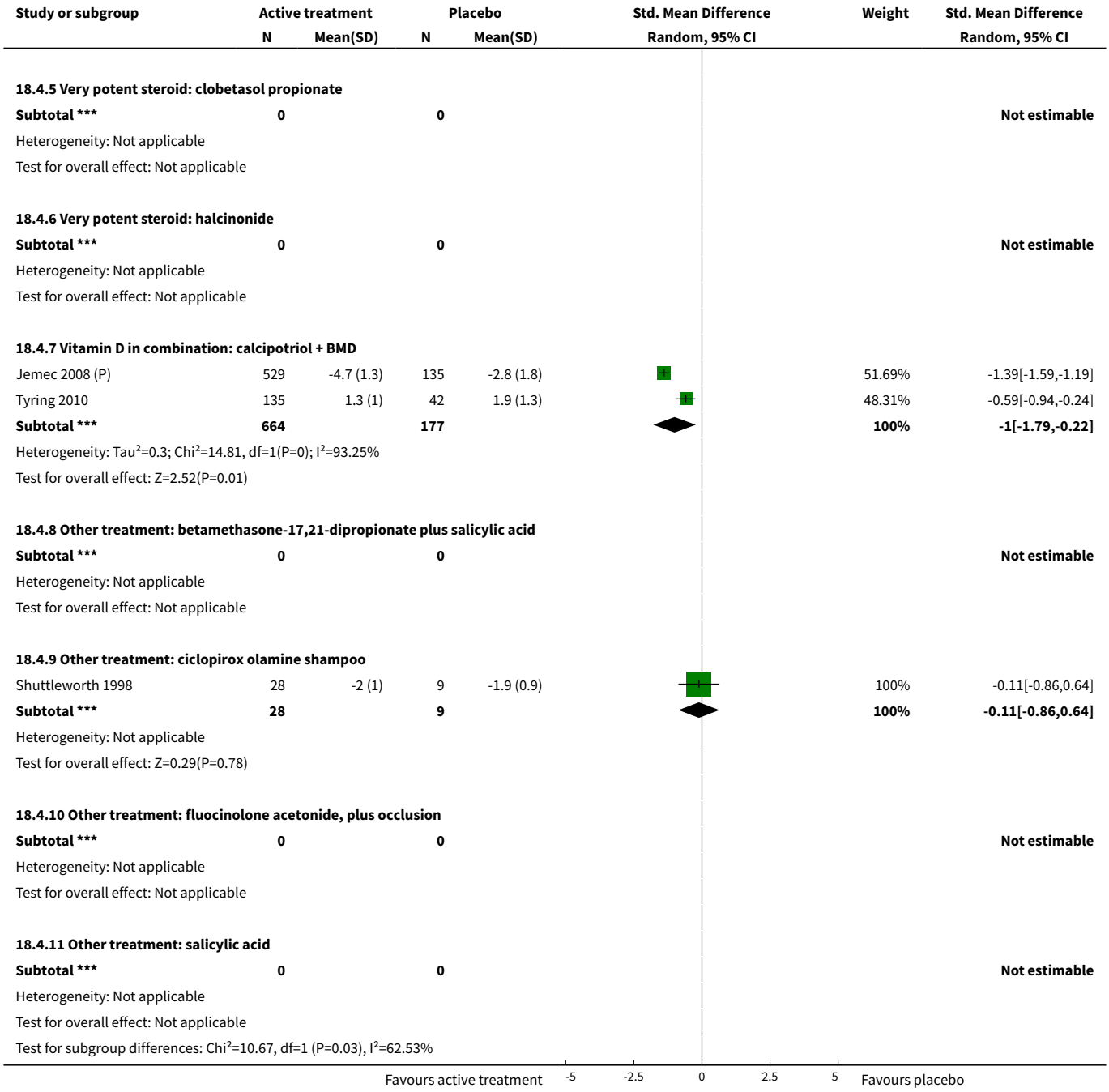
Study or subgroup	Active treatment N	Mean(SD)	Placebo N	Mean(SD)	Std. Mean Difference Random, 95% CI	Weight	Std. Mean Difference Random, 95% CI
18.2.1 Vitamin D: calcipotriol							
Green 1994	25	3.6 (2.7)	24	5.3 (2.5)		11.53%	-0.64[-1.22,-0.07]
Jemec 2008 (P)	272	3.4 (2.4)	136	4.4 (2.4)		88.47%	-0.42[-0.62,-0.21]
Subtotal ***	**297**		**160**			**100%**	**-0.44[-0.64,-0.25]**
Heterogeneity: Tau^2=0; Chi^2=0.53, df=1(P=0.47); I^2=0%							
Test for overall effect: Z=4.43(P<0.0001)							
18.2.2 Potent steroid: betamethasone dipropionate							
Elie 1983	10	2.2 (2.3)	10	3.9 (2.3)		4.39%	-0.71[-1.62,0.2]
Jemec 2008 (P)	556	2.2 (2.1)	136	4.4 (2.4)		95.61%	-1.02[-1.21,-0.82]
Subtotal ***	**566**		**146**			**100%**	**-1[-1.19,-0.81]**
Heterogeneity: Tau^2=0; Chi^2=0.41, df=1(P=0.52); I^2=0%							
Test for overall effect: Z=10.31(P<0.0001)							
18.2.3 Potent steroid: betamethasone valerate							
Franz 1999	115	2.8 (2.3)	57	6 (2.3)		100%	-1.4[-1.75,-1.05]
Subtotal ***	**115**		**57**			**100%**	**-1.4[-1.75,-1.05]**
Heterogeneity: Not applicable							
Test for overall effect: Z=7.81(P<0.0001)							
18.2.4 Very potent steroid: amcinonide							
Ellis 1988	59	-6.3 (2.3)	67	-2.7 (2.3)		100%	-1.58[-1.98,-1.18]
Subtotal ***	**59**		**67**			**100%**	**-1.58[-1.98,-1.18]**
Heterogeneity: Tau^2=0; Chi^2=0, df=0(P<0.0001); I^2=100%							
Test for overall effect: Z=7.7(P<0.0001)							
18.2.5 Very potent steroid: clobetasol propionate							
Franz 2000	125	2.1 (2.3)	63	5.4 (2.3)		30.59%	-1.45[-1.78,-1.11]
Jarratt 2004	95	3.2 (1.7)	47	5.5 (1.7)		26.3%	-1.31[-1.69,-0.93]
Olsen 1991	188	2.4 (2.3)	189	6.3 (2.3)		43.11%	-1.71[-1.95,-1.48]
Subtotal ***	**408**		**299**			**100%**	**-1.53[-1.77,-1.28]**
Heterogeneity: Tau^2=0.02; Chi^2=3.73, df=2(P=0.16); I^2=46.31%							
Test for overall effect: Z=12.14(P<0.0001)							
18.2.6 Very potent steroid: halcinonide							
Subtotal ***	**0**		**0**				**Not estimable**
Heterogeneity: Not applicable							
Test for overall effect: Not applicable							
18.2.7 Vitamin D in combination: calcipotriol + BMD							
Jemec 2008 (P)	541	1.9 (2.1)	136	4.4 (2.4)		54.39%	-1.15[-1.35,-0.96]
Tyring 2010	135	2.1 (2.4)	42	3.7 (2.6)		45.61%	-0.65[-1,-0.3]
Subtotal ***	**676**		**178**			**100%**	**-0.92[-1.42,-0.43]**
Heterogeneity: Tau^2=0.11; Chi^2=5.95, df=1(P=0.01); I^2=83.19%							
Test for overall effect: Z=3.69(P=0)							
18.2.8 Other treatment: betamethasone-17,21-dipropionate plus salicylic acid							
Elie 1983	10	1.2 (2.3)	10	3.9 (2.3)		100%	-1.15[-2.11,-0.19]
Subtotal ***	**10**		**10**			**100%**	**-1.15[-2.11,-0.19]**
Heterogeneity: Not applicable							



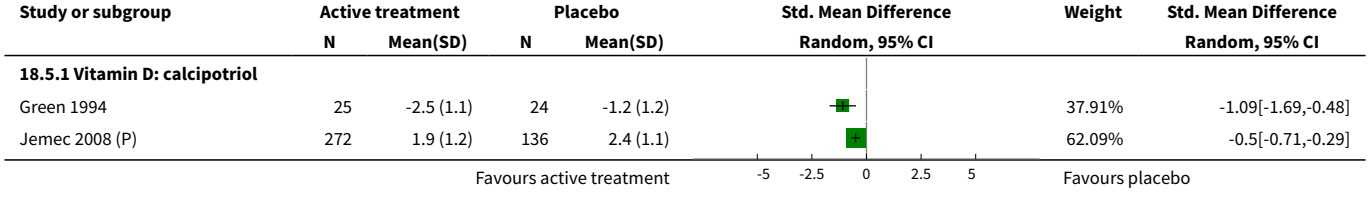


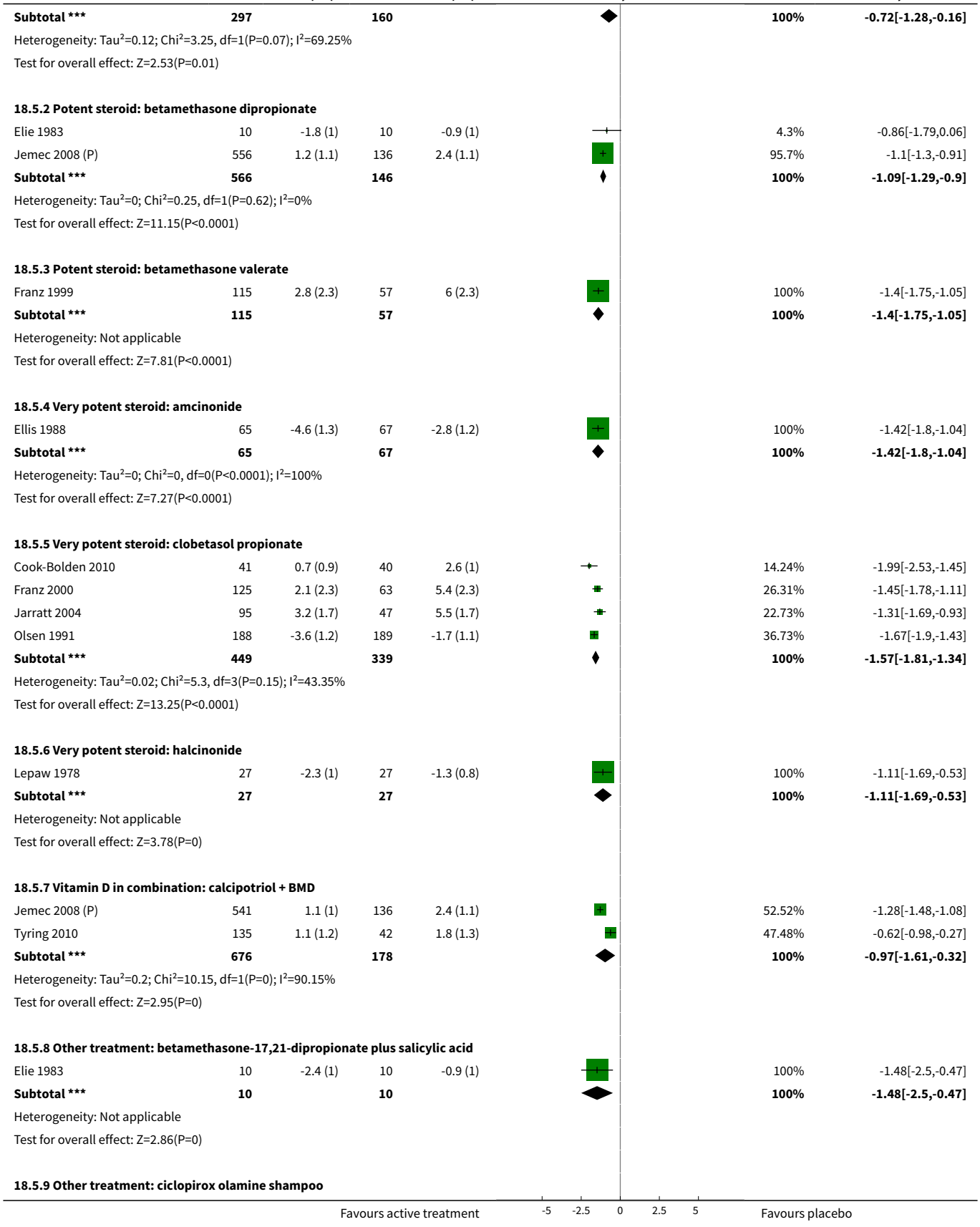
Analysis 18.4. Comparison 18 Scalp psoriasis: placebo-controlled trials, Outcome 4 PAGI.

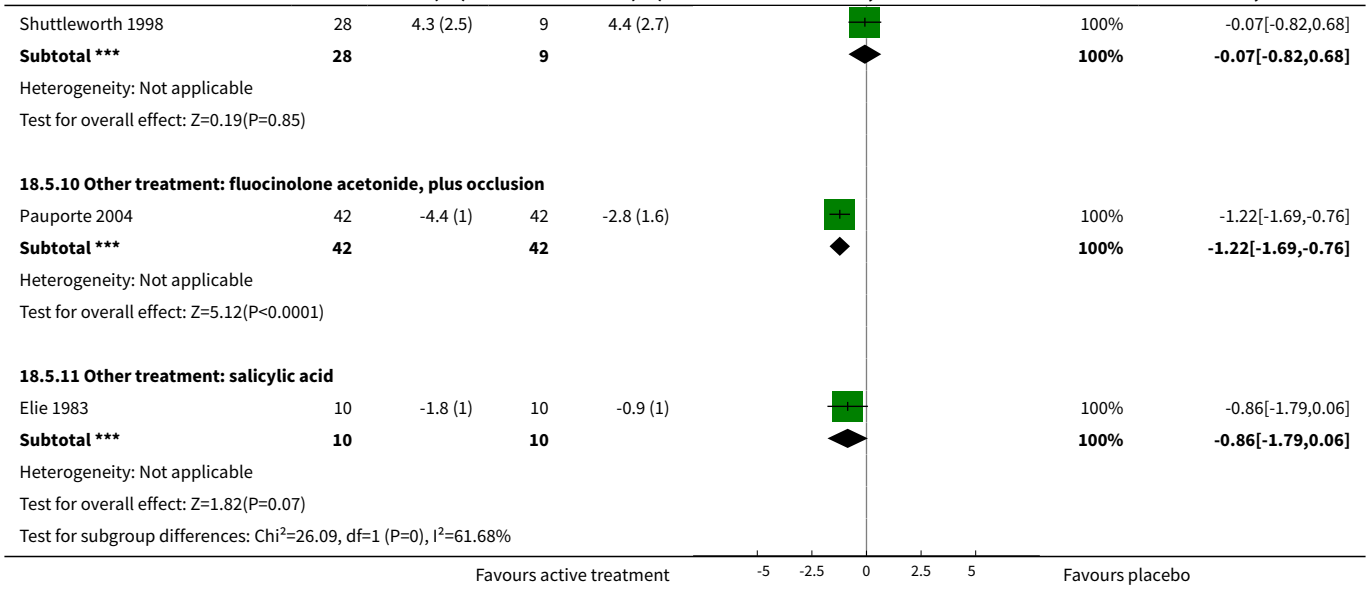




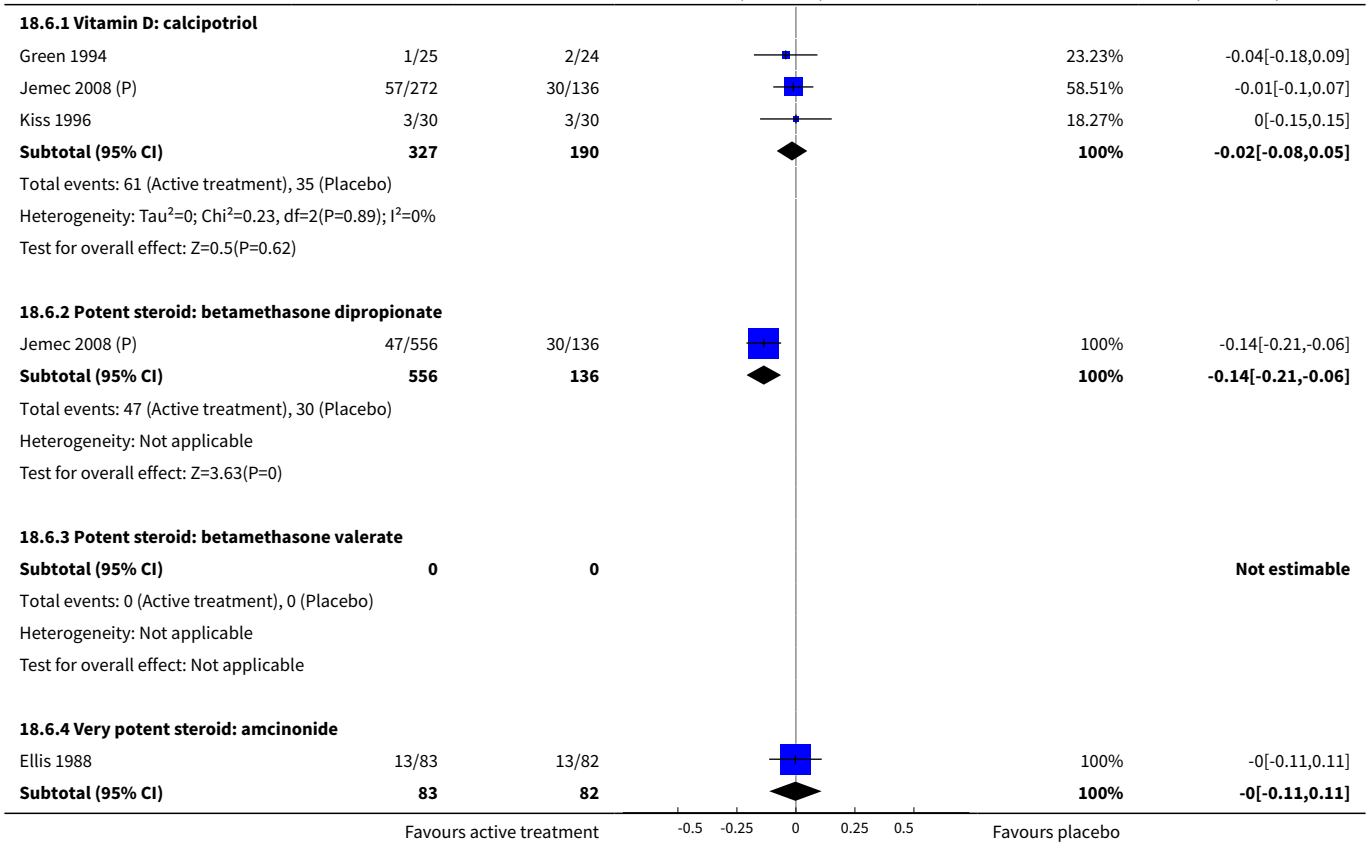
Analysis 18.5. Comparison 18 Scalp psoriasis: placebo-controlled trials, Outcome 5 Combined end point (IAGI/TSS/PASI/PAGI).



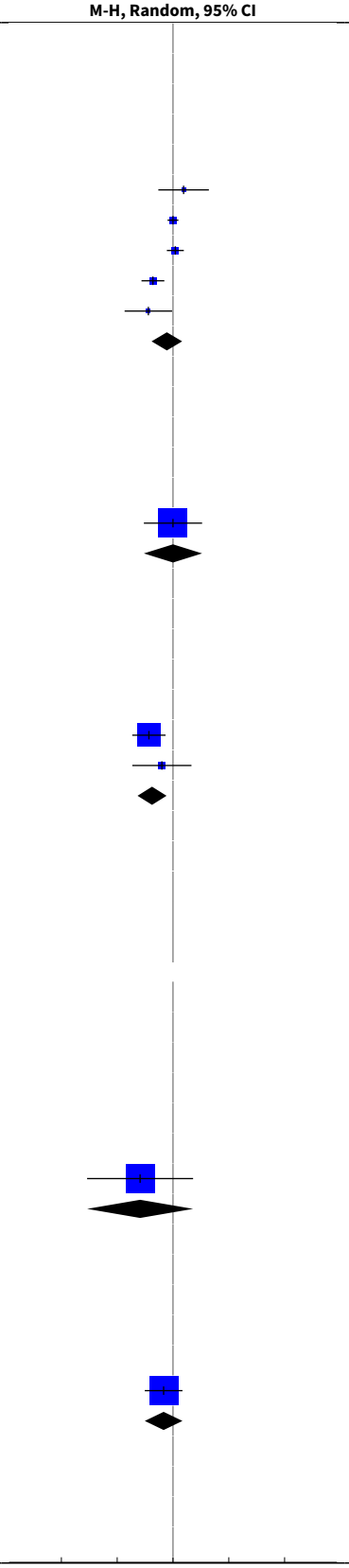




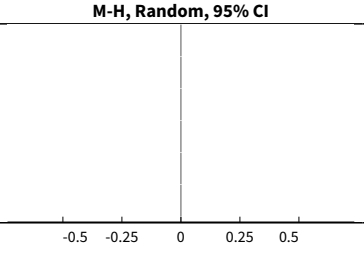
Analysis 18.6. Comparison 18 Scalp psoriasis: placebo-controlled trials, Outcome 6 Total withdrawals.



Study or subgroup	Active treatment n/N	Placebo n/N	Risk Difference M-H, Random, 95% CI	Weight	Risk Difference M-H, Random, 95% CI
Total events: 13 (Active treatment), 13 (Placebo)					
Heterogeneity: Not applicable					
Test for overall effect: Z=0.03(P=0.97)					
18.6.5 Very potent steroid: clobetasol propionate					
Cook-Bolden 2010	4/41	2/40		14.88%	0.05[-0.07,0.16]
Franz 2000	0/125	0/63		24.28%	0[-0.02,0.02]
Jarratt 2004	1/95	0/47		23.25%	0.01[-0.03,0.05]
Olsen 1991	5/189	22/189		21.98%	-0.09[-0.14,-0.04]
Poulin 2010	16/106	29/111		15.61%	-0.11[-0.22,-0]
Subtotal (95% CI)	**556**	**450**		**100%**	**-0.03[-0.1,0.04]**
Total events: 26 (Active treatment), 53 (Placebo)					
Heterogeneity: Tau^2=0; Chi^2=36.71, df=4(P<0.0001); I^2=89.1%					
Test for overall effect: Z=0.79(P=0.43)					
18.6.6 Very potent steroid: halcinonide					
Lepaw 1978	2/29	2/29		100%	0[-0.13,0.13]
Subtotal (95% CI)	**29**	**29**		**100%**	**0[-0.13,0.13]**
Total events: 2 (Active treatment), 2 (Placebo)					
Heterogeneity: Not applicable					
Test for overall effect: Not applicable					
18.6.7 Vitamin D in combination: calcipotriol + BMD					
Jemec 2008 (P)	61/541	30/136		75.91%	-0.11[-0.18,-0.03]
Tyring 2010	19/135	8/42		24.09%	-0.05[-0.18,0.08]
Subtotal (95% CI)	**676**	**178**		**100%**	**-0.09[-0.16,-0.03]**
Total events: 80 (Active treatment), 38 (Placebo)					
Heterogeneity: Tau^2=0; Chi^2=0.56, df=1(P=0.45); I^2=0%					
Test for overall effect: Z=2.83(P=0)					
18.6.8 Other treatment: betamethasone-17,21-dipropionate plus salicylic acid					
Subtotal (95% CI)	**0**	**0**			**Not estimable**
Total events: 0 (Active treatment), 0 (Placebo)					
Heterogeneity: Not applicable					
Test for overall effect: Not applicable					
18.6.9 Other treatment: ciclopirox olamine shampoo					
Shuttleworth 1998	1/29	2/11		100%	-0.15[-0.38,0.09]
Subtotal (95% CI)	**29**	**11**		**100%**	**-0.15[-0.38,0.09]**
Total events: 1 (Active treatment), 2 (Placebo)					
Heterogeneity: Not applicable					
Test for overall effect: Z=1.22(P=0.22)					
18.6.10 Other treatment: fluocinolone acetonide, plus occlusion					
Pauporte 2004	1/43	3/46		100%	-0.04[-0.13,0.04]
Subtotal (95% CI)	**43**	**46**		**100%**	**-0.04[-0.13,0.04]**
Total events: 1 (Active treatment), 3 (Placebo)					
Heterogeneity: Not applicable					
Test for overall effect: Z=0.97(P=0.33)					

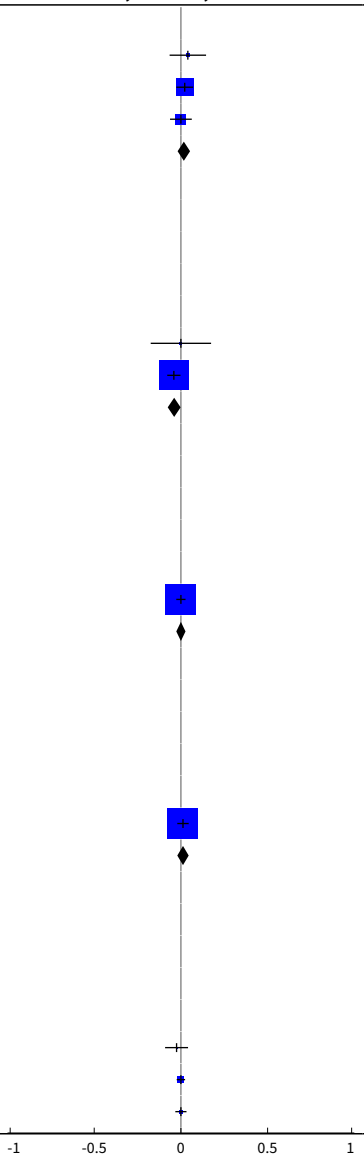


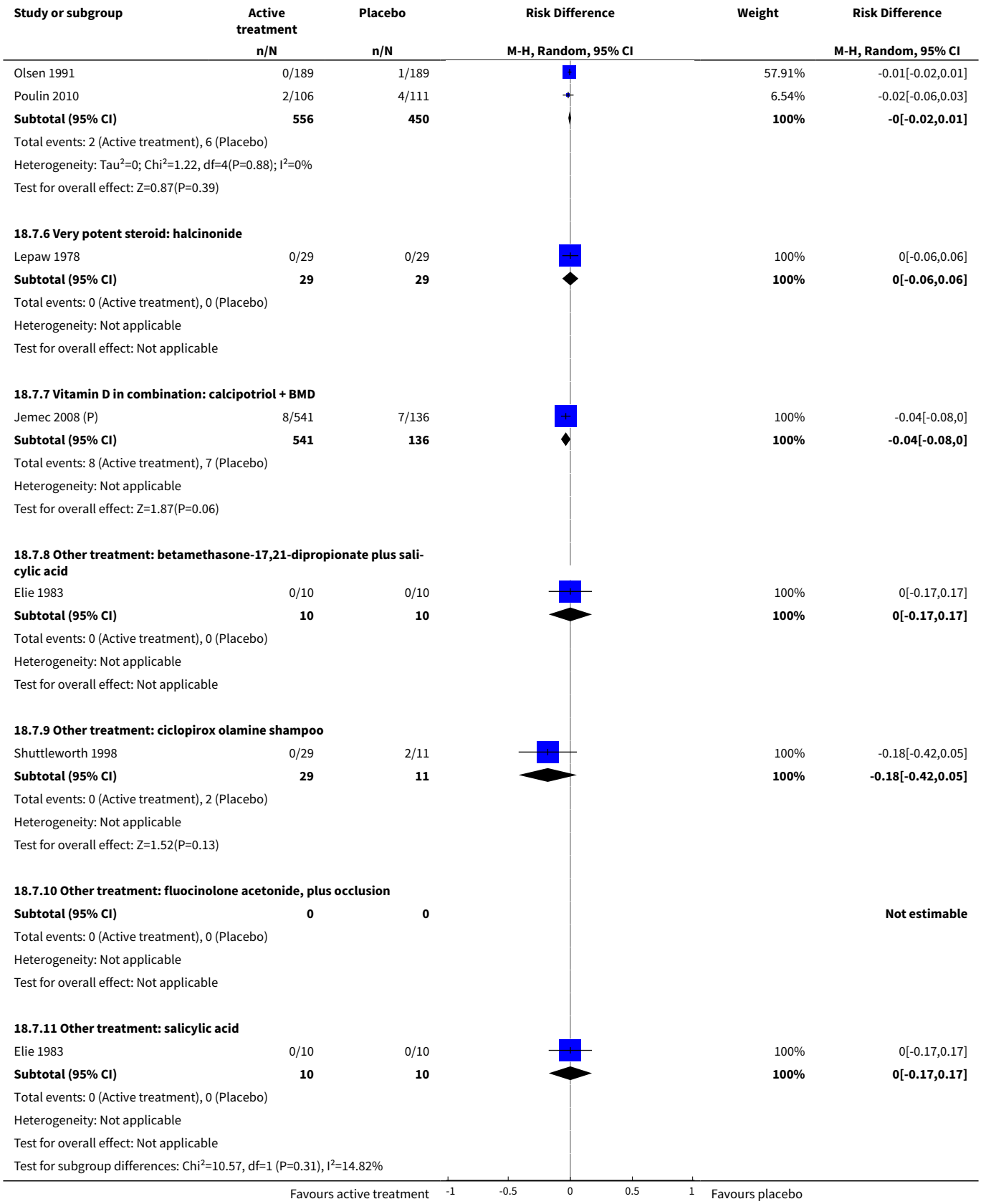
Study or subgroup	Active treatment n/N	Placebo n/N	Risk Difference M-H, Random, 95% CI	Weight	Risk Difference M-H, Random, 95% CI
18.6.11 Other treatment: salicylic acid					
Subtotal (95% CI)	**0**	**0**			**Not estimable**
Total events: 0 (Active treatment), 0 (Placebo)					
Heterogeneity: Not applicable					
Test for overall effect: Not applicable					
Test for subgroup differences: Chi^2=10.25, df=1 (P=0.17), I^2=31.7%					



Analysis 18.7. Comparison 18 Scalp psoriasis: placebo-controlled trials, Outcome 7 Withdrawals due to adverse events.

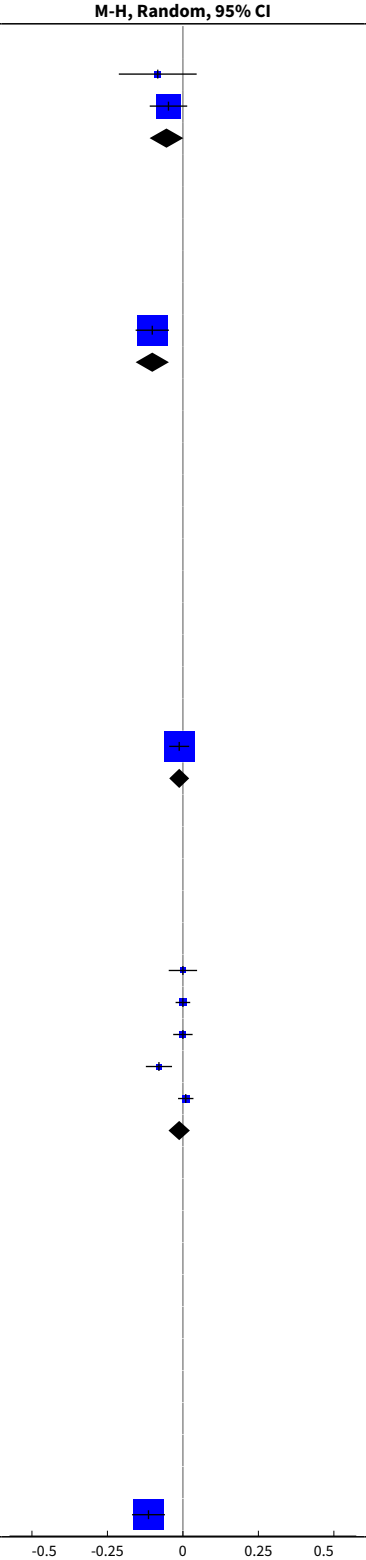
Study or subgroup	Active treatment n/N	Placebo n/N	Risk Difference M-H, Random, 95% CI	Weight	Risk Difference M-H, Random, 95% CI
18.7.1 Vitamin D: calcipotriol					
Green 1994	1/25	0/24		11.73%	0.04[-0.07,0.15]
Jemec 2008 (P)	20/272	7/136		55.33%	0.02[-0.03,0.07]
Kiss 1996	0/30	0/30		32.94%	0[-0.06,0.06]
Subtotal (95% CI)	**327**	**190**		**100%**	**0.02[-0.02,0.05]**
Total events: 21 (Active treatment), 7 (Placebo)					
Heterogeneity: Tau^2=0; Chi^2=0.56, df=2(P=0.76); I^2=0%					
Test for overall effect: Z=0.92(P=0.36)					
18.7.2 Potent steroid: betamethasone dipropionate					
Elie 1983	0/10	0/10		4.57%	0[-0.17,0.17]
Jemec 2008 (P)	6/556	7/136		95.43%	-0.04[-0.08,-0]
Subtotal (95% CI)	**566**	**146**		**100%**	**-0.04[-0.08,-0]**
Total events: 6 (Active treatment), 7 (Placebo)					
Heterogeneity: Tau^2=0; Chi^2=0.2, df=1(P=0.65); I^2=0%					
Test for overall effect: Z=2.04(P=0.04)					
18.7.3 Potent steroid: betamethasone valerate					
Franz 1999	0/115	0/57		100%	0[-0.03,0.03]
Subtotal (95% CI)	**115**	**57**		**100%**	**0[-0.03,0.03]**
Total events: 0 (Active treatment), 0 (Placebo)					
Heterogeneity: Not applicable					
Test for overall effect: Not applicable					
18.7.4 Very potent steroid: amcinonide					
Ellis 1988	1/83	0/82		100%	0.01[-0.02,0.04]
Subtotal (95% CI)	**83**	**82**		**100%**	**0.01[-0.02,0.04]**
Total events: 1 (Active treatment), 0 (Placebo)					
Heterogeneity: Not applicable					
Test for overall effect: Z=0.72(P=0.47)					
18.7.5 Very potent steroid: clobetasol propionate					
Cook-Bolden 2010	0/41	1/40		2.8%	-0.02[-0.09,0.04]
Franz 2000	0/125	0/63		20.9%	0[-0.02,0.02]
Jarratt 2004	0/95	0/47		11.86%	0[-0.03,0.03]

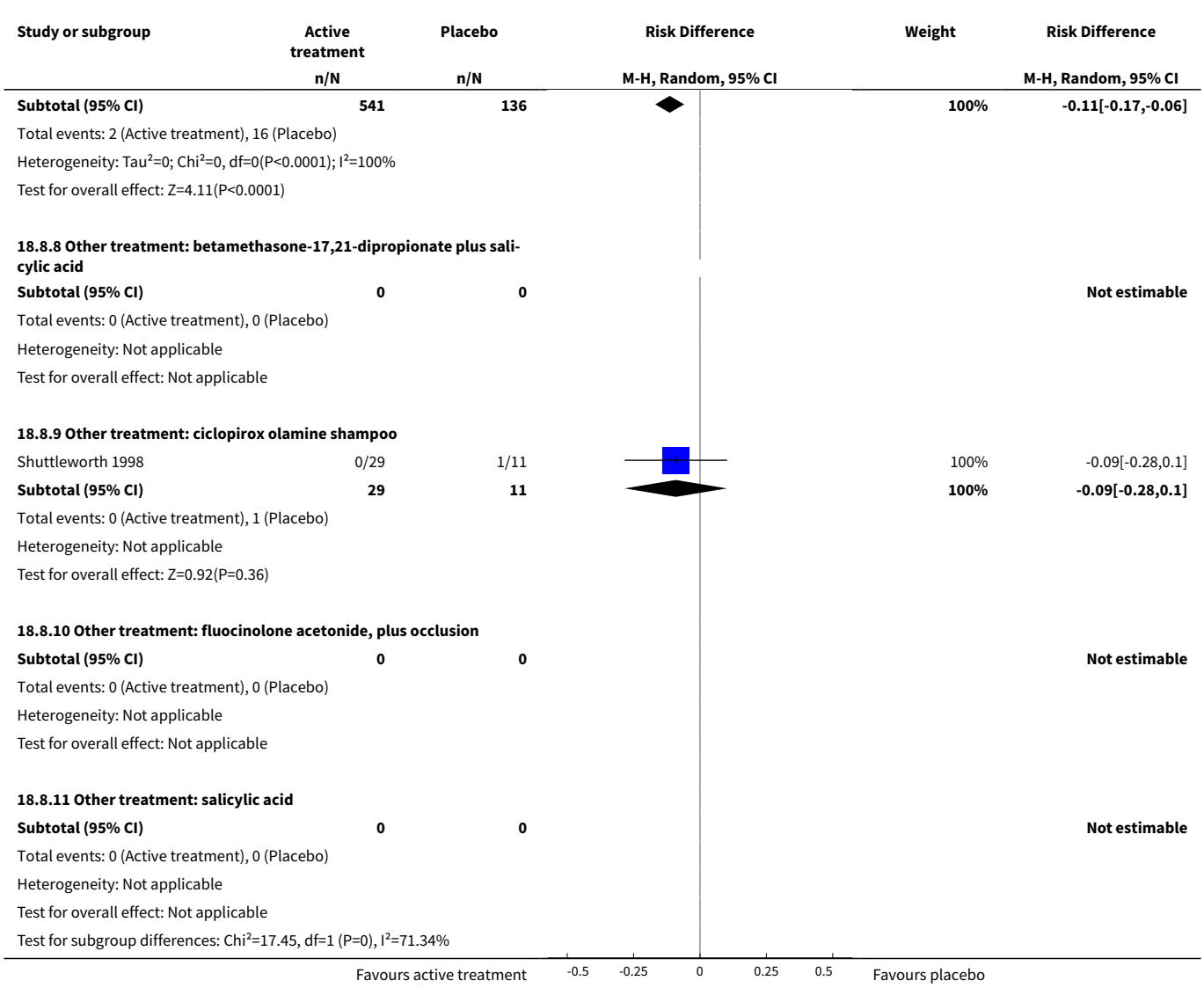




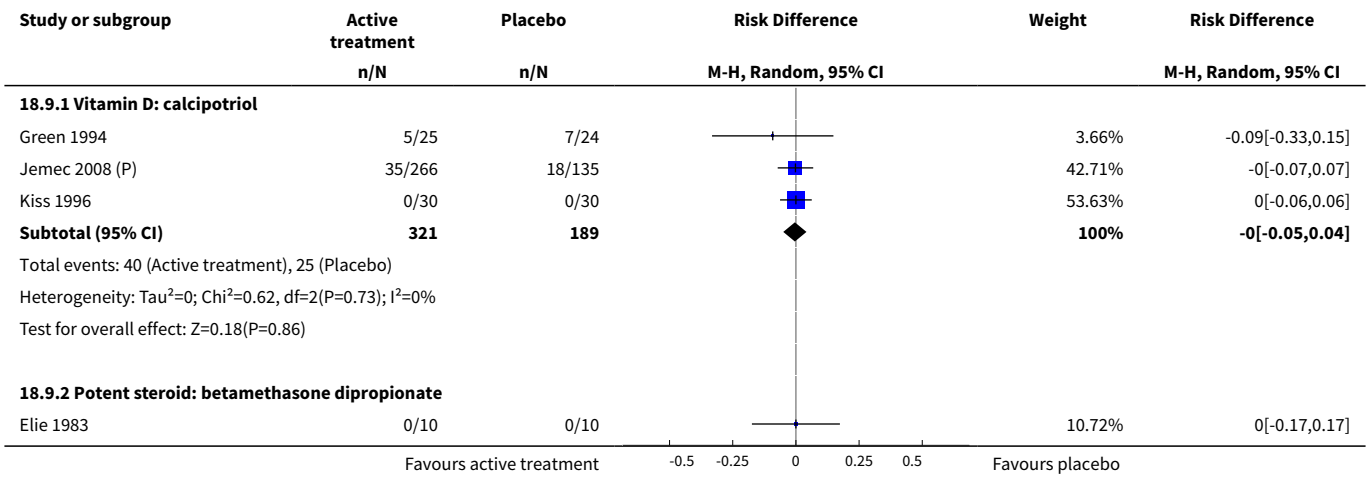
Analysis 18.8. Comparison 18 Scalp psoriasis: placebo-controlled trials, Outcome 8 Withdrawals due to treatment failure.

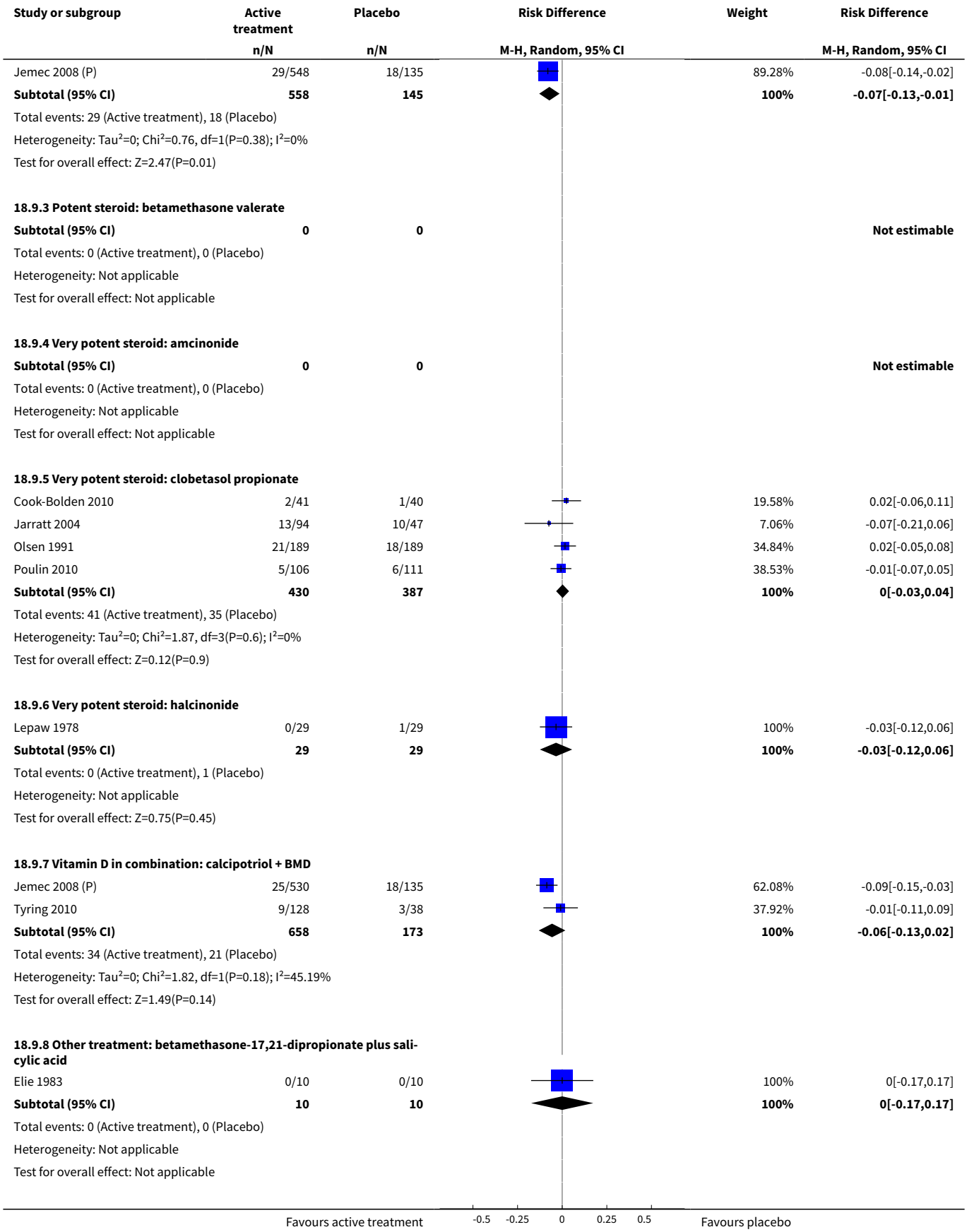
Study or subgroup	Active treatment n/N	Placebo n/N	Risk Difference M-H, Random, 95% CI	Weight	Risk Difference M-H, Random, 95% CI
18.8.1 Vitamin D: calcipotriol					
Green 1994	0/25	2/24		18.81%	-0.08[-0.21,0.05]
Jemec 2008 (P)	19/272	16/136		81.19%	-0.05[-0.11,0.01]
Subtotal (95% CI)	**297**	**160**		**100%**	**-0.05[-0.11,0]**
Total events: 19 (Active treatment), 18 (Placebo)					
Heterogeneity: Tau^2=0; Chi^2=0.24, df=1(P=0.62); I^2=0%					
Test for overall effect: Z=1.91(P=0.06)					
18.8.2 Potent steroid: betamethasone dipropionate					
Jemec 2008 (P)	9/556	16/136		100%	-0.1[-0.16,-0.05]
Subtotal (95% CI)	**556**	**136**		**100%**	**-0.1[-0.16,-0.05]**
Total events: 9 (Active treatment), 16 (Placebo)					
Heterogeneity: Not applicable					
Test for overall effect: Z=3.61(P=0)					
18.8.3 Potent steroid: betamethasone valerate					
Subtotal (95% CI)	**0**	**0**			**Not estimable**
Total events: 0 (Active treatment), 0 (Placebo)					
Heterogeneity: Not applicable					
Test for overall effect: Not applicable					
18.8.4 Very potent steroid: amcinonide					
Ellis 1988	0/83	1/82		100%	-0.01[-0.05,0.02]
Subtotal (95% CI)	**83**	**82**		**100%**	**-0.01[-0.05,0.02]**
Total events: 0 (Active treatment), 1 (Placebo)					
Heterogeneity: Not applicable					
Test for overall effect: Z=0.72(P=0.47)					
18.8.5 Very potent steroid: clobetasol propionate					
Cook-Bolden 2010	0/41	0/40		17.26%	0[-0.05,0.05]
Franz 2000	0/125	0/63		22.18%	0[-0.02,0.02]
Jarratt 2004	0/95	0/47		20.56%	0[-0.03,0.03]
Olsen 1991	2/189	17/189		18.07%	-0.08[-0.12,-0.04]
Poulin 2010	1/106	0/111		21.94%	0.01[-0.02,0.03]
Subtotal (95% CI)	**556**	**450**		**100%**	**-0.01[-0.05,0.02]**
Total events: 3 (Active treatment), 17 (Placebo)					
Heterogeneity: Tau^2=0; Chi^2=23.9, df=4(P<0.0001); I^2=83.27%					
Test for overall effect: Z=0.68(P=0.5)					
18.8.6 Very potent steroid: halcinonide					
Subtotal (95% CI)	**0**	**0**			**Not estimable**
Total events: 0 (Active treatment), 0 (Placebo)					
Heterogeneity: Not applicable					
Test for overall effect: Not applicable					
18.8.7 Vitamin D in combination: calcipotriol + BMD					
Jemec 2008 (P)	2/541	16/136		100%	-0.11[-0.17,-0.06]

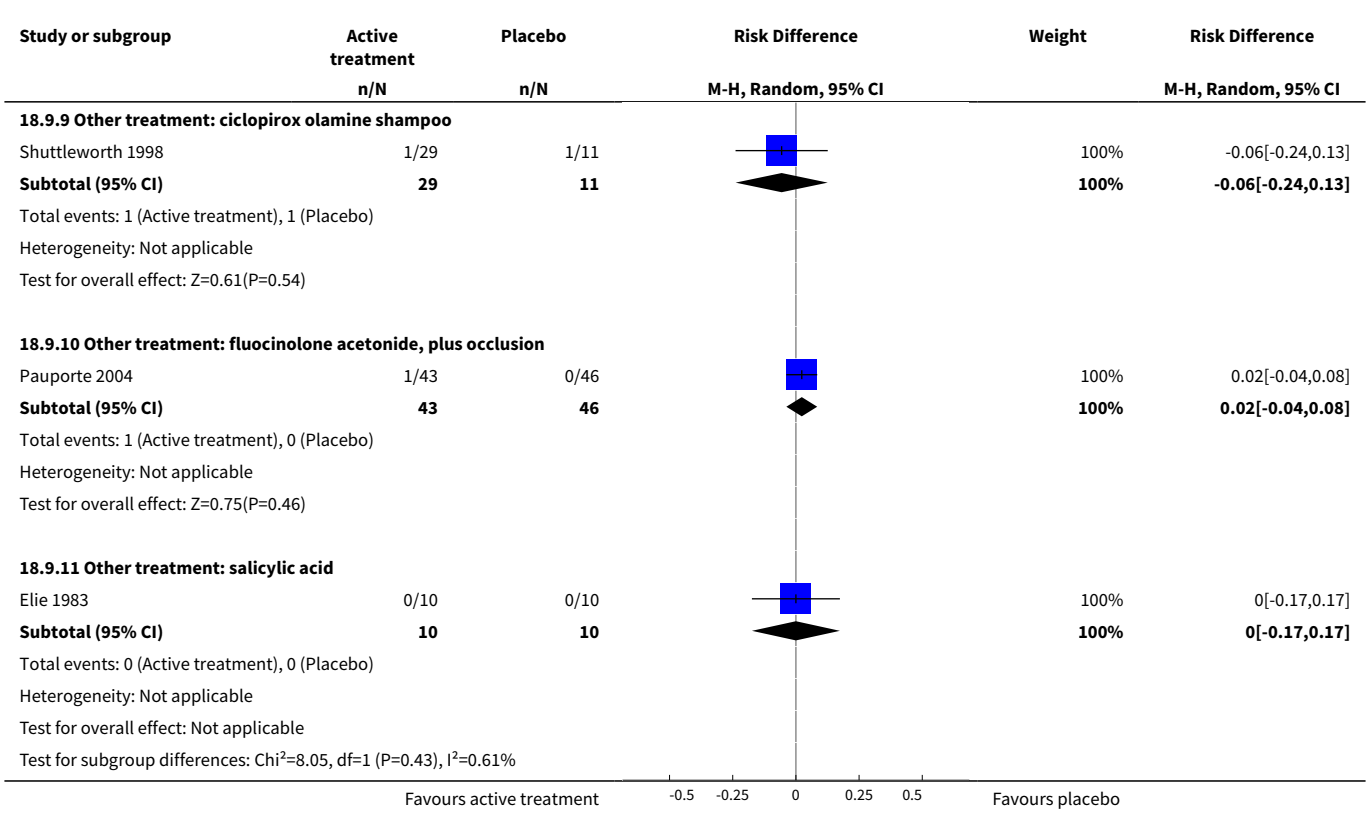




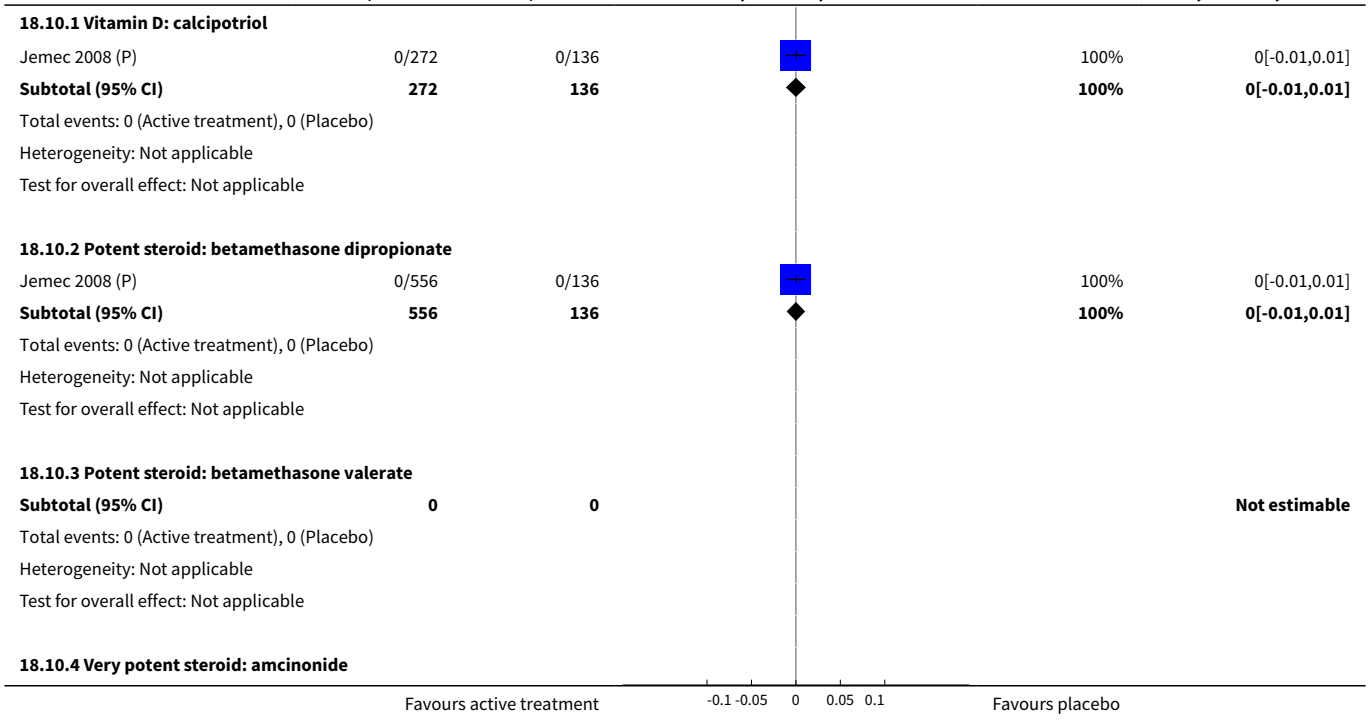
Analysis 18.9. Comparison 18 Scalp psoriasis: placebo-controlled trials, Outcome 9 Adverse events (local).

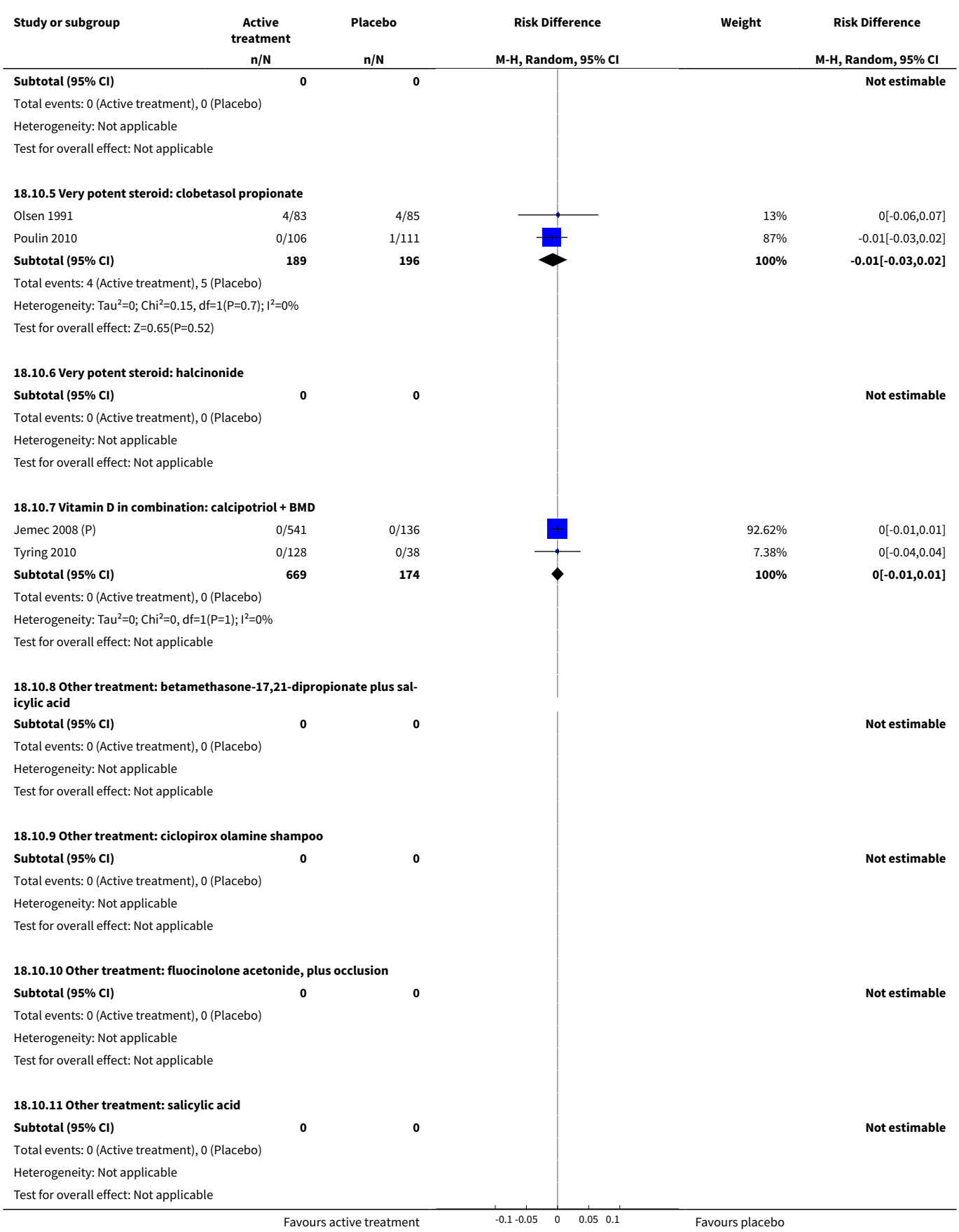


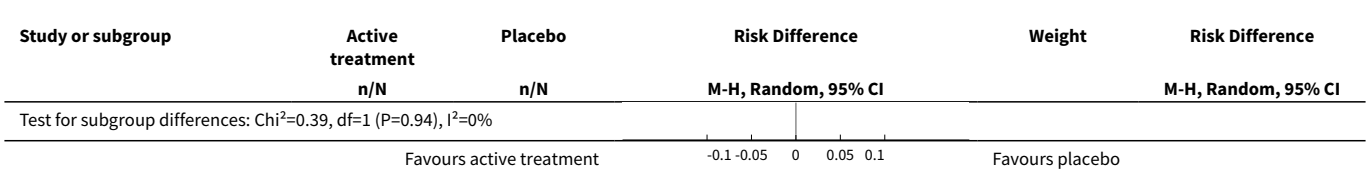




Analysis 18.10. Comparison 18 Scalp psoriasis: placebo-controlled trials, Outcome 10 Adverse events (systemic).







Comparison 19. Scalp psoriasis: vitamin D alone or in combination versus other treatments

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 IAGI	9		Std. Mean Difference (IV, Random, 95% CI)	Subtotals only
1.1 Vitamin D vs. corticosteroid (potent): calcipotriol vs. BMD	2	1676	Std. Mean Difference (IV, Random, 95% CI)	0.48 [0.32, 0.64]
1.2 Vitamin D vs. corticosteroid (potent): calcipotriol vs. BMV	2	510	Std. Mean Difference (IV, Random, 95% CI)	0.37 [0.20, 0.55]
1.3 Vitamin D vs. corticosteroid (very potent): calcipotriol vs. clobetasol propionate	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
1.4 Vitamin D + corticosteroid vs. corticosteroid: calcipotriol + BMD vs. BMD	3	2444	Std. Mean Difference (IV, Random, 95% CI)	-0.18 [-0.26, -0.10]
1.5 Vitamin D vs. vitamin D + corticosteroid: calcipotriol vs. calcipotriol + BMD	4	2581	Std. Mean Difference (IV, Random, 95% CI)	0.64 [0.44, 0.84]
1.6 Vitamin D vs. other treatments: calcipotriol vs. coal tar polytherapy	2	748	Std. Mean Difference (IV, Random, 95% CI)	-0.24 [-0.73, 0.25]
2 TSS	10		Std. Mean Difference (IV, Random, 95% CI)	Subtotals only
2.1 Vitamin D vs. corticosteroid (potent): calcipotriol vs. BMD	2	1676	Std. Mean Difference (IV, Random, 95% CI)	0.45 [0.28, 0.63]
2.2 Vitamin D vs. corticosteroid (potent): calcipotriol vs. BMV	2	487	Std. Mean Difference (IV, Random, 95% CI)	0.09 [-0.09, 0.27]
2.3 Vitamin D vs. corticosteroid (very potent): calcipotriol vs. clobetasol propionate	1	151	Std. Mean Difference (IV, Random, 95% CI)	0.37 [0.05, 0.69]
2.4 Vitamin D + corticosteroid vs. corticosteroid: calcipotriol + BMD vs. BMD	3	2444	Std. Mean Difference (IV, Random, 95% CI)	-0.19 [-0.27, -0.11]
2.5 Vitamin D vs. vitamin D + corticosteroid: calcipotriol vs. calcipotriol + BMD	3	1978	Std. Mean Difference (IV, Random, 95% CI)	0.70 [0.56, 0.84]
2.6 Vitamin D vs. other treatments: calcipotriol vs. coal tar polytherapy	3	925	Std. Mean Difference (IV, Random, 95% CI)	-0.30 [-0.84, 0.24]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
3 PASI	0		Std. Mean Difference (IV, Random, 95% CI)	Subtotals only
3.1 Vitamin D vs. corticosteroid (potent): calcipotriol vs. BMD	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
3.2 Vitamin D vs. corticosteroid (potent): calcipotriol vs. BMV	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
3.3 Vitamin D vs. corticosteroid (very potent): calcipotriol vs. clobetasol propionate	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
3.4 Vitamin D + corticosteroid vs. corticosteroid: calcipotriol + BMD vs. BMD	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
3.5 Vitamin D vs. vitamin D + corticosteroid: calcipotriol vs. calcipotriol + BMD	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
3.6 Vitamin D vs. other treatments: calcipotriol vs. coal tar polytherapy	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
4 PAGI	5		Std. Mean Difference (IV, Random, 95% CI)	Subtotals only
4.1 Vitamin D vs. corticosteroid (potent): calcipotriol vs. BMD	2	1654	Std. Mean Difference (IV, Random, 95% CI)	0.56 [0.31, 0.81]
4.2 Vitamin D vs. corticosteroid (potent): calcipotriol vs. BMV	1	468	Std. Mean Difference (IV, Random, 95% CI)	0.41 [0.22, 0.59]
4.3 Vitamin D vs. corticosteroid (very potent): calcipotriol vs. clobetasol propionate	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
4.4 Vitamin D + corticosteroid vs. corticosteroid: calcipotriol + BMD vs. BMD	3	2414	Std. Mean Difference (IV, Random, 95% CI)	-0.17 [-0.25, -0.09]
4.5 Vitamin D vs. vitamin D + corticosteroid: calcipotriol vs. calcipotriol + BMD	3	1952	Std. Mean Difference (IV, Random, 95% CI)	0.84 [0.61, 1.08]
4.6 Vitamin D vs. other treatments: calcipotriol vs. coal tar polytherapy	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
5 Combined end point (IAGI/TSS/PASI/PAGI)	11		Std. Mean Difference (IV, Random, 95% CI)	Subtotals only
5.1 Vitamin D vs. corticosteroid (potent): calcipotriol vs. BMD	2	1676	Std. Mean Difference (IV, Random, 95% CI)	0.48 [0.32, 0.64]
5.2 Vitamin D vs. corticosteroid (potent): calcipotriol vs. BMV	2	510	Std. Mean Difference (IV, Random, 95% CI)	0.37 [0.20, 0.55]

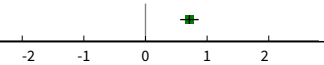
Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
5.3 Vitamin D vs. corticosteroid (very potent): calcipotriol vs. clobetasol propionate	1	151	Std. Mean Difference (IV, Random, 95% CI)	0.37 [0.05, 0.69]
5.4 Vitamin D + corticosteroid vs. corticosteroid: calcipotriol + BMD vs. BMD	3	2444	Std. Mean Difference (IV, Random, 95% CI)	-0.18 [-0.26, -0.10]
5.5 Vitamin D vs. vitamin D + corticosteroid: calcipotriol vs. calcipotriol + BMD	4	2581	Std. Mean Difference (IV, Random, 95% CI)	0.64 [0.44, 0.84]
5.6 Vitamin D vs. other treatments: calcipotriol vs. coal tar polytherapy	3	835	Std. Mean Difference (IV, Random, 95% CI)	-0.45 [-0.92, 0.02]
6 Total withdrawals	10		Risk Difference (M-H, Random, 95% CI)	Subtotals only
6.1 Vitamin D vs. corticosteroid (potent): calcipotriol vs. BMD	2	1676	Risk Difference (M-H, Random, 95% CI)	0.07 [-0.04, 0.18]
6.2 Vitamin D vs. corticosteroid (potent): calcipotriol vs. BMV	2	516	Risk Difference (M-H, Random, 95% CI)	0.04 [-0.00, 0.08]
6.3 Vitamin D vs. corticosteroid (very potent): calcipotriol vs. clobetasol propionate	2	194	Risk Difference (M-H, Random, 95% CI)	0.05 [-0.07, 0.18]
6.4 Vitamin D + corticosteroid vs. corticosteroid: calcipotriol + BMD vs. BMD	3	2444	Risk Difference (M-H, Random, 95% CI)	0.01 [-0.04, 0.06]
6.5 Vitamin D vs. vitamin D + corticosteroid: calcipotriol vs. calcipotriol + BMD	4	2847	Risk Difference (M-H, Random, 95% CI)	0.11 [0.05, 0.18]
6.6 Vitamin D vs. other treatments: calcipotriol vs. coal tar polytherapy	1	475	Risk Difference (M-H, Random, 95% CI)	0.01 [-0.07, 0.09]
7 Withdrawals due to adverse events	10		Risk Difference (M-H, Random, 95% CI)	Subtotals only
7.1 Vitamin D vs. corticosteroid (potent): calcipotriol vs. BMD	2	1676	Risk Difference (M-H, Random, 95% CI)	0.04 [-0.01, 0.09]
7.2 Vitamin D vs. corticosteroid (potent): calcipotriol vs. BMV	2	516	Risk Difference (M-H, Random, 95% CI)	0.03 [0.01, 0.06]
7.3 Vitamin D vs. corticosteroid (very potent): calcipotriol vs. clobetasol propionate	2	194	Risk Difference (M-H, Random, 95% CI)	0.05 [-0.05, 0.15]
7.4 Vitamin D + corticosteroid vs. corticosteroid: calcipotriol + BMD vs. BMD	3	2444	Risk Difference (M-H, Random, 95% CI)	-0.00 [-0.01, 0.01]
7.5 Vitamin D vs. vitamin D + corticosteroid: calcipotriol vs. calcipotriol + BMD	4	2847	Risk Difference (M-H, Random, 95% CI)	0.06 [0.02, 0.09]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
7.6 Vitamin D vs. other treatments: calcipotriol vs. coal tar polytherapy	1	445	Risk Difference (M-H, Random, 95% CI)	0.08 [0.02, 0.14]
8 Withdrawals due to treatment failure	8		Risk Difference (M-H, Random, 95% CI)	Subtotals only
8.1 Vitamin D vs. corticosteroid (potent): calcipotriol vs. BMD	2	1676	Risk Difference (M-H, Random, 95% CI)	0.03 [-0.01, 0.07]
8.2 Vitamin D vs. corticosteroid (potent): calcipotriol vs. BMV	2	516	Risk Difference (M-H, Random, 95% CI)	0.01 [-0.01, 0.03]
8.3 Vitamin D vs. corticosteroid (very potent): calcipotriol vs. clobetasol propionate	2	194	Risk Difference (M-H, Random, 95% CI)	0.01 [-0.02, 0.04]
8.4 Vitamin D + corticosteroid vs. corticosteroid: calcipotriol + BMD vs. BMD	3	2444	Risk Difference (M-H, Random, 95% CI)	-0.01 [-0.02, -0.00]
8.5 Vitamin D vs. vitamin D + corticosteroid: calcipotriol vs. calcipotriol + BMD	3	2535	Risk Difference (M-H, Random, 95% CI)	0.05 [0.01, 0.10]
8.6 Vitamin D vs. other treatments: calcipotriol vs. coal tar polytherapy	0	0	Risk Difference (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
9 Adverse events (local)	10		Risk Difference (M-H, Random, 95% CI)	Subtotals only
9.1 Vitamin D vs. corticosteroid (potent): calcipotriol vs. BMD	2	1652	Risk Difference (M-H, Random, 95% CI)	0.07 [0.04, 0.11]
9.2 Vitamin D vs. corticosteroid (potent): calcipotriol vs. BMV	2	516	Risk Difference (M-H, Random, 95% CI)	0.17 [0.01, 0.33]
9.3 Vitamin D vs. corticosteroid (very potent): calcipotriol vs. clobetasol propionate	2	194	Risk Difference (M-H, Random, 95% CI)	0.19 [0.10, 0.28]
9.4 Vitamin D + corticosteroid vs. corticosteroid: calcipotriol + BMD vs. BMD	3	2415	Risk Difference (M-H, Random, 95% CI)	-0.00 [-0.02, 0.01]
9.5 Vitamin D vs. vitamin D + corticosteroid: calcipotriol vs. calcipotriol + BMD	4	2801	Risk Difference (M-H, Random, 95% CI)	0.09 [0.06, 0.12]
9.6 Vitamin D vs. other treatments: calcipotriol vs. coal tar polytherapy	1	445	Risk Difference (M-H, Random, 95% CI)	0.24 [0.15, 0.33]
10 Adverse events (systemic)	6		Risk Difference (M-H, Random, 95% CI)	Subtotals only
10.1 Vitamin D vs. corticosteroid (potent): calcipotriol vs. BMD	2	1666	Risk Difference (M-H, Random, 95% CI)	0.0 [-0.00, 0.00]
10.2 Vitamin D vs. corticosteroid (potent): calcipotriol vs. BMV	1	474	Risk Difference (M-H, Random, 95% CI)	0.0 [-0.01, 0.01]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
10.3 Vitamin D vs. corticosteroid (very potent): calcipotriol vs. clobetasol propionate	1	151	Risk Difference (M-H, Random, 95% CI)	0.0 [-0.03, 0.03]
10.4 Vitamin D + corticosteroid vs. corticosteroid: calcipotriol + BMD vs. BMD	2	2216	Risk Difference (M-H, Random, 95% CI)	0.0 [-0.00, 0.00]
10.5 Vitamin D vs. vitamin D + corticosteroid: calcipotriol vs. calcipotriol + BMD	3	1970	Risk Difference (M-H, Random, 95% CI)	0.0 [-0.00, 0.00]
10.6 Vitamin D vs. other treatments: calcipotriol vs. coal tar polytherapy	1	445	Risk Difference (M-H, Random, 95% CI)	0.0 [-0.01, 0.01]

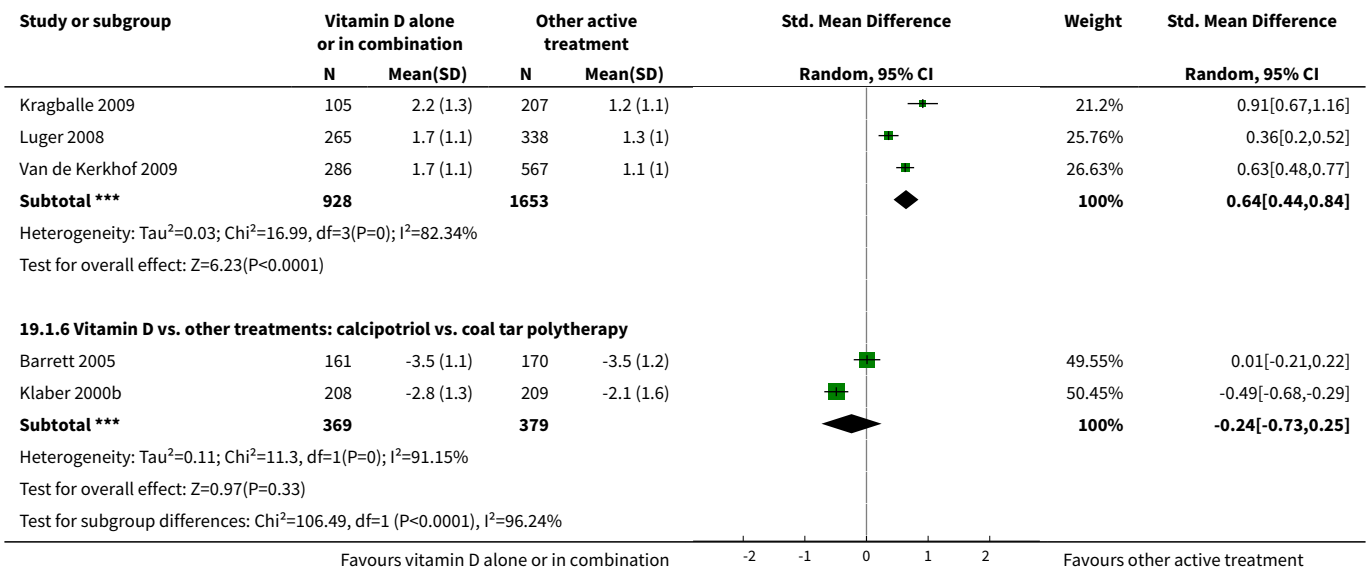
Analysis 19.1. Comparison 19 Scalp psoriasis: vitamin D alone or in combination versus other treatments, Outcome 1 IAGI.

Study or subgroup	Vitamin D alone or in combination		Other active treatment		Std. Mean Difference	Weight	Std. Mean Difference
	N	Mean(SD)	N	Mean(SD)	Random, 95% CI		Random, 95% CI
19.1.1 Vitamin D vs. corticosteroid (potent): calcipotriol vs. BMD							
Jemec 2008 (H)	272	1.9 (1.2)	556	1.2 (1.1)		49.46%	0.56[0.42,0.71]
Van de Kerkhof 2009	286	1.7 (1.1)	562	1.3 (1.1)		50.54%	0.4[0.25,0.54]
Subtotal ***	**558**		**1118**			**100%**	**0.48[0.32,0.64]**
Heterogeneity: Tau^2=0.01; Chi^2=2.53, df=1(P=0.11); I^2=60.42%							
Test for overall effect: Z=5.75(P<0.0001)							
19.1.2 Vitamin D vs. corticosteroid (potent): calcipotriol vs. BMV							
Duweb 2000	24	-2.6 (0.9)	18	-2.8 (0.9)		8.17%	0.22[-0.39,0.83]
Klaber 1994	236	-2.5 (1.1)	232	-2.9 (1)		91.83%	0.39[0.2,0.57]
Subtotal ***	**260**		**250**			**100%**	**0.37[0.2,0.55]**
Heterogeneity: Tau^2=0; Chi^2=0.27, df=1(P=0.61); I^2=0%							
Test for overall effect: Z=4.18(P<0.0001)							
19.1.3 Vitamin D vs. corticosteroid (very potent): calcipotriol vs. clobetasol propionate							
Subtotal ***	**0**		**0**				**Not estimable**
Heterogeneity: Not applicable							
Test for overall effect: Not applicable							
19.1.4 Vitamin D + corticosteroid vs. corticosteroid: calcipotriol + BMD vs. BMD							
Buckley 2008	108	0.8 (0.9)	110	1.1 (1)		8.88%	-0.26[-0.53,0]
Jemec 2008 (H)	541	1.1 (1)	556	1.2 (1.1)		44.98%	-0.13[-0.25,-0.02]
Van de Kerkhof 2009	567	1.1 (1)	562	1.3 (1.1)		46.14%	-0.21[-0.33,-0.1]
Subtotal ***	**1216**		**1228**			**100%**	**-0.18[-0.26,-0.1]**
Heterogeneity: Tau^2=0; Chi^2=1.27, df=2(P=0.53); I^2=0%							
Test for overall effect: Z=4.48(P<0.0001)							
19.1.5 Vitamin D vs. vitamin D + corticosteroid: calcipotriol vs. calcipotriol + BMD							
Jemec 2008 (H)	272	1.9 (1.2)	541	1.1 (1)		26.4%	0.71[0.56,0.86]

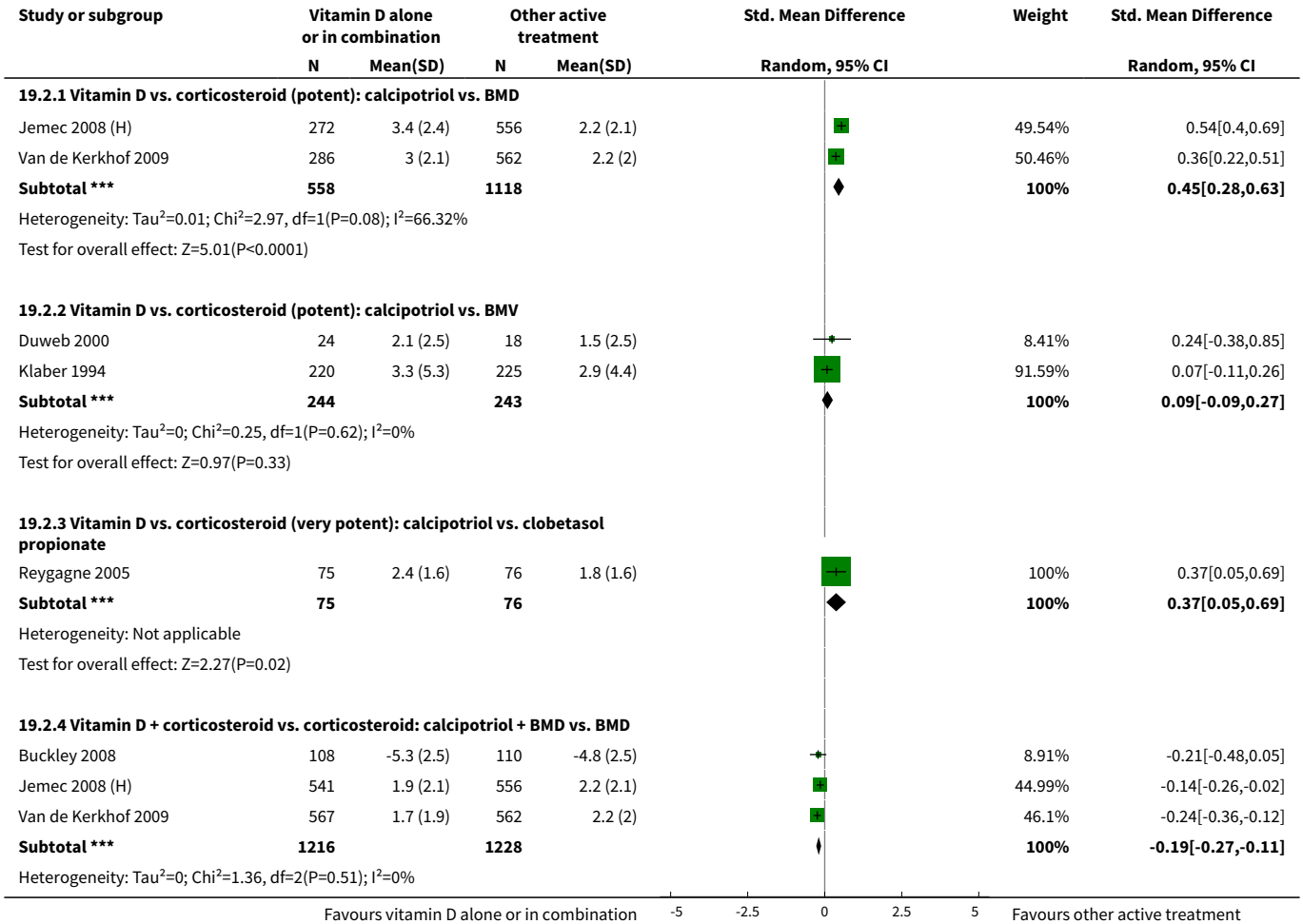


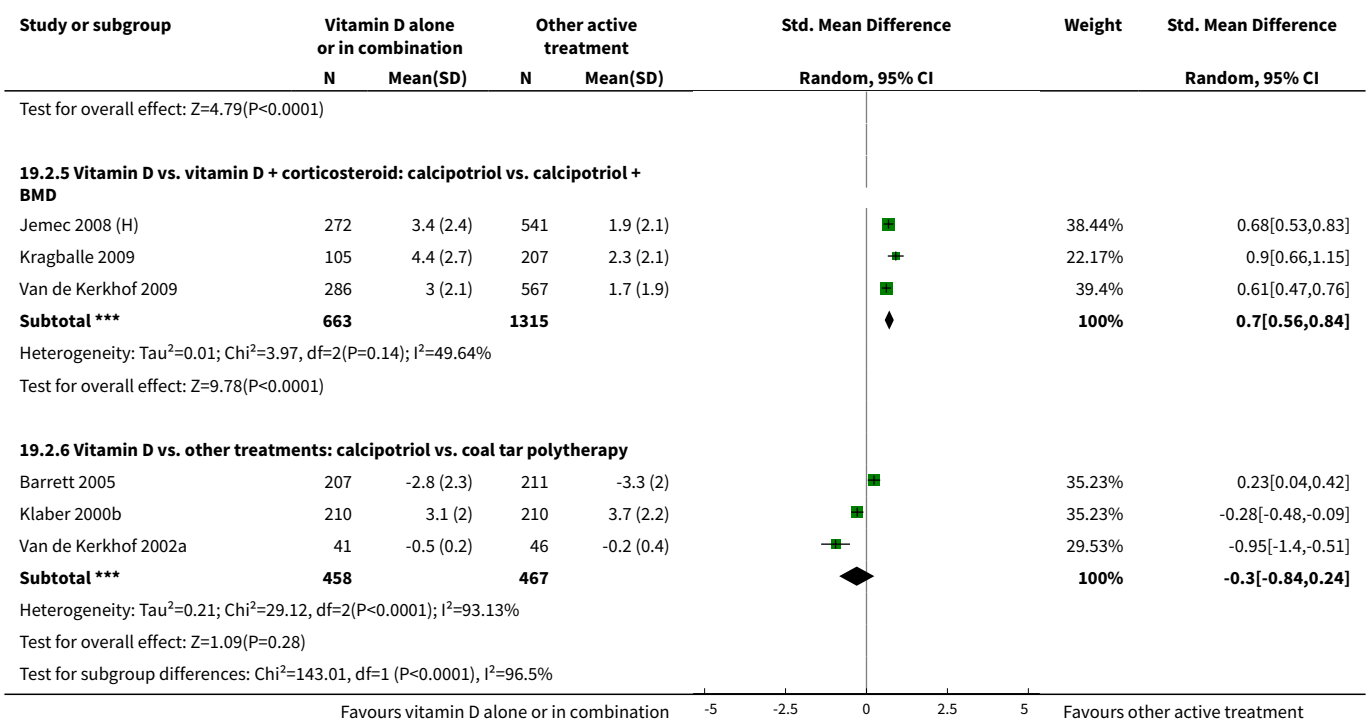
Favours vitamin D alone or in combination

Favours other active treatment

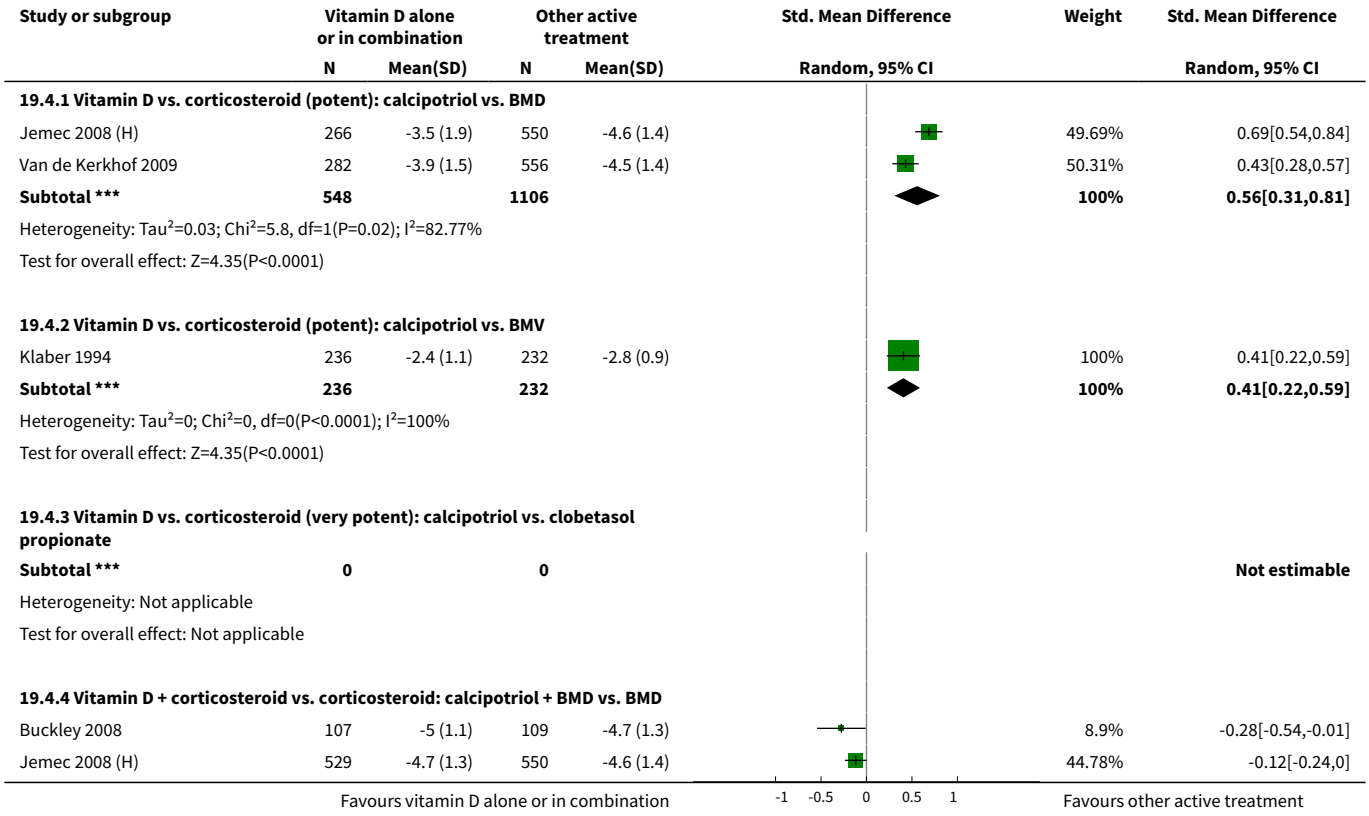


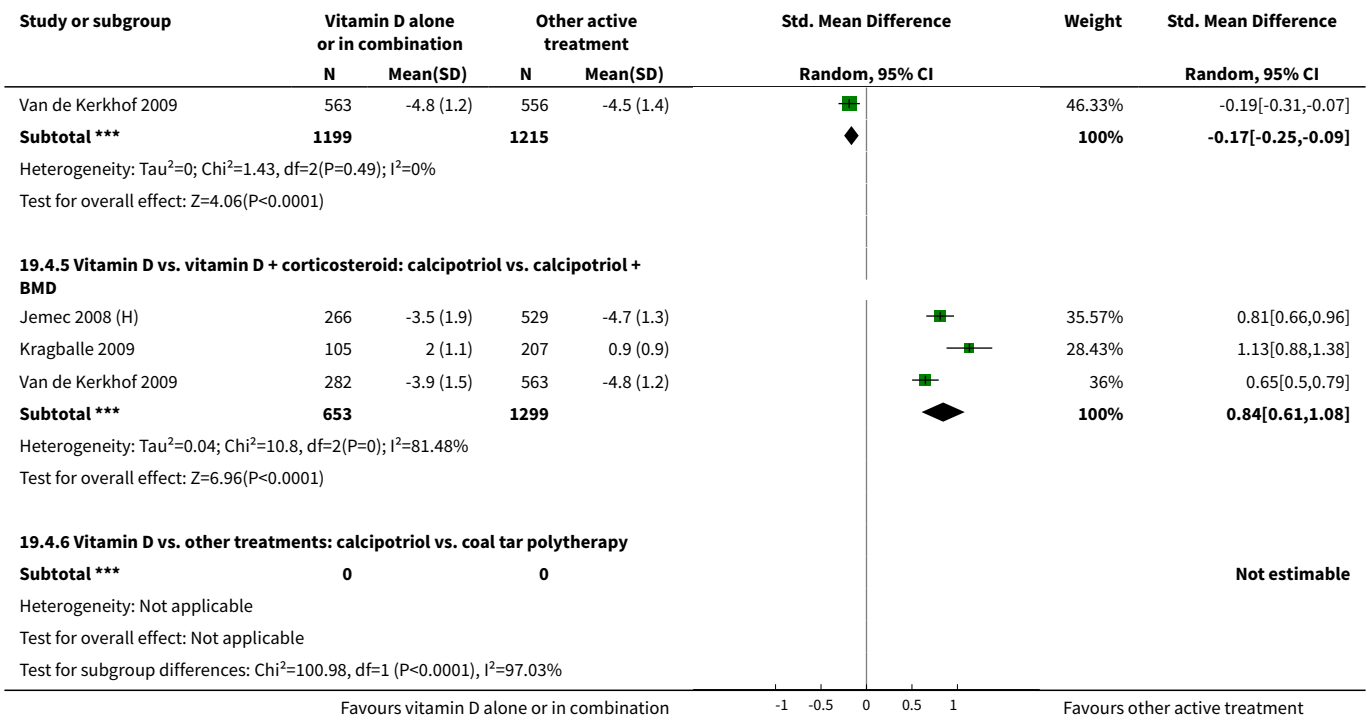
Analysis 19.2. Comparison 19 Scalp psoriasis: vitamin D alone or in combination versus other treatments, Outcome 2 TSS.



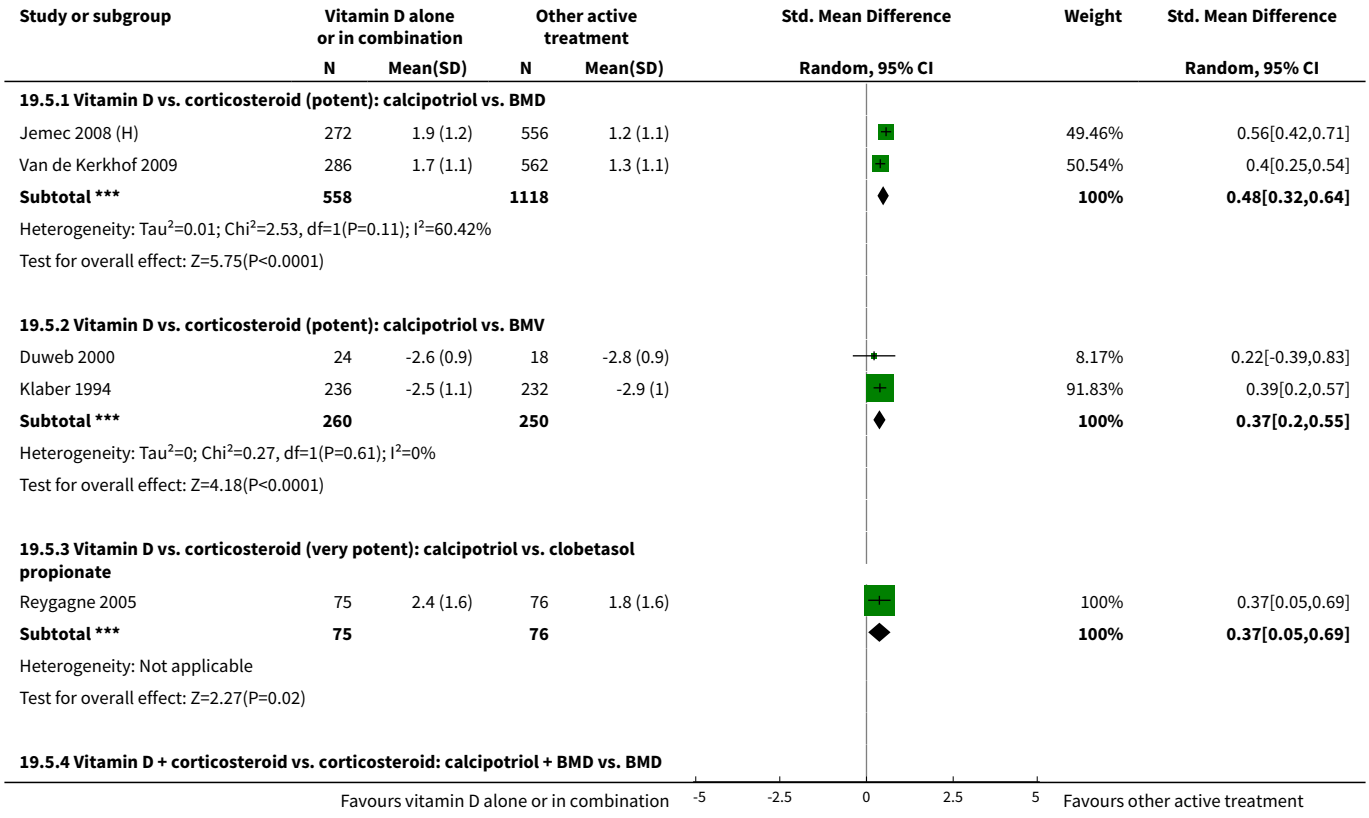


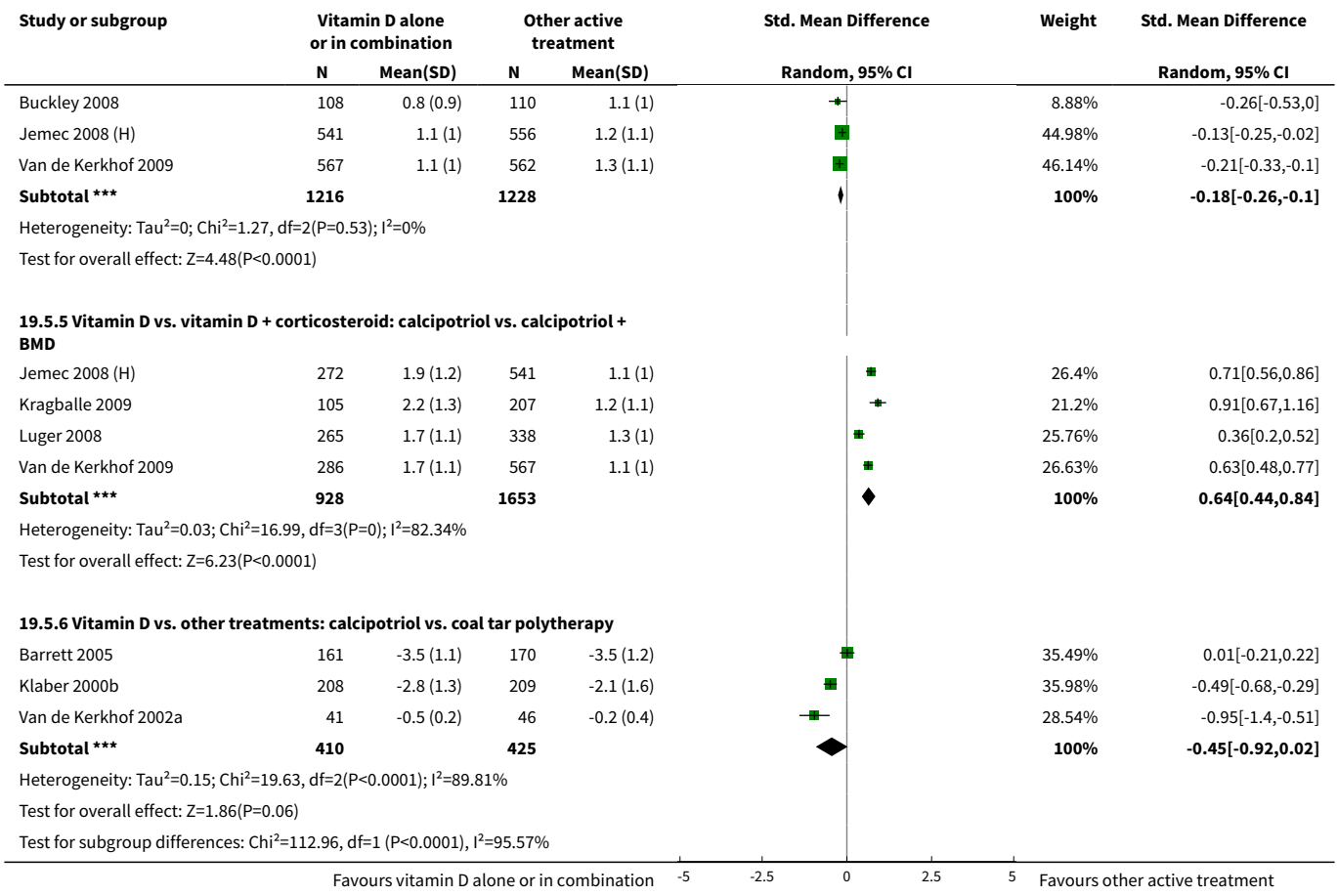
Analysis 19.4. Comparison 19 Scalp psoriasis: vitamin D alone or in combination versus other treatments, Outcome 4 PAGI.



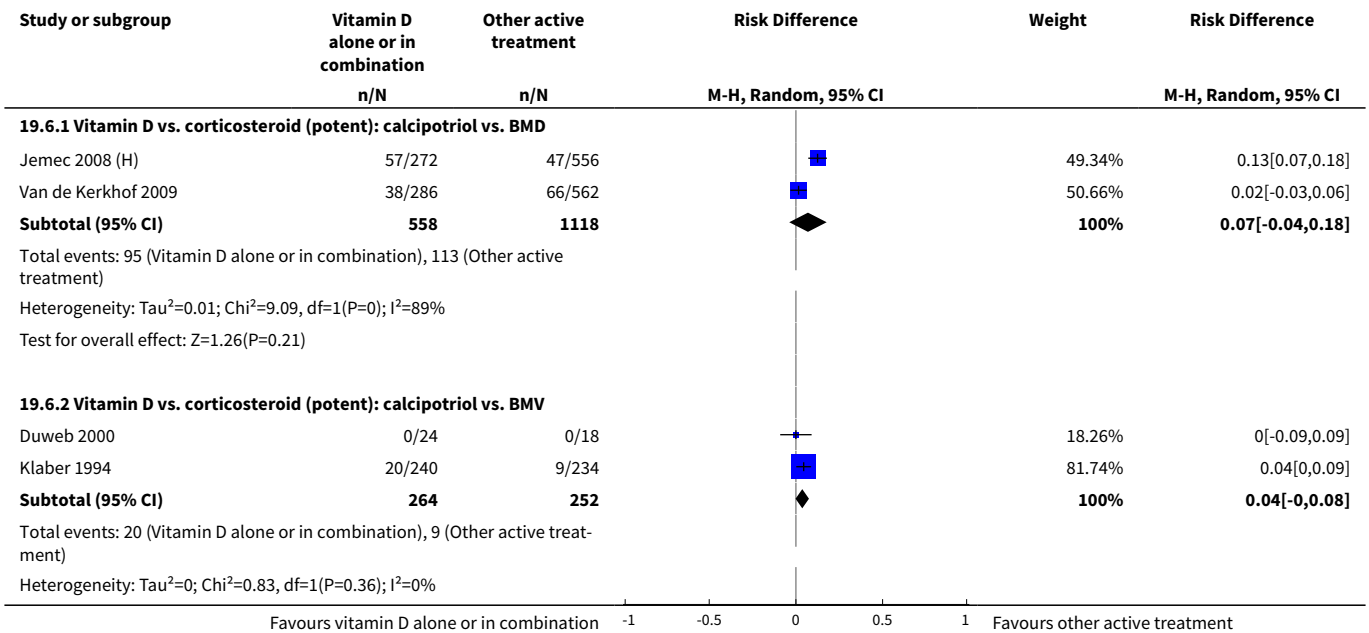


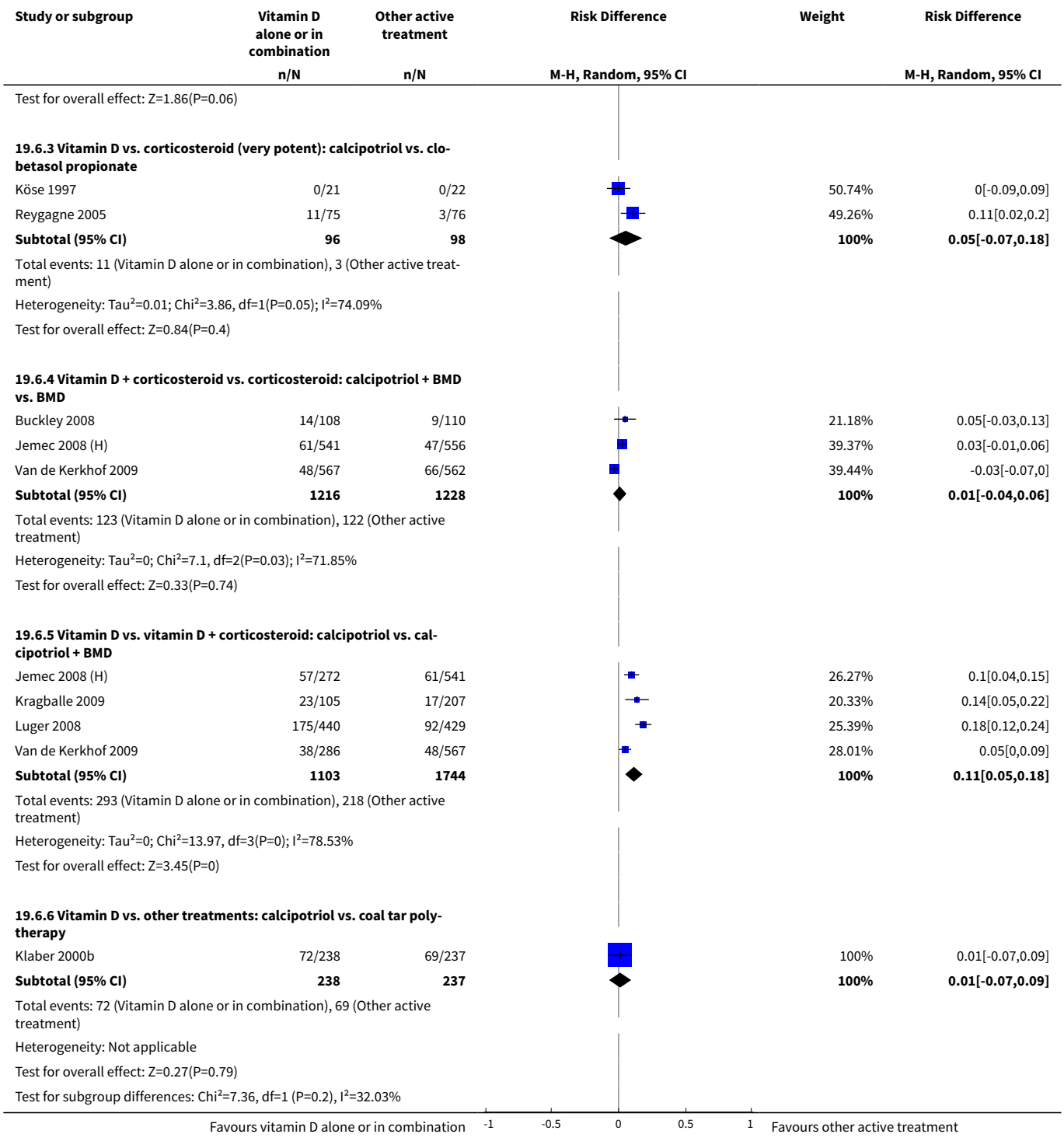
Analysis 19.5. Comparison 19 Scalp psoriasis: vitamin D alone or in combination versus other treatments, Outcome 5 Combined end point (IAGI/TSS/PASI/PAGI).





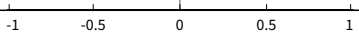
Analysis 19.6. Comparison 19 Scalp psoriasis: vitamin D alone or in combination versus other treatments, Outcome 6 Total withdrawals.





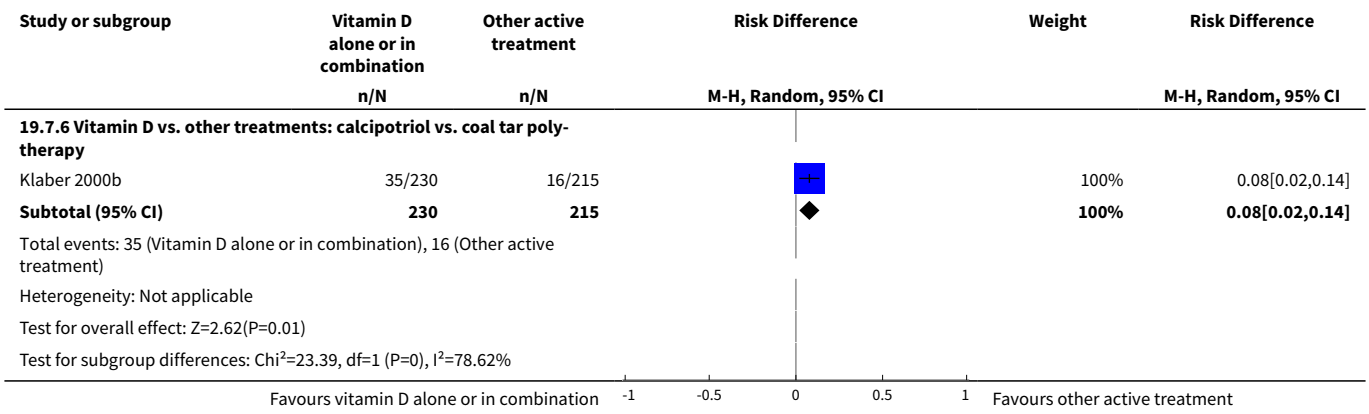
Analysis 19.7. Comparison 19 Scalp psoriasis: vitamin D alone or in combination versus other treatments, Outcome 7 Withdrawals due to adverse events.

Study or subgroup	Vitamin D alone or in combination	Other active treatment	Risk Difference	Weight	Risk Difference
	n/N	n/N	M-H, Random, 95% CI		M-H, Random, 95% CI
19.7.1 Vitamin D vs. corticosteroid (potent): calcipotriol vs. BMD					
Jemec 2008 (H)	20/272	6/556		47.07%	0.06[0.03,0.09]
Van de Kerkhof 2009	8/286	7/562		52.93%	0.02[-0.01,0.04]
Subtotal (95% CI)	**558**	**1118**		**100%**	**0.04[-0.01,0.09]**
Total events: 28 (Vitamin D alone or in combination), 13 (Other active treatment)					
Heterogeneity: Tau^2=0; Chi^2=6.74, df=1(P=0.01); I^2=85.15%					
Test for overall effect: Z=1.48(P=0.14)					
19.7.2 Vitamin D vs. corticosteroid (potent): calcipotriol vs. BMV					
Duweb 2000	0/24	0/18		9.29%	0[-0.09,0.09]
Klaber 1994	11/240	2/234		90.71%	0.04[0.01,0.07]
Subtotal (95% CI)	**264**	**252**		**100%**	**0.03[0.01,0.06]**
Total events: 11 (Vitamin D alone or in combination), 2 (Other active treatment)					
Heterogeneity: Tau^2=0; Chi^2=0.59, df=1(P=0.44); I^2=0%					
Test for overall effect: Z=2.4(P=0.02)					
19.7.3 Vitamin D vs. corticosteroid (very potent): calcipotriol vs. clobetasol propionate					
Köse 1997	0/21	0/22		46.53%	0[-0.09,0.09]
Reygagne 2005	7/75	0/76		53.47%	0.09[0.02,0.16]
Subtotal (95% CI)	**96**	**98**		**100%**	**0.05[-0.05,0.15]**
Total events: 7 (Vitamin D alone or in combination), 0 (Other active treatment)					
Heterogeneity: Tau^2=0; Chi^2=3.07, df=1(P=0.08); I^2=67.43%					
Test for overall effect: Z=1.01(P=0.31)					
19.7.4 Vitamin D + corticosteroid vs. corticosteroid: calcipotriol + BMD vs. BMD					
Buckley 2008	1/108	2/110		7.36%	-0.01[-0.04,0.02]
Jemec 2008 (H)	8/541	6/556		39.47%	0[-0.01,0.02]
Van de Kerkhof 2009	4/567	7/562		53.17%	-0.01[-0.02,0.01]
Subtotal (95% CI)	**1216**	**1228**		**100%**	**-0[-0.01,0.01]**
Total events: 13 (Vitamin D alone or in combination), 15 (Other active treatment)					
Heterogeneity: Tau^2=0; Chi^2=1.32, df=2(P=0.52); I^2=0%					
Test for overall effect: Z=0.46(P=0.65)					
19.7.5 Vitamin D vs. vitamin D + corticosteroid: calcipotriol vs. calcipotriol + BMD					
Jemec 2008 (H)	20/272	8/541		25.73%	0.06[0.03,0.09]
Kragballe 2009	9/105	2/207		18.17%	0.08[0.02,0.13]
Luger 2008	44/440	9/429		26.26%	0.08[0.05,0.11]
Van de Kerkhof 2009	8/286	4/567		29.83%	0.02[0,0.04]
Subtotal (95% CI)	**1103**	**1744**		**100%**	**0.06[0.02,0.09]**
Total events: 81 (Vitamin D alone or in combination), 23 (Other active treatment)					
Heterogeneity: Tau^2=0; Chi^2=14.23, df=3(P=0); I^2=78.92%					
Test for overall effect: Z=3.13(P=0)					

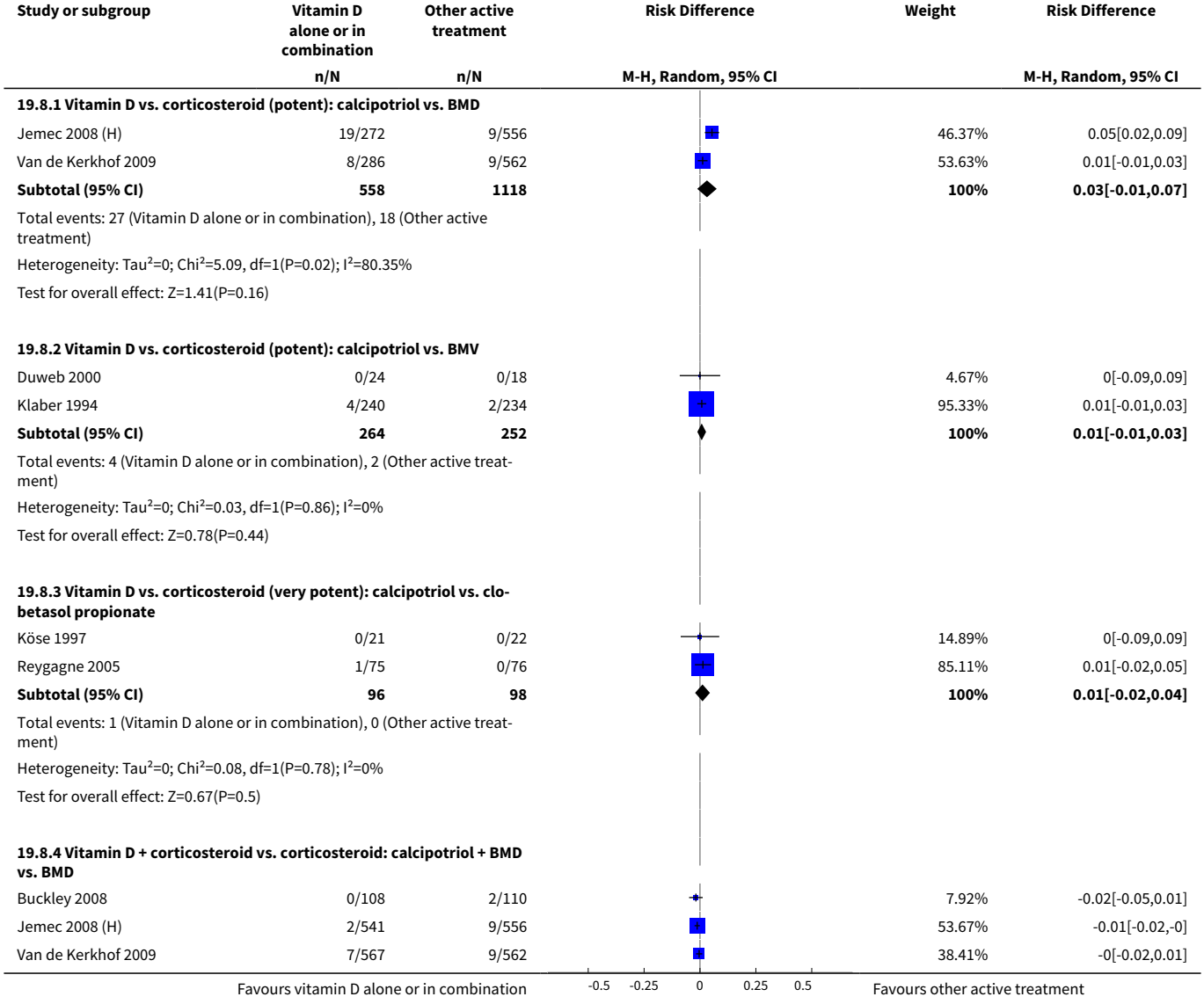


Favours vitamin D alone or in combination

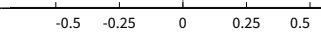
Favours other active treatment



Analysis 19.8. Comparison 19 Scalp psoriasis: vitamin D alone or in combination versus other treatments, Outcome 8 Withdrawals due to treatment failure.



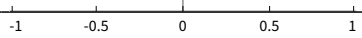
Study or subgroup	Vitamin D alone or in combination n/N	Other active treatment n/N	Risk Difference M-H, Random, 95% CI	Weight	Risk Difference M-H, Random, 95% CI
Subtotal (95% CI)	**1216**	**1228**		**100%**	**-0.01[-0.02,-0]**
Total events: 9 (Vitamin D alone or in combination), 20 (Other active treatment)					
Heterogeneity: Tau^2=0; Chi^2=1.27, df=2(P=0.53); I^2=0%					
Test for overall effect: Z=2.19(P=0.03)					
19.8.5 Vitamin D vs. vitamin D + corticosteroid: calcipotriol vs. calcipotriol + BMD					
Jemec 2008 (H)	19/272	2/541		32.85%	0.07[0.04,0.1]
Luger 2008	51/440	14/429		31.77%	0.08[0.05,0.12]
Van de Kerkhof 2009	8/286	7/567		35.38%	0.02[-0.01,0.04]
Subtotal (95% CI)	**998**	**1537**		**100%**	**0.05[0.01,0.1]**
Total events: 78 (Vitamin D alone or in combination), 23 (Other active treatment)					
Heterogeneity: Tau^2=0; Chi^2=16.89, df=2(P=0); I^2=88.16%					
Test for overall effect: Z=2.21(P=0.03)					
19.8.6 Vitamin D vs. other treatments: calcipotriol vs. coal tar polytherapy					
Subtotal (95% CI)	**0**	**0**			**Not estimable**
Total events: 0 (Vitamin D alone or in combination), 0 (Other active treatment)					
Heterogeneity: Not applicable					
Test for overall effect: Not applicable					
Test for subgroup differences: Chi^2=11.94, df=1 (P=0.02), I^2=66.5%					



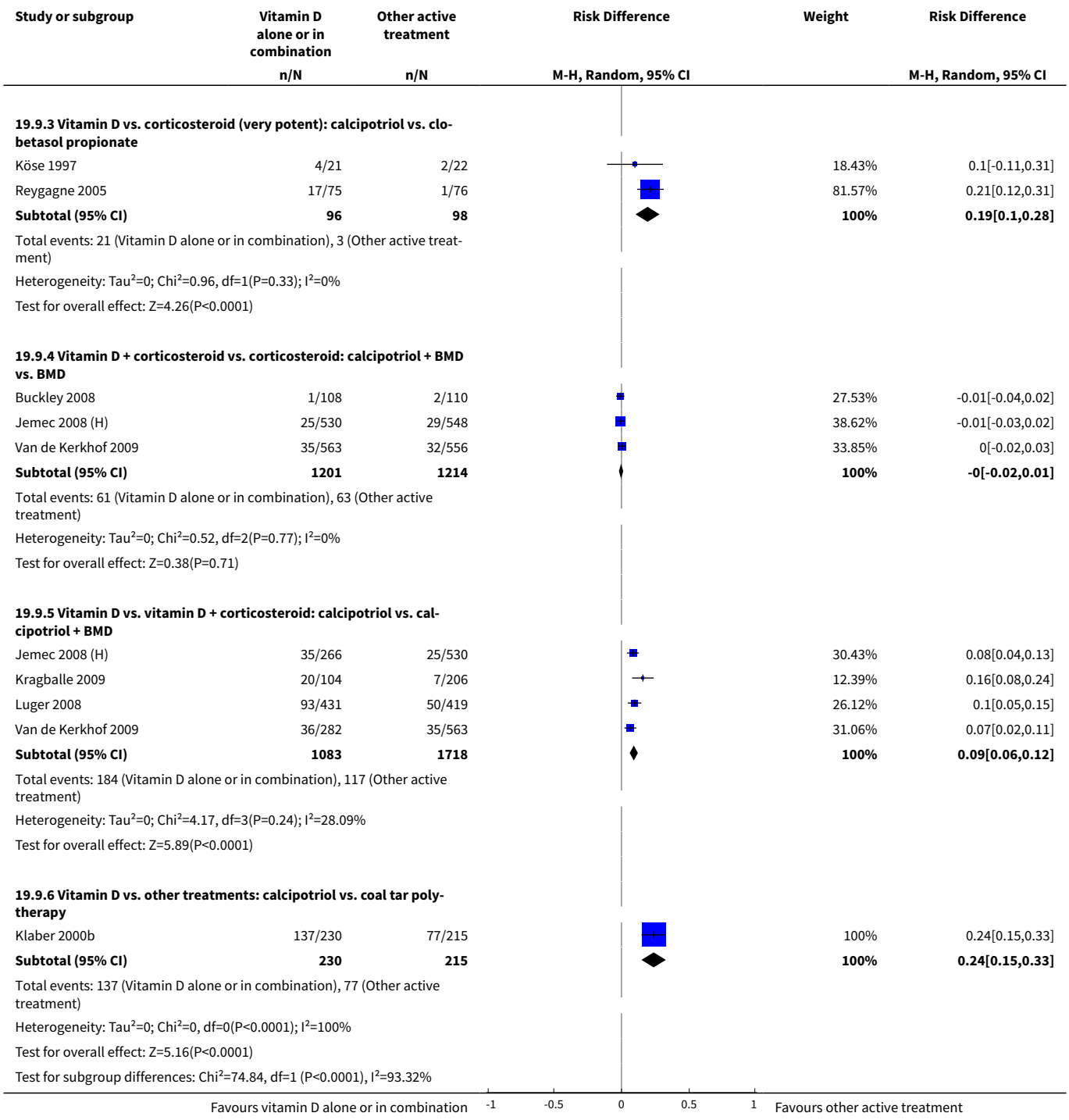
Favours vitamin D alone or in combination — Favours other active treatment

Analysis 19.9. Comparison 19 Scalp psoriasis: vitamin D alone or in combination versus other treatments, Outcome 9 Adverse events (local).

Study or subgroup	Vitamin D alone or in combination n/N	Other active treatment n/N	Risk Difference M-H, Random, 95% CI	Weight	Risk Difference M-H, Random, 95% CI
19.9.1 Vitamin D vs. corticosteroid (potent): calcipotriol vs. BMD					
Jemec 2008 (H)	35/266	29/548		48.59%	0.08[0.03,0.12]
Van de Kerkhof 2009	36/282	32/556		51.41%	0.07[0.03,0.11]
Subtotal (95% CI)	**548**	**1104**		**100%**	**0.07[0.04,0.11]**
Total events: 71 (Vitamin D alone or in combination), 61 (Other active treatment)					
Heterogeneity: Tau^2=0; Chi^2=0.07, df=1(P=0.79); I^2=0%					
Test for overall effect: Z=4.67(P<0.0001)					
19.9.2 Vitamin D vs. corticosteroid (potent): calcipotriol vs. BMV					
Duweb 2000	2/24	0/18		43.34%	0.08[-0.05,0.22]
Klaber 1994	84/240	26/234		56.66%	0.24[0.17,0.31]
Subtotal (95% CI)	**264**	**252**		**100%**	**0.17[0.01,0.33]**
Total events: 86 (Vitamin D alone or in combination), 26 (Other active treatment)					
Heterogeneity: Tau^2=0.01; Chi^2=4.25, df=1(P=0.04); I^2=76.48%					
Test for overall effect: Z=2.11(P=0.03)					

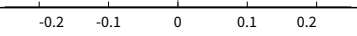


Favours vitamin D alone or in combination — Favours other active treatment



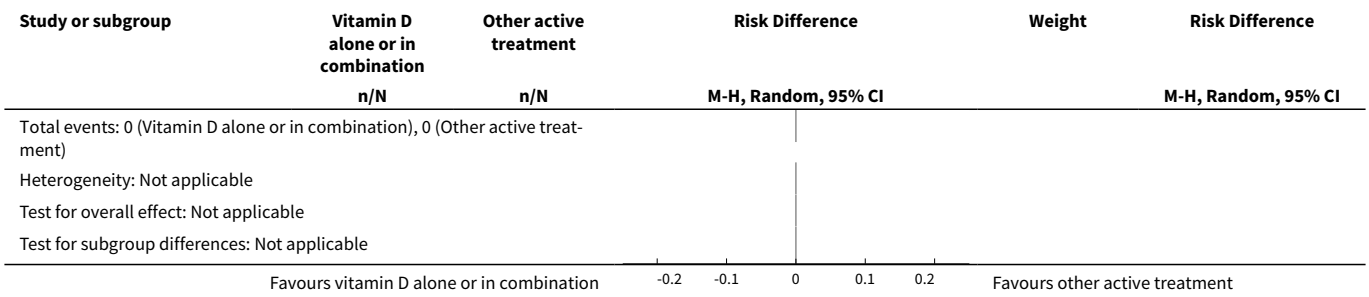
Analysis 19.10. Comparison 19 Scalp psoriasis: vitamin D alone or in combination versus other treatments, Outcome 10 Adverse events (systemic).

Study or subgroup	Vitamin D alone or in combination n/N	Other active treatment n/N	Risk Difference M-H, Random, 95% CI	Weight	Risk Difference M-H, Random, 95% CI
19.10.1 Vitamin D vs. corticosteroid (potent): calcipotriol vs. BMD					
Jemec 2008 (H)	0/272	0/556		48.56%	0[-0.01,0.01]
Van de Kerkhof 2009	0/282	0/556		51.44%	0[-0.01,0.01]
Subtotal (95% CI)	**554**	**1112**		**100%**	**0[-0,0]**
Total events: 0 (Vitamin D alone or in combination), 0 (Other active treatment)					
Heterogeneity: $Tau^2=0$; $Chi^2=0$, df=1(P=1); $I^2=0\%$					
Test for overall effect: Not applicable					
19.10.2 Vitamin D vs. corticosteroid (potent): calcipotriol vs. BMV					
Klaber 1994	0/240	0/234		100%	0[-0.01,0.01]
Subtotal (95% CI)	**240**	**234**		**100%**	**0[-0.01,0.01]**
Total events: 0 (Vitamin D alone or in combination), 0 (Other active treatment)					
Heterogeneity: Not applicable					
Test for overall effect: Not applicable					
19.10.3 Vitamin D vs. corticosteroid (very potent): calcipotriol vs. clobetasol propionate					
Reygagne 2005	0/75	0/76		100%	0[-0.03,0.03]
Subtotal (95% CI)	**75**	**76**		**100%**	**0[-0.03,0.03]**
Total events: 0 (Vitamin D alone or in combination), 0 (Other active treatment)					
Heterogeneity: Not applicable					
Test for overall effect: Not applicable					
19.10.4 Vitamin D + corticosteroid vs. corticosteroid: calcipotriol + BMD vs. BMD					
Jemec 2008 (H)	0/541	0/556		49%	0[-0,0]
Van de Kerkhof 2009	0/563	0/556		51%	0[-0,0]
Subtotal (95% CI)	**1104**	**1112**		**100%**	**0[-0,0]**
Total events: 0 (Vitamin D alone or in combination), 0 (Other active treatment)					
Heterogeneity: $Tau^2=0$; $Chi^2=0$, df=1(P=1); $I^2=0\%$					
Test for overall effect: Not applicable					
19.10.5 Vitamin D vs. vitamin D + corticosteroid: calcipotriol vs. calcipotriol + BMD					
Jemec 2008 (H)	0/272	0/541		44.91%	0[-0.01,0.01]
Kragballe 2009	0/105	0/207		6.76%	0[-0.01,0.01]
Van de Kerkhof 2009	0/282	0/563		48.33%	0[-0.01,0.01]
Subtotal (95% CI)	**659**	**1311**		**100%**	**0[-0,0]**
Total events: 0 (Vitamin D alone or in combination), 0 (Other active treatment)					
Heterogeneity: $Tau^2=0$; $Chi^2=0$, df=2(P=1); $I^2=0\%$					
Test for overall effect: Not applicable					
19.10.6 Vitamin D vs. other treatments: calcipotriol vs. coal tar polytherapy					
Klaber 2000b	0/230	0/215		100%	0[-0.01,0.01]
Subtotal (95% CI)	**230**	**215**		**100%**	**0[-0.01,0.01]**



Favours vitamin D alone or in combination

Favours other active treatment



ADDITIONAL TABLES

Table 1. List of acronyms

Acronym	Full name
BC	baseline comparability demonstrated (clinical/demographic)
BD	twice daily
BMD	betamethasone dipropionate
BMV	betamethasone valerate
BSA	Body Surface Area
Btw-patient	Between-patient
CI	confidence interval
dys	days
EQ-5D	EuroQOL
FU	follow up (includes treatment period)
I^2	heterogeneity statistic
IAGI	Investigator Assessment of Global Improvement (change score)
IGA	Investigator Global Assessment (static score)
IQR	interquartile range
ISGA	Investigator's Static Global Assessment Score
LAE	local adverse effects
LCD	liquor carbonis distillate
LF	loss to follow up (per cent of participants randomised, not contributing to primary outcome measure)
MEMS	Medication Event Monitoring System

Table 1. List of acronyms *(Continued)*

mPASI	modified Psoriasis Area Severity Index
NA	not available/not applicable
NR	not reported
OD	once daily
OM	once in the morning
ON	once at night
ODS	overall disease severity
PAGI	Patient Assessment of Global Improvement (change score)
PASI	Psoriasis Area Severity Index
PDI	Psoriasis Disability Index
PGA	Patient Global Assessment (static score)
PMAQ-3w	Medication Adherence Questionnaire, version 3W
pt	point
QOL	quality of life
RD	risk difference
SD	standard deviation
SMD	standardised mean difference
TCP	two-compound product
TD	three times daily
TLPSS	Total Local Psoriasis Severity Score
TSS	Total Severity Score/total sum score
UV	ultra violet
VDRE	Vitamin D-Responsive Element
wks	weeks
yrs	years

Table 2. Overview of outcome measures on effectiveness

Outcome	Acronym	Construct	Scale, minimum	Scale, maximum	Notes

Table 2. Overview of outcome measures on effectiveness *(Continued)*

* Investigator's Assessment of Overall Global Improvement	IAGI	Improvement from baseline variably defined. Common taxonomy ranges from worse to cleared	4-pt	7-pt	Calculated means and standard deviations by assigning zero to 'worse' (or equivalent). Higher scores indicate greater improvement
Investigator's Global Assessment of Disease Severity	IGA	Static equivalent of the IAGI	4-pt	7-pt	Calculated means and standard deviations by assigning zero to 'clear' (or equivalent). Higher scores indicate more severe disease
Total Severity Score	TSS	Redness (erythema), thickness (infiltration) and scaling (sometimes also itching (pruritis)) of target plaque(s). Scored separately then summed	0 to 3	0 to 24	Also known as the Local Psoriasis Severity Index or the Total Sum Score. Higher scores indicate more severe disease
Psoriasis Area and Severity Index	PASI	Redness, thickness, and scaliness of the lesions (each graded on a 0 to 4 scale), weighted by the area of involvement (0 to 6) and summed	0 to 68 (without head)	0 to 72 (including head)	Higher scores indicate more severe disease
* Patient's Assessment of Overall Global Improvement	PAGI	Assessed as IAGI	4-pt	7-pt	Less often reported than IAGI. Majority of included trials use 5-pt scale
Patient's Global Assessment of Disease Severity	PGA	Assessed as IGA	4-pt	5-pt	Rarely reported (5/177 studies)

* IAGI/PAGI data are entered as a negative values; thus, a reduction denotes a positive improvement for the active treatment consistent with TSS and PASI measures.

Table 3. Summary of imputed standard deviation values

Type of study/score	Placebo IAGI (change)/ IGA (end point)	Placebo TSS	Placebo PASI	Placebo PAGI (change)/ PGA (end point)	H2H IAGI (change)/ IGA (end point)	H2H TSS	H2H PASI	H2H PAGI (change)/ PGA (end point)
Between-patient (end point)	0.93	1.33	3.76	1.13	1.01	1.65	3.61	1.12
Within-patient (end point)	1.08	1.49	7.17	NA	NA	1.50	2.58	NA
Between-patient (change)	1.17	1.52	5.75	1.31	1.10	1.73	7.85	1.20
Within-patient (change)	1.02	1.58	NA	1.53	0.96	1.94	NA	0.83
Within-patient (% change)	NA	0.18	NA	NA	NA	NA	NA	NA
Between-patient (% change)	NA	NA	0.37	NA	NA	0.13	0.33	NA
Scalp between-patient (end point)	1.08	1.74	NA	1.06	1.06	1.94	NA	1.18
Scalp within-patient (end point)	1.33	NA	NA	NA	NA	NA	NA	NA
Scalp between-patient (change)	1.20	NA	NA	1.28	1.30	1.75	NA	1.20
Scalp between-patient (% change)	NA	NA	NA	NA	NA	0.25	NA	NA

NA: not available; H2H: head-to-head; IGA [PGA]: Investigator [Patient] Global Assessment of Disease Severity;

IAGI [PAGI]: Investigator (patient) Assessment of Global Improvement; TSS: Total Severity Score; PASI: Psoriasis Area and Severity Index

Table 4. Overview of analyses: evidence of effectiveness outcomes

Comparison No.	Comparison Label	No. studies (NB: a study may contribute to more than one comparison)	Per cent studies with between-patient design	No. participants
01	Vitamin D analogues vs. placebo	30	60%	4986
02	Corticosteroid (potent) vs. placebo	13	85%	2216
03	Corticosteroid (very potent) vs. placebo	10	70%	1264
04	Dithranol vs. placebo	3	0%	47
05	Vitamin D combination products vs. placebo	5	100%	2058
06	Other treatment vs. placebo	26	46%	1450
07	Vitamin D analogues vs. corticosteroid (potent)	14	64%	3542
08	Vitamin D analogues vs. corticosteroid (very potent)	2	100%	82
09	Vitamin D combined with corticosteroid vs. corticosteroid	5	100%	2113
10	Vitamin D alone or in combination vs. dithranol	8	88%	1284
11	Vitamin D alone or in combination vs. other vitamin D analogue	4	75%	513
12	Vitamin D alone or in combination vs. vitamin D + corticosteroid	17	94%	5856
13	Vitamin D alone or in combination vs. other treatments: complex regimens	9	89%	2936
14	Vitamin D alone or in combination vs. other treatment: long-term studies (> 24 wks)	1	100%	297
15	Vitamin D analogues vs. other treatment	19	68%	2364
16	Flexural/facial psoriasis: placebo-controlled trials	2	100%	122
17	Flexural/facial psoriasis: vitamin D alone or in combination vs. other treatment	4	75%	588
18	Scalp psoriasis: placebo-controlled trials	14	93%	3011
19	Scalp psoriasis: vitamin D alone or in combination vs. other treatments	12	100%	5413

Table 5. Analysis 01: Trial characteristics and outcomes: vitamin D vs. placebo

Subcategory	Measure	01 IAGI/IGA	02 TSS	03 PASI	04 PAGI/PGA	05 Combined end point
01 Calcipotriol OD/BD	Effect size [CI]	(SMD -0.93; 95% CI -1.17 to -0.68)	(SMD -1.15; 95% CI -1.41 to -0.89)	(SMD -0.65; 95% CI -0.75 to -0.55)	(SMD -0.64; 95% CI -0.97 to -0.30)	(SMD -0.96; 95% CI -1.15 to -0.77)
02 Calcipotriol plus occlusion	Effect size [CI]	NA	(SMD -0.15; 95% CI -0.44 to 0.14)	-	-	(SMD -0.15; 95% CI -0.44 to 0.14)
03 Calcitriol OD/BD	Effect size [CI]	(SMD -1.03; 95% CI -1.71 to -0.36)	(SMD -1.22; 95% CI -2.38 to -0.07)	-	(SMD -0.59; 95% CI -0.76 to -0.41)	(SMD -0.92; 95% CI -1.54 to -0.29)
04 Tacalcitol OD	Effect size [CI]	(SMD -0.84; 95% CI -1.41 to -0.26)	(SMD -0.66; 95% CI -0.95 to -0.36)	(SMD -0.27; 95% CI -0.56 to 0.03)	(SMD -0.24; 95% CI -0.53 to 0.05)	(SMD -0.73; 95% CI -1.09 to -0.37)
05 Maxacalcitol OD	Effect size [CI]	(SMD -1.43; 95% CI -1.91 to -0.96)	(SMD -1.61; 95% CI -2.10 to -1.12)	-	-	(SMD -1.43; 95% CI -1.91 to -0.96)
06 Paricalcitol OD	Effect size [CI]	(SMD -1.66; 95% CI -2.66 to -0.67)	(SMD -2.15; 95% CI -3.24 to -1.06)	-	-	(SMD -1.66; 95% CI -2.66 to -0.67)
07 Becocalcidiol OD	Effect size [CI]	(SMD -0.22; 95% CI -0.58 to 0.14)	(SMD -0.02; 95% CI -0.37 to 0.34)	-	-	(SMD -0.22; 95% CI -0.58 to 0.14)
08 Becocalcidiol BD	Effect size [CI]	(SMD -0.67; 95% CI -1.04 to -0.30)	(SMD -0.46; 95% CI -0.83 to -0.10)	-	-	(SMD -0.67; 95% CI -1.04 to -0.30)
All treatments	Effect size [CI]; I^2 statistic	(SMD -0.95; 95% CI -1.17 to -0.74): I^2 statistic: 89.0%	(SMD -1.04; 95% CI -1.33 to -0.74) I^2 statistic: 93.0%	(SMD -0.58; 95% CI -0.71 to -0.45): I^2 statistic: 42.3%	(SMD -0.54; 95% CI -0.72 to -0.36): I^2 statistic: 55.5%	(SMD -0.90; 95% CI -1.07 to -0.72); I^2 statistic: 87.5%
-	No. participants	3771	2647	2357	1467	4986
-	Between-patient design	13	9	8	5	18
-	Within-patient design	7	10	1	0	12
-	Treatment duration	4 wks to 12 wks	4 wks to 12 wks	3 wks to 8 wks	8 wks to 8 wks	3 wks to 12 wks

Table 5. Analysis 01: Trial characteristics and outcomes: vitamin D vs. placebo *(Continued)*

Sensitivity analyses	Within-patient trials	-	-	-	-	(SMD -1.11; 95% CI -1.58 to -0.64)
-	Between-patient trials	-	-	-	-	(SMD -0.80; 95% CI -0.96 to -0.63)
-	Calcitriol, Perez 1996 removed	-	-	-		(SMD -0.60; 95% CI -0.78 to -0.41)
-	Calcipotriol BD	-	-	-	-	(SMD -1.02; 95% CI -1.23 to -0.82)
-	Calcipotriol OD	-	-	-	-	(SMD -0.76; 95% CI -1.13 to -0.40)
-	correlation coefficient (rho) = 0 All trials	-	-	-	-	(SMD -0.85; 95% CI -1.00 to -0.71); I^2 statistic: 87.8%
-	rho = 0 Btw-patient trials rho = 0.25 Within-patient trials	-	-	-	-	(SMD -0.87; 95% CI -1.01 to -0.72); I^2 statistic: 88.8%
-	rho = 0 Btw-patient trials rho = 0.50 Within-patient trials	-	-	-	-	(SMD -0.88; 95% CI -1.03 to -0.73); I^2 statistic = 90.3%
-	rho = 0 Btw-patient trials rho = 0.75 Within-patient trials	-	-	-	-	(SMD -0.91; 95% CI -1.07 to -0.75); I^2 statistic: 93.2%

For acronyms, see Table 1.

Table 6. Analysis 02: Trial characteristics and outcomes: potent steroids vs. placebo

Subcategory	Measure	01 IAGI/IGA	02 TSS	03 PASI	04 PAGI/PGA	05 Combined end point
01 Betamethasone dipropionate OD	Effect size [CI]	(SMD -0.81; 95% CI -0.98 to -0.64)	(SMD -0.74; 95% CI -1.16 to -0.32)	(SMD -0.79; 95% CI -1.44 to -0.14)	-	(SMD -0.80; 95% CI -0.96 to -0.64)
02 Betametha-	Effect size [CI]	(SMD -1.35; 95% CI -1.56 to -1.15)	(SMD -0.77; 95% CI -1.48 to -0.06)	(SMD -1.21; 95% CI	-	(SMD -1.35; 95% CI -1.56 to -1.15)

Table 6. Analysis 02: Trial characteristics and outcomes: potent steroids vs. placebo *(Continued)*

sone dipropionate BD				-1.44 to -0.97)		
03 Betamethasone dipropionate, maintenance	Effect size [CI]		(SMD -0.95; 95% CI -1.62 to -0.27)	-	-	(SMD -0.95; 95% CI -1.62 to -0.27)
04 Betamethasone valerate	Effect size [CI]	(SMD -1.41; 95% CI -1.92 to -0.90)	(SMD -1.09; 95% CI -2.00 to -0.18)	-	-	(SMD -1.33; 95% CI -1.78 to -0.89)
05 Budesonide	Effect size [CI]	-	-	-	-	-
06 Desonide	Effect size [CI]	(SMD -0.81; 95% CI -1.34 to -0.28)	(SMD -1.16; 95% CI -1.70 to -0.61)	-	-	(SMD -0.81; 95% CI -1.34 to -0.28)
07 Diflorasone diacetate	Effect size [CI]	-	(SMD -0.32; 95% CI -0.73 to 0.09)	-	-	(SMD -0.32; 95% CI -0.73 to 0.09)
08 Fluticasone propionate	Effect size [CI]	(SMD -0.93; 95% CI -1.14 to -0.72)	-	-	-	(SMD -0.93; 95% CI -1.14 to -0.72)
09 Hydrocortisone buteprate	Effect size [CI]	-	(SMD -0.46; 95% CI -0.77 to -0.15)	-	-	(SMD -0.46; 95% CI -0.77 to -0.15)
10 Mometasone furoate	Effect size [CI]	(SMD -0.75; 95% CI -1.17 to -0.34)	(SMD -1.12; 95% CI -1.55 to -0.68)	-	-	(SMD -0.75; 95% CI -1.17 to -0.34)
All treatments	Effect size [CI]; I^2 statistic	(SMD -1.00; 95% CI -1.18 to -0.82); I^2 statistic: 57.6%	(SMD -0.77; 95% CI -1.01 to -0.52); I^2 statistic: 46.7%	(SMD -0.97; 95% CI -1.31 to -0.62); I^2 statistic: 79.6%	-	(SMD -0.89; 95% CI -1.06 to -0.72); I^2 statistic: 65.1%
-	No. participants	1867	553	1158	0	2216
-	Between-patient design	8	6	3	0	11
-	Within-patient design	1	1	0	0	2
-	Treatment duration	3 wks to 12 wks	2 wks to 12 wks	4 wks to 8 wks	-	2 wks to 12 wks
Sensitivity analyses	Within-patient trials	-	-	-	-	(SMD -1.33; 95% CI -1.78 to -0.89)

Table 6. Analysis 02: Trial characteristics and outcomes: potent steroids vs. placebo *(Continued)*

-	Between-patient trials	-	-	-	-	(SMD -0.85; 95% CI -1.03 to -0.67)
-	correlation coefficient (rho) = 0 All trials	-	-	-	-	(SMD -0.89; 95% CI -1.06 to -0.72) I^2 statistic: 77.7%
-	rho = 0 Btw-patient trials rho = 0.25 Within-patient trials	-	-	-	-	(SMD -0.89; 95% CI -1.06 to -0.72) I^2 statistic: 78.0%
-	rho = 0 Btw-patient trials rho = 0.50 Within-patient trials	-	-	-	-	(SMD -0.90; 95% CI -1.07 to -0.73) I^2 statistic: 78.6%
-	rho = 0 Btw-patient trials rho = 0.75 Within-patient trials	-	-	-	-	(SMD -0.91; 95% CI -1.08 to -0.74) I^2 statistic: 80.2%

For acronyms, see Table 1. Both within-patient trials compared betamethasone valerate with placebo.

Table 7. Analysis 03: Trial characteristics and outcomes: v. potent steroids vs. placebo

Subcategory	Measure	01 IAGI/IGA	02 TSS	03 PASI	04 PAGI/PGA	05 Combined end point
01 Clobetasol propionate	Effect size [CI]	(SMD -1.89; 95% CI -2.53 to -1.24)	(SMD -1.35; 95% CI -1.80 to -0.89)	-	(SMD -1.01; 95% CI -1.55 to -0.47)	(SMD -1.65; 95% CI -2.10 to -1.20)
02 Halcinonide	Effect size [CI]	-	-	-	-	-
03 Halobetasol	Effect size [CI]	(SMD -1.81; 95% CI -2.37 to -1.24)	-	-	(SMD -1.25; 95% CI -1.46 to -1.04)	(SMD -1.36; 95% CI -1.65 to -1.07)
All treatments	Effect size [CI], N, I^2	(SMD -1.87; 95% CI -2.38 to -1.36); I^2 statistic: 78.7%	(SMD -1.35; 95% CI -1.80 to -0.89); I^2 statistic: 75.3%	-	(SMD -1.22; 95% CI -1.42 to -1.02); I^2 statistic: 0%	(SMD -1.56; 95% CI -1.87 to -1.26); I^2 statistic: 81.7%

Table 7. Analysis 03: Trial characteristics and outcomes: v. potent steroids vs. placebo *(Continued)*

-	No. participants	515	545	0	283	1264
-	Between-patient design	4	3	0	1	7
-	Within-patient design	1	0	0	2	3
-	Treatment duration	2 wks to 4 wks	2 wks to 4 wks		2 wks to 2 wks	2 wks to 4 wks
Sensitivity analyses	Within-patient trials	-	-	-	-	(SMD -1.52; 95% CI -2.02 to -1.02)
-	Between-patient trials	-	-	-	-	(SMD -1.58; 95% CI -1.99 to -1.17)
-	correlation coefficient (rho) = 0 All trials	-	-	-	-	(SMD -1.52; 95% CI -1.80 to -1.24) I^2 statistic: 81.6%
-	rho = 0 Btw-patient trials rho = 0.25 Within-patient trials	-	-	-	-	(SMD -1.52; 95% CI -1.80 to -1.25) I^2 statistic: 82.2%
-	rho = 0 Btw-patient trials rho = 0.50 Within-patient trials	-	-	-	-	(SMD -1.53; 95% CI -1.80 to -1.26) I^2 statistic: 83.3%
-	rho = 0 Btw-patient trials rho = 0.75 Within-patient trials	-	-	-	-	(SMD -1.55; 95% CI -1.80 to -1.29) I^2 statistic: 85.9%

For acronyms, see Table 1.

Table 8. Analysis 05: Trial characteristics and outcomes: vitamin D combination vs. placebo

Subcategory	Measure	01 IAGI/IGA	02 TSS	03 PASI	04 PAGI/ PGA	05 Combined end point
01 Combination calcipotriol/betamethasone dipropionate, OD	Effect size [CI]	(SMD -1.21; 95% CI -1.50 to -0.91)	-	(SMD -1.14; 95% CI -1.57 to -0.70)	(SMD -0.69; 95% CI -0.98 to -0.40)	(SMD -1.21; 95% CI -1.50 to -0.91)
02 Combination calcipotriol/be-	Effect size [CI]	(SMD -1.90; 95% CI -2.09 to -1.71)	-	(SMD -1.41; 95% CI -1.86 to -0.97)	-	(SMD -1.90; 95% CI -2.09 to -1.71)

Table 8. Analysis 05: Trial characteristics and outcomes: vitamin D combination vs. placebo *(Continued)*

tamethasone dipropionate, BD						
All treatments	Effect size [CI], N, I^2 statistic	(SMD -1.44; 95% CI -1.76 to -1.12); I^2 statistic: 89.4%	-	(SMD -1.24; 95% CI -1.53 to -0.95); I^2 statistic: 87.6%	(SMD -0.69; 95% CI -0.98 to -0.40); I^2 statistic: NA	(SMD -1.44; 95% CI -1.76 to -1.12); I^2 statistic: 89.4%
-	No. participants	2058	0	2056	235	2058
-	Between-patient design	5	0	5	1	5
-	Within-patient design	0	0	0	0	0
-	Treatment duration	4 wks to 8 wks	-	4 wks to 8 wks	8 wks	4 wks to 8 wks

For acronyms, see Table 1.

Table 9. Analysis 06: Trial characteristics and outcomes: other treatments vs. placebo

Subcategory	Measure	01 IAGI/IGA	02 TSS	03 PASI	04 PAGI/PGA	05 Combined end point
01 Aloe vera extract	Effect size [CI]	-	-	(SMD -1.58; 95% CI -2.16 to -0.99)	-	(SMD -1.58; 95% CI -2.16 to -0.99)
02 Anti-IL-8 monoclonal antibody cream	Effect size [CI]	(SMD -0.59; 95% CI -1.01 to -0.16)	(SMD -0.70; 95% CI -1.13 to -0.27)	-	-	(SMD -0.59; 95% CI -1.01 to -0.16)
03 Betamethasone 17-valerate 21-acetate plus tretinoine plus salicylic acid	Effect size [CI]	(SMD -0.76; 95% CI -1.21 to -0.31)	-	(SMD -0.54; 95% CI -0.99 to -0.10)	(SMD -0.80; 95% CI -1.26 to -0.35)	(SMD -0.76; 95% CI -1.21 to -0.31)
04 Caffeine (topical) 10%, TD	Effect size [CI]	-	-	(SMD -0.39; 95% CI -0.84 to 0.06)	-	(SMD -0.39; 95% CI -0.84 to 0.06)
05 Calcipotriene 0.005% ointment + nicotinamide 0.05% or 0.1% or 0.7% or 1.4%, BD	Effect size [CI]	-	(SMD -0.48; 95% CI -0.81 to -0.15)	-	-	(SMD -0.48; 95% CI -0.81 to -0.15)
06 Dead sea salts emollient lotion	Effect size [CI]	-	-	(SMD 0.57; 95% CI -0.36 to 1.51)	-	(SMD 0.57; 95% CI -0.36 to 1.51)

Table 9. Analysis 06: Trial characteristics and outcomes: other treatments vs. placebo *(Continued)*

07 Fish oil plus occlusion	Effect size [CI]	-	(SMD -1.05; 95% CI -1.64 to -0.46)	-	-	(SMD -1.05; 95% CI -1.64 to -0.46)
08 Herbal skin care (Dr Michaels® cleansing gel, ointment and skin conditioner), BD	Effect size [CI]			(SMD -2.96; 95% CI -4.19 to -1.74)	-	(SMD -2.96; 95% CI -4.19 to -1.74)
09 Hexafluoro-1,25-dihydroxyvitamin D3	Effect size [CI]	(SMD -0.62; 95% CI -1.35 to 0.12)	(SMD -1.13; 95% CI -1.91 to -0.35)	-	-	(SMD -0.62; 95% CI -1.35 to 0.12)
10 Indigo naturalis 1.4% ointment	Effect size [CI]	(SMD -2.14; 95% CI -2.74 to -1.53)	(SMD -1.64; 95% CI -2.13 to -1.15)	-	-	(SMD -2.09; 95% CI -2.62 to -1.56)
11 Kukui nut oil, TD	Effect size [CI]	(SMD 0.00; 95% CI -0.80 to 0.80)	(SMD 0.33; 95% CI -0.48 to 1.14)	(SMD -0.03; 95% CI -0.84 to 0.77)	(SMD 0.00; 95% CI -0.80 to 0.80)	(SMD 0.00; 95% CI -0.80 to 0.80)
12 *Mahonia aquifolium* (Reliéva™), BD	Effect size [CI]	-	-	-	-	(SMD -0.77; 95% CI -1.06 to -0.48)
13 Methotrexate gel	Effect size [CI]	(SMD -0.56; 95% CI -1.01 to -0.12)	(SMD -0.48; 95% CI -0.92 to -0.04)	(SMD -1.58; 95% CI -2.16 to -0.99)	-	(SMD -1.05; 95% CI -2.04 to -0.06)
14 Mycophenolic acid ointment	Effect size [CI]	-	(SMD -1.44; 95% CI -2.67 to -0.22)	-	-	(SMD -1.44; 95% CI -2.67 to -0.22)
15 NG-monomethyl-L-arginine (L-NMMA) cream	Effect size [CI]	-	(SMD 0.08; 95% CI -0.60 to 0.75)	-	-	(SMD 0.08; 95% CI -0.60 to 0.75)
16 Nicotinamide 1.4%, BD	Effect size [CI]	-	(SMD -0.20; 95% CI -0.60 to 0.20)	-	-	(SMD -0.20; 95% CI -0.60 to 0.20)
17 Oleum horwathiensis	Effect size [CI]	(SMD -0.02; 95% CI -0.63 to 0.58)	(SMD -0.77; 95% CI -1.40 to -0.14)	-	-	(SMD -0.02; 95% CI -0.63 to 0.58)
18 Omega-3-polyunsaturated fatty acids ointment	Effect size [CI]	-	-	-	-	-
19 Platelet aggregation activating factor (PAF) (Ro 24-0238)	Effect size [CI]	(SMD -0.07; 95% CI -0.50 to 0.37)	-		-	(SMD -0.07; 95% CI -0.50 to 0.37)
20 Polymyxin B cream, 200,000 U/g	Effect size [CI]	-	(SMD 0.13; 95% CI -0.59 to 0.85)	-	-	(SMD 0.13; 95% CI -0.59 to 0.85)

Table 9. Analysis 06: Trial characteristics and outcomes: other treatments vs. placebo *(Continued)*

21 PTH (1-34) in Novasome A® liposomal cream, BD	Effect size [CI]	-	(SMD -2.31; 95% CI -3.26 to -1.36)	-	-	(SMD -2.31; 95% CI -3.26 to -1.36)
22 Sirolimus (topical), 2.2% for 6 wks, then 8% for a further 6 wks	Effect size [CI]	-	(SMD -0.39; 95% CI -0.98 to 0.21)	-	-	(SMD -0.39; 95% CI -0.98 to 0.21)
23 Tacrolimus ointment	Effect size [CI]	-	(SMD 0.06; 95% CI -0.52 to 0.63)	-	-	(SMD 0.06; 95% CI -0.52 to 0.63)
24 Tar	Effect size [CI]	-	(SMD -0.45; 95% CI -1.11 to 0.22)	-	-	(SMD -0.45; 95% CI -1.11 to 0.22)
25 Tazarotene	Effect size [CI]	-	(SMD -0.86; 95% CI -1.11 to -0.62)	-	-	(SMD -0.86; 95% CI -1.11 to -0.62)
26 Theophylline 1% ointment, BD	Effect size [CI]	-	-	(SMD -2.87; 95% CI -4.13 to -1.62)	-	(SMD -2.87; 95% CI -4.13 to -1.62)
All treatments	(not pooled)	-	-	-	-	-
-	No. participants	364	907	529	105	1450
-	Between-patient design	4	5	8	2	12
-	Within-patient design	4	12	1	0	14
-	Treatment duration	3 wks to 12 wks	3 wks to 12 wks	2 wks to 12 wks	3 wks to 12 wks	2 wks to 12 wks

For acronyms, see Table 1.

Table 10. Analysis 07: Trial characteristics and outcomes: vitamin D vs. potent steroids

Subcategory	Measure	01 IAGI/IGA	02 TSS	03 PASI	04 PAGI/PGA	05 Combined end point
01 Calcipotriol vs. betamethasone dipropionate	Effect size [CI]	(SMD 0.43; 95% CI 0.28 to 0.58)	-	(SMD 0.36; 95% CI 0.22 to 0.51)	-	(SMD 0.43; 95% CI 0.28 to 0.58)
02 Calcipotriol vs. betamethasone valerate	Effect size [CI]	(SMD -0.02; 95% CI -0.21 to 0.17)	(SMD -0.26; 95% CI -0.41 to -0.11)	(SMD -0.12; 95% CI -0.22 to -0.02)	(SMD -0.26; 95% CI -0.38 to -0.14)	(SMD -0.12; 95% CI -0.26 to 0.02)

Table 10. Analysis 07: Trial characteristics and outcomes: vitamin D vs. potent steroids *(Continued)*

03 Calcipotriol vs. desoxymetasone	Effect size [CI]	-	-	(SMD 0.15; 95% CI -0.73 to 1.02)	-	(SMD 0.15; 95% CI -0.73 to 1.02)
04 Calcipotriol vs. diflorasone diacetate	Effect size [CI]	(SMD 0.27; 95% CI 0.02 to 0.52)	(SMD 0.40; 95% CI 0.15 to 0.65)	-	-	(SMD 0.27; 95% CI 0.02 to 0.52)
05 Calcipotriol vs. fluocinonide	Effect size [CI]	(SMD -0.58; 95% CI -0.99 to -0.18)	(SMD -0.50; 95% CI -0.92 to -0.07)	-	-	(SMD -0.58; 95% CI -0.99 to -0.18)
06 Calcitriol vs. betamethasone dipropionate	Effect size [CI]	(SMD 0.21; 95% CI -0.04 to 0.45)	(SMD 0.27; 95% CI 0.02 to 0.51)	(SMD 0.39; 95% CI 0.14 to 0.63)	-	(SMD 0.21; 95% CI -0.04 to 0.45)
07 Calcitriol vs. betamethasone valerate	Effect size [CI]	(SMD -0.19; 95% CI -0.91 to 0.53)	-	-	-	(SMD -0.19; 95% CI -0.91 to 0.53)
08 Tacalcitol vs. betamethasone valerate	Effect size [CI]	-	(SMD 0.41; 95% CI 0.09 to 0.74)	-	-	(SMD 0.41; 95% CI 0.09 to 0.74)
All treatments	Effect size [CI]; I^2 statistic	(SMD 0.17; 95% CI -0.04 to 0.37); I^2 statistic: 83.4%	(SMD 0.11; 95% CI -0.22 to 0.44); I^2 statistic: 86.7%	(SMD 0.12; 95% CI -0.07 to 0.32); I^2 statistic: 86.2%	(SMD -0.26; 95% CI -0.38 to -0.14); I^2 statistic: 0%	(SMD 0.11; 95% CI -0.07 to 0.30); I^2 statistic: 85.6%
-	No. participants	2655	891	3185	738	3542
-	Between-patient design	7	2	7	1	9
-	Within-patient design	1	4	2	1	5
-	Treatment duration	3 wks to 8 wks	3 wks to 6 wks	4 wks to 8 wks	6 wks	3 wks to 8 wks
Sensitivity analyses	Within-patient trials	-	-	-	-	(SMD 0.17; 95% CI -0.20 to 0.54)
-	Between-patient trials	-	-	-	-	(SMD 0.10; 95% CI -0.11 to 0.31)
-	correlation coefficient (rho) = 0 All trials	-	-	-	-	(SMD 0.10; 95% CI -0.08 to 0.28); I^2 statistic: 90.5%
-	rho = 0	-	-	-	-	(SMD 0.10; 95% CI -0.07 to 0.28)

Table 10. Analysis 07: Trial characteristics and outcomes: vitamin D vs. potent steroids *(Continued)*

	Btw-patient trials rho = 0.25 Within-patient trials					I^2 statistic: 91.3%
-	rho = 0 Btw-patient trials rho = 0.50 Within-patient trials	-	-	-	-	(SMD 0.11; 95% CI -0.07 to 0.29) I^2 statistic: 92.4%
-	rho = 0 Btw-patient trials rho = 0.75 Within-patient trials	-	-	-	-	(SMD 0.12; 95% CI -0.06 to 0.30) I^2 statistic: 94.3%

For acronyms, see Table 1.

Table 11. Analysis 08: Trial characteristics and outcomes: vitamin D vs. v. potent steroids

Subcategory	Measure	01 IAGI/IGA	02 TSS	03 PASI	04 PAGI/ PGA	05 Combined end point
01 Calcipotriol vs. clobetasol propionate	Effect size [CI]	(SMD 0.19; 95% CI -0.42 to 0.80)	-	(SMD -0.32; 95% CI -0.95 to 0.30)	(SMD 0.42; 95% CI -0.20 to 1.03)	(SMD -0.06; 95% CI -0.57 to 0.44); I^2 statistic: 25.7%
All treatments	No. participants	42	0	40	42	82
-	Between-patient design	1	0	1	1	2
-	Within-patient design	0	0	0	0	0
-	Treatment duration	2 wks	-	6 wks	2 wks	2 wks to 6 wks

Table 12. Analysis 09: Trial characteristics and outcomes: vitamin D + steroid vs. steroid

Subcategory	Measure	01 IAGI/IGA	02 TSS	03 PASI	04 PAGI/ PGA	05 Combined end point
01 Calcipotriol + betamethasone dipropionate vs. betamethasone dipropionate	Effect size [CI]	(SMD -0.40; 95% CI -0.52 to -0.27)	-	(SMD -0.44; 95% CI -0.55 to -0.33)	-	(SMD -0.40; 95% CI -0.52 to -0.27)
02 Calcipotriol + betamethasone dipropionate vs. clobetasol propionate	Effect size [CI]	-	(SMD 0.45; 95% CI 0.09 to 0.81)	-	-	(SMD 0.45; 95% CI 0.09 to 0.81)

Table 12. Analysis 09: Trial characteristics and outcomes: vitamin D + steroid vs. steroid *(Continued)*

03 Calcipotriol + clobetasol propionate vs. clobetasol propionate	Effect size [CI]	(SMD -0.69; 95% CI -1.22 to -0.15)	-	-	(SMD -0.28; 95% CI -0.80 to 0.24)	(SMD -0.69; 95% CI -1.22 to -0.15)
-	Effect size [CI], I^2	(SMD -0.41; 95% CI -0.53 to -0.29); I^2 statistic: 32.0%	(SMD 0.45; 95% CI 0.09 to 0.81): I^2 statistic: NA	(SMD -0.44; 95% CI -0.55 to -0.33) I^2 statistic: 22.4%	(SMD -0.28; 95% CI -0.80 to 0.24) I^2 statistic: NA	(SMD -0.26; 95% CI -0.52 to -0.00); I^2 statistic: 84.4%
-	No. participants	1991	122	1876	65	2113
-	Between-patient design	4	1	3	1	5
-	Within-patient design	0	0	0	0	0
-	Treatment duration	2 wks to 8 wks	4 wks	4 wks to 8 wks	2 wks	2 wks to 8 wks

Table 13. Analysis 10: Trial characteristics and outcomes: vitamin D vs. dithranol

Subcategory	Measure	01 IAGI/IGA	02 TSS	03 PASI	04 PAGI/PGA	05 Combined end point
01 Calcipotriol vs. dithranol	Effect size [CI]	(SMD -0.43; 95% CI -0.85 to -0.01)	(SMD -0.54; 95% CI -1.16 to 0.08)	(SMD 0.73; 95% CI -0.55 to 2.00)	(SMD -0.05; 95% CI -0.90 to 0.80)	(SMD 0.07; 95% CI -0.57 to 0.71)
02 Calcitriol vs. dithranol	Effect size [CI]	(SMD 0.51; 95% CI 0.13 to 0.88)	(SMD 0.13; 95% CI -0.24 to 0.50)	(SMD -0.21; 95% CI -0.58 to 0.16)	-	(SMD 0.51; 95% CI 0.13 to 0.88)
03 Tacalcitol vs. dithranol	Effect size [CI]	-	(SMD -0.18; 95% CI -0.60 to 0.25)	(SMD -0.07; 95% CI -0.50 to 0.36)	-	(SMD -0.18; 95% CI -0.60 to 0.25)
All treatments	Effect size [CI], I^2 statistic	(SMD -0.24; 95% CI -0.72 to 0.25); I^2 statistic:93.0%	(SMD -0.27; 95% CI -0.73 to 0.20); I^2 statistic: 80.6%	(SMD 0.36; 95% CI -0.33 to 1.04); I^2 statistic: 94.5%	(SMD -0.05; 95% CI -0.90 to 0.80); I^2 statistic: 92.5%	(SMD 0.09; 95% CI -0.44 to 0.63); I^2 statistic: 94.9%
-	No. participants	1108	386	796	544	1284
-	Between-patient design	5	3	5	2	7

Table 13. Analysis 10: Trial characteristics and outcomes: vitamin D vs. dithranol *(Continued)*

-	Within-patient design	0	1	0	0	1
-	Treatment duration	8 wks to 12 wks	4 wks to 8 wks	8 wks to 12 wks	8 wks to 12 wks	4 wks to 12 wks

Table 14. Analysis 11: Trial characteristics and outcomes: vitamin D vs. vitamin D

Subcategory	Measure	01 IAGI/IGA	02 TSS	03 PASI	04 PAGI/PGA	05 Combined end point
01 Calcipotriol vs. calcitriol	Effect size [CI]	(SMD 0.00; 95% CI -0.25 to 0.25)	(SMD -0.32; 95% CI -0.57 to -0.07)	(SMD -1.11; 95% CI -2.22 to 0.01)	(SMD 0.04; 95% CI -0.21 to 0.29)	(SMD -0.41; 95% CI -1.46 to 0.64)
02 Calcipotriol vs. tacalcitol	Effect size [CI]	(SMD -0.47; 95% CI -0.73 to -0.21)	(SMD -0.45; 95% CI -0.68 to -0.22)	-	-	(SMD -0.47; 95% CI -0.73 to -0.21)
03 Calcipotriol vs. maxacalcitol	Effect size [CI]	(SMD 0.43; 95% CI -0.12 to 0.98)	(SMD 0.13; 95% CI -0.41 to 0.68)	-	-	(SMD 0.43; 95% CI -0.12 to 0.98)
All treatments	Effect size [CI], I^2	(SMD -0.06; 95% CI -0.51 to 0.38); I^2 statistic: 82.2%	(SMD -0.31; 95% CI -0.55 to -0.06); I^2 statistic: 46.9%	(SMD -1.11; 95% CI -2.22 to 0.01); I^2 statistic: NA	(SMD 0.04; 95% CI -0.21 to 0.29); I^2 statistic: NA	(SMD -0.17; 95% CI -0.62 to 0.27); I^2 statistic: 78.5%
-	No. participants	498	563	15	250	513
-	Between-patient design	2	2	1	1	3
-	Within-patient design	1	1	0	0	1
-	Treatment duration	8 wks to 12 wks	8 wks to 12 wks	8 wks	12 wks	8 wks to 12 wks
Sensitivity analyses	TSS data from Ji 2008 used in combined end point: 01 Calcipotriol vs. calcitriol		-	-	-	(SMD -0.52; 95% CI -1.19 to 0.15; I^2 statistic: 44.9%)
-	TSS data from Ji 2008 used in combined end point: all treatments		-	-	-	(SMD -0.28; 95% CI -0.66 to 0.10; I^2 statistic: 70.6%)

Table 15. Analysis 12: Trial characteristics and outcomes: vitamin D vs. vitamin D + steroid

Subcategory	Measure	01 IAGI/IGA	02 TSS	03 PASI	04 PAGI/PGA	05 Combined end point
01 Calcipotriol BD vs. calcipotriol OM, BMD ON	Effect size [CI]	(SMD 0.56; 95% CI 0.23 to 0.88)	-	(SMD 0.46; 95% CI 0.10 to 0.82)	-	(SMD 0.56; 95% CI 0.23 to 0.88)
02 Calcipotriol OD vs. combined calcipotriol + BMD OD	Effect size [CI]	(SMD 0.66; 95% CI 0.31 to 1.02)	-	(SMD 0.67; 95% CI 0.23 to 1.11)	-	(SMD 0.66; 95% CI 0.31 to 1.02)
03 Calcipotriol BD vs. combined calcipotriol + BMD OD	Effect size [CI]	(SMD 0.27; 95% CI 0.06 to 0.48)	(SMD 0.25; 95% CI 0.03 to 0.48)	(SMD 0.52; 95% CI 0.38 to 0.67)	-	(SMD 0.43; 95% CI 0.20 to 0.66)
04 Calcipotriol BD vs. combined calcipotriol + BMD BD	Effect size [CI]	(SMD 0.66; 95% CI 0.40 to 0.93)	-	(SMD 0.64; 95% CI 0.46 to 0.83)	-	(SMD 0.66; 95% CI 0.40 to 0.93)
05 Calcipotriol BD vs. calcipotriol OM, BMV ON	Effect size [CI]	(SMD 0.27; 95% CI -0.19 to 0.74)	-	(SMD 0.43; 95% CI -0.07 to 0.93)	-	(SMD 0.27; 95% CI -0.19 to 0.74)
06 Calcipotriol BD vs. calcipotriol OM, clobetasone butyrate ON	Effect size [CI]	(SMD 0.27; 95% CI 0.05 to 0.48)	-	(SMD 0.17; 95% CI -0.04 to 0.38)	-	(SMD 0.27; 95% CI 0.05 to 0.48)
07 Calcipotriol BD vs. calcipotriol BD + clobetasol propionate BD	Effect size [CI]	(SMD 0.88; 95% CI 0.34 to 1.42)	-	-	(SMD 0.70; 95% CI 0.16 to 1.23)	(SMD 0.88; 95% CI 0.34 to 1.42)
08 Calcipotriol BD vs. calcipotriol OM, diflucortolone valerate ON	Effect size [CI]	-	-	(SMD 0.08; 95% CI -0.29 to 0.44)	-	(SMD 0.08; 95% CI -0.29 to 0.44)
09 Calcipotriol OD vs. calcipotriol OM, fluocinonide acetonide ON	Effect size [CI]	-	-	(SMD 0.53; 95% CI -0.11 to 1.18)	-	(SMD 0.53; 95% CI -0.11 to 1.18)
10 Calcipotriol OD vs. combined calcipotriol + hydrocortisone OD	Effect size [CI]	(SMD 0.14; 95% CI -0.06 to 0.33)	-	(SMD 0.08; 95% CI -0.11 to 0.28)	-	(SMD 0.14; 95% CI -0.06 to 0.33)
11 calcitriol BD vs. diflucortolone valerate OM, calcitriol ON	Effect size [CI]	-	-	(SMD 0.24; 95% CI -0.09 to 0.57)	-	(SMD 0.24; 95% CI -0.09 to 0.57)
12 Tacalcitol OD vs. combined calcipotriol + BMD OD	Effect size [CI]	(SMD 0.48; 95% CI 0.26 to 0.70)	-	(SMD 0.47; 95% CI 0.25 to 0.69)	(SMD 0.46; 95% CI 0.24 to 0.68)	(SMD 0.48; 95% CI 0.26 to 0.70)
All treatments	Effect size [CI], I^2 statistic	(SMD 0.48; 95% CI 0.32 to 0.65), I^2 statistic: 86.9%	(SMD 0.25; 95% CI 0.03 to 0.48)	(SMD 0.47; 95% CI 0.34 to 0.59), I^2 statistic: 82.3%	(SMD 0.49; 95% CI 0.29 to 0.69), I^2 statistic: 0%	(SMD 0.46; 95% CI 0.33 to 0.59), I^2 statistic: 83.3%

Table 15. Analysis 12: Trial characteristics and outcomes: vitamin D vs. vitamin D + steroid *(Continued)*

-	No. participants	4791	301	5703	399	5856
-	Between-patient design	11	1	15	2	16
-	Within-patient design	0	0	1	0	1
-	Treatment duration	2 wks to 8 wks	4 wks	2 wks to 12 wks	2 wks to 8 wks	2 wks to 12 wks

For acronyms, see Table 1.

Table 16. Analysis 13: Trial characteristics and outcomes: vitamin D vs. other treatments: complex regimens

Subcategory	Measure	01 IAGI/IGA	02 TSS	03 PASI	04 PAGI/PGA	05 Combined end point
01 Calcipotriol (12 wks) vs. combined calcipotriol + BMD (8 wks); then calcipotriol (4 wks)	Effect size [CI]	(SMD -0.12; 95% CI -0.29 to 0.04)	-	(SMD -0.04; 95% CI -0.19 to 0.11)	(SMD -0.14; 95% CI -0.30 to 0.02)	(SMD -0.12; 95% CI -0.29 to 0.04)
02 Calcipotriol (12 wks) vs. combined calcipotriol + BMD (4 wks); then calcipotriol (8 wks)	Effect size [CI]	-	-	(SMD 0.29; 95% CI -0.04 to 0.62)	-	(SMD 0.29; 95% CI -0.04 to 0.62)
03 Calcipotriol (12 wks) vs. combined calcipotriol + BMD (4 wks); then calcipotriol (w/dy) & combined calcipotriol + BMD (w/e) (8 wks)	Effect size [CI]	(SMD 0.13; 95% CI -0.04 to 0.29)	-	(SMD 0.10; 95% CI -0.05 to 0.25)	(SMD 0.10; 95% CI -0.06 to 0.26)	(SMD 0.13; 95% CI -0.04 to 0.29)
04 Calcipotriol (6 wks) vs. clobetasol propionate (2 wks); then calcipotriol (4 wks)	Effect size [CI]	(SMD 0.60; 95% CI 0.18 to 1.02)	(SMD 0.63; 95% CI 0.21 to 1.05)	-	-	(SMD 0.60; 95% CI 0.18 to 1.02)
05 Calcipotriol (6 wks) vs. calcipotriol OM, fluocinonide acetonide ON (2 wks); then calcipotriol BD (4 wks)	Effect size [CI]	-	-	(SMD 0.66; 95% CI 0.01 to 1.32)	-	(SMD 0.66; 95% CI 0.01 to 1.32)
06 Calcipotriol (6 wks) vs. halometasone OM, calcipotriol ON (2 wks); then calcipotriol BD (w/dy), halometasone (w/e) (2 wks); then calcipotriol BD (2wks)	Effect size [CI]	(SMD 0.41; 95% CI -0.05 to 0.86)	-	(SMD 1.13; 95% CI 0.64 to 1.62)	-	(SMD 0.41; 95% CI -0.05 to 0.86)
07 Calcipotriol ON, clobetasol propionate OM (2 to 4 wks); then calcipotriol BD (to wk12) vs. calcitriol ON, clobetasol propionate OM (2 to 4 wks); then calcitriol BD (to wk12)	Effect size [CI]	(SMD -0.19; 95% CI -0.54 to 0.16)	-	(SMD -0.27; 95% CI -0.62 to 0.09)	-	(SMD -0.19; 95% CI -0.54 to 0.16)

Table 16. Analysis 13: Trial characteristics and outcomes: vitamin D vs. other treatments: complex regimens *(Continued)*

08 Combined calcipotriol + BMD (4 wks); then placebo ointment BD (8 wks) vs. combined calcipotriol + BMD (4 wks); then calcipotriol ointment BD (8 wks)	Effect size [CI]	(SMD 0.27; 95% CI 0.12 to 0.41)	-	(SMD 0.25; 95% CI 0.10 to 0.39)	(SMD 0.28; 95% CI 0.13 to 0.42)	(SMD 0.27; 95% CI 0.12 to 0.41)
09 Combined calcipotriol + BMD (4 wks); then placebo ointment BD (8 wks) vs. combined calcipotriol + BMD (4 wks); then calcipotriol (w/dy)+ combined calcipotriol + BMD (w/e) (8 wks)	Effect size [CI]	(SMD 0.51; 95% CI 0.37 to 0.66)	-	(SMD 0.59; 95% CI 0.45 to 0.74)	(SMD 0.71; 95% CI 0.56 to 0.85)	(SMD 0.51; 95% CI 0.37 to 0.66)
10 combined calcipotriol + BMD (4 wks); then calcipotriol ointment BD (8 wks) vs. combined calcipotriol + BMD (4 wks); then calcipotriol (w/dy) + combined calcipotriol + BMD (w/e) (8 wks)	Effect size [CI]	(SMD 0.26; 95% CI 0.11 to 0.40)	-	(SMD 0.30; 95% CI 0.16 to 0.45)	(SMD 0.44; 95% CI 0.29 to 0.58)	(SMD 0.26; 95% CI 0.11 to 0.40)
11 Combined calcipotriol + BMD (8 wks); then calcipotriol (4 wks) vs. combined calcipotriol + BMD (4 wks); then calcipotriol (w/dy) & combined calcipotriol + BMD (w/e) (8 wks)	Effect size [CI]	(SMD 0.24; 95% CI 0.08 to 0.40)	-	(SMD 0.15; 95% CI -0.01 to 0.30)	(SMD 0.23; 95% CI 0.07 to 0.39)	(SMD 0.24; 95% CI 0.08 to 0.40)
12 Tacalcitol (8 wks) vs. combined calcipotriol + BMD (4 wks); then calcipotriol (4 wks)	Effect size [CI]	(SMD 0.54; 95% CI 0.36 to 0.72)	-	(SMD 0.49; 95% CI 0.31 to 0.67)	(SMD 0.54; 95% CI 0.36 to 0.72)	(SMD 0.54; 95% CI 0.36 to 0.72)
All treatments	(not pooled)	-	-	-	-	-
-	No. participants	2755	46	2991	2508	2936
-	Between-patient design	6	0	8	4	8
-	Within-patient design	1	1	0	0	1
-	Treatment duration	6 wks to 12 wks	6 wks	2 wks to 12 wks	8 wks to 12 wks	2 wks to 12 wks

For acronyms, see Table 1.

Table 17. Analysis 14: Trial characteristics and outcomes: vitamin D vs. other treatment: long-term studies (> 24 wks)

Subcategory	Measure	01 IAGI/IGA	02 TSS	03 PASI	04 PAGI/PGA	05 Combined end point
01 Combined calcipotriol + BMD (52 wks) vs. alternating: combined calcipotriol + BMD (4 wks); then calcipotriol (4 wks)	Effect size [CI]	(SMD -0.09; 95% CI -0.36 to 0.18)	-	-	-	(SMD -0.09; 95% CI -0.36 to 0.18)

Table 17. Analysis 14: Trial characteristics and outcomes: vitamin D vs. other treatment: long-term studies (> 24 wks) *(Continued)*

02 Combined calcipotriol+BMD (52 wks) vs. combined calcipotriol+ BMD (4 wks); then calcipotriol (48 wks)	Effect size [CI]	(SMD -0.18; 95% CI -0.47 to 0.10)	-	-	-	(SMD -0.18; 95% CI -0.47 to 0.10)
03 Alternating: combined calcipotriol + BMD (4 wks); then calcipotriol (4 wks) vs. combined calcipotriol + BMD (4 wks); then calcipotriol (48 wks)	Effect size [CI]	(SMD -0.09; 95% CI -0.37 to 0.19)	-	-	-	(SMD -0.09; 95% CI -0.37 to 0.19)
All treatments	(no pooling)	-	-	-	-	-
-	No. participants	297	0	0	0	297
-	Between-patient design	1	0	0	0	1
-	Within-patient design	0	0	0	0	0
-	Treatment duration	52 wks	-	-	-	52 wks

For acronyms, see Table 1.

Table 18. Analysis 15: Trial characteristics and outcomes: vitamin D/other treatment

Subcategory	Measure	01 IAGI/IGA	02 TSS	03 PASI	04 PAGI/ PGA	05 Combined end point
01 Calcipotriol vs. coal tar	Effect size [CI]	(SMD -0.53; 95% CI -1.74 to 0.68)	-	(SMD -0.10; 95% CI -1.54 to 1.35)	(SMD -0.10; 95% CI -1.54 to 1.35)	(SMD -0.53; 95% CI -1.74 to 0.68)
02 Calcipotriol vs. coal tar polytherapy	Effect size [CI]	(SMD -0.59; 95% CI -0.87 to -0.31)	(SMD -0.51; 95% CI -0.86 to -0.16)	(SMD -0.63; 95% CI -1.06 to -0.20)	(SMD -0.63; 95% CI -1.06 to -0.20)	(SMD -0.59; 95% CI -0.87 to -0.31)
03 Calcipotriol vs. nicotinamide 1.4%, BD	Effect size [CI]	-	(SMD -0.09; 95% CI -0.49 to 0.31)	-	-	(SMD -0.09; 95% CI -0.49 to 0.31)
04 Calcipotriol vs. calcipotriol + nicotinamide 1.4%, BD	Effect size [CI]	-	(SMD 0.19; 95% CI -0.14 to 0.52)	-	-	(SMD 0.19; 95% CI -0.14 to 0.52)
05 Calcipotriol vs. corticosteroid + salicylic acid	Effect size [CI]	(SMD -0.06; 95% CI	-	(SMD -0.05; 95% CI	(SMD -0.49; 95% CI	(SMD -0.05; 95% CI -0.26 to 0.15)

Table 18. Analysis 15: Trial characteristics and outcomes: vitamin D/other treatment *(Continued)*

		-0.33 to 0.22)		-0.36 to 0.26)	-0.79 to -0.20)	
06 Calcipotriol vs. propylthiouracil cream	Effect size [CI]	-	-	(SMD -2.24; 95% CI -3.23 to -1.25)	-	(SMD -2.24; 95% CI -3.23 to -1.25)
07 Calcipotriol vs. tacrolimus ointment	Effect size [CI]	-	(SMD -0.35; 95% CI -1.51 to 0.81)		(SMD -0.13; 95% CI -0.51 to 0.24)	(SMD -0.55; 95% CI -1.28 to 0.17)
08 Calcipotriol vs. tazarotene	Effect size [CI]	(SMD -0.22; 95% CI -0.60 to 0.16)	(SMD -0.05; 95% CI -0.33 to 0.23)	-	(SMD -0.35; 95% CI -0.99 to 0.29)	(SMD -0.10; 95% CI -0.35 to 0.16)
09 Calcipotriol vs. tazarotene gel plus mometasone furoate cream	Effect size [CI]	-	-	-	-	-
10 Calcipotriol vs. vitamin B12 cream	Effect size [CI]	(SMD -0.55; 95% CI -1.33 to 0.24)	-	(SMD -0.01; 95% CI -0.78 to 0.75)	(SMD -0.55; 95% CI -1.33 to 0.24)	(SMD -0.55; 95% CI -1.33 to 0.24)
11 Head-to-head vitamin D alone or in combination: dosing	Effect size [CI]	(SMD -0.24; 95% CI -0.38 to -0.09)	-	(SMD -0.12; 95% CI -0.25 to 0.00)	-	(SMD -0.20; 95% CI -0.32 to -0.07)
12 Head-to-head vitamin D alone or in combination: occlusion	Effect size [CI]	-	(SMD -0.18; 95% CI -2.04 to 1.68)	-	-	(SMD -0.18; 95% CI -2.04 to 1.68)
All treatments	(not pooled)	-	-	-	-	-
-	No. participants	1386	898	1228	456	2364
-	Between-patient design	8	5	6	3	13
-	Within-patient design	2	2	3	3	6
-	Treatment duration	4 wks to 12 wks	6 wks to 12 wks	4 wks to 12 wks	4 wks to 12 wks	4 wks to 12 wks

For acronyms, see Table 1.

Table 19. Analysis 16: Trial characteristics and outcomes: flexural/facial psoriasis: placebo trials

Subcategory	Measure	01 IAGI/IGA	02 TSS	03 PASI	04 PAGI/PGA	05 Combined end point

Table 19. Analysis 16: Trial characteristics and outcomes: flexural/facial psoriasis: placebo trials *(Continued)*

01 Betamethasone valerate 0.1%, OD	Effect size [CI]	-	-	(SMD -2.83; 95% CI -3.79 to -1.88)	-	(SMD -2.83; 95% CI -3.79 to -1.88)
02 Calcipotriol ointment, OD	Effect size [CI]	-	-	(SMD -1.08; 95% CI -1.77 to -0.40)	-	(SMD -1.08; 95% CI -1.77 to -0.40)
03 Pimecrolimus cream, 1% OD/BD	Effect size [CI]	(SMD -1.07; 95% CI -1.69 to -0.45)	(SMD -1.37; 95% CI -1.95 to -0.79)	(SMD -0.62; 95% CI -1.27 to 0.02)	(SMD -0.65; 95% CI -1.24 to -0.06)	(SMD -0.86; 95% CI -1.30 to -0.41)
04 Tacrolimus ointment 0.1%, BD	Effect size [CI]	-	-	-	-	-
All treatments	(no pooling)	-	-	-	-	-
-	No. participants	47	57	75	47	122
-	Between-patient design	1	1	1	1	2
-	Within-patient design	0	0	0	0	0
-	Treatment duration	8 wks	8 wks	4 wks	8 wks	4 wks to 8 wks

For acronyms, see Table 1.

Table 20. Analysis 17: Trial characteristics and outcomes: flexural/facial psoriasis: vitamin D vs. other treatment

Subcategory	Measure	01 IAGI/IGA	02 TSS	03 PASI	04 PAGI/PGA	05 Combined end point
01 Calcipotriol vs. BMV	Effect size [CI]	-	-	(SMD 2.02; 95% CI 1.20 to 2.84)	-	(SMD 2.02; 95% CI 1.20 to 2.84)
02 Calcipotriol vs. calcipotriol + hydrocortisone	Effect size [CI]	(SMD 0.30; 95% CI 0.11 to 0.50)	-	(SMD 0.32; 95% CI 0.12 to 0.51)	-	(SMD 0.30; 95% CI 0.11 to 0.50)
03 Calcipotriol vs. calcitriol	Effect size [CI]	-	(SMD 0.61; 95% CI 0.28 to 0.94)	-	-	(SMD 0.61; 95% CI 0.28 to 0.94)
04 Calcipotriol vs. pimecrolimus	Effect size [CI]	-	-	(SMD -0.53; 95% CI -1.17 to 0.11)		(SMD -0.53; 95% CI -1.17 to 0.11)
05 Calcitriol vs. tacrolimus	Effect size [CI]	(SMD 0.42; 95% CI -0.15 to 0.98)	(SMD 0.29; 95% CI -0.27 to 0.85)	-	-	(SMD 0.42; 95% CI -0.15 to 0.98)
All treatments	(no pooling)	-	-	-	-	-

Table 20. Analysis 17: Trial characteristics and outcomes: flexural/facial psoriasis: vitamin D vs. other treatment *(Continued)*

-	No. participants	457	124	464	0	588
-	Between-patient design	2	1	2	0	3
-	Within-patient design	0	1	0	0	1
-	Treatment duration	6 wks to 8 wks	6 wks	4 wks to 8 wks	0	4 wks to 8 wks

For acronyms, see Table 1.

Table 21. Analysis 18: Trial characteristics and outcomes: scalp psoriasis: placebo-controlled trials

Subcategory	Measure	01 IAGI/IGA	02 TSS	03 PASI	04 PAGI/ PGA	05 Combined end point
01 Vitamin D: calcipotriol	Effect size [CI]	(SMD -0.72; 95% CI -1.28 to -0.16)	(SMD -0.44; 95% CI -0.64 to -0.25)	-	(SMD -0.66; 95% CI -1.28 to -0.05)	(SMD -0.72; 95% CI -1.28 to -0.16)
02 Potent steroid: betamethasone dipropionate	Effect size [CI]	(SMD -1.09; 95% CI -1.29 to -0.90)	(SMD -1.00; 95% CI -1.19 to -0.81)	-	(SMD -1.23; 95% CI -1.43 to -1.03)	(SMD -1.09; 95% CI -1.29 to -0.90)
03 Potent steroid: betamethasone valerate	Effect size [CI]	-	(SMD -1.40; 95% CI -1.75 to -1.05)	-	-	(SMD -1.40; 95% CI -1.75 to -1.05)
04 Very potent steroid: amcinonide	Effect size [CI]	(SMD -1.42; 95% CI -1.80 to -1.04)	(SMD -1.58; 95% CI -1.98 to -1.18)	-	(SMD -0.97; 95% CI -1.33 to -0.61)	(SMD -1.42; 95% CI -1.80 to -1.04)
05 Very potent steroid: clobetasol propionate	Effect size [CI]	(SMD -1.73; 95% CI -1.99 to -1.48)	(SMD -1.53; 95% CI -1.77 to -1.28)	-	-	(SMD -1.57; 95% CI -1.81 to -1.34)
06 Very potent steroid: halcinonide	Effect size [CI]	(SMD -1.11; 95% CI -1.69 to -0.53)	-	-	-	(SMD -1.11; 95% CI -1.69 to -0.53)
07 Vitamin D in combination: calcipotriol + BMD	Effect size [CI]	(SMD -0.97; 95% CI -1.61 to -0.32)	(SMD -0.92; 95% CI -1.42 to -0.43)	-	(SMD -1.00; 95% CI -1.79 to -0.22)	(SMD -0.97; 95% CI -1.61 to -0.32)
08 Other treatment: betamethasone-17,21-dipropionate plus salicylic acid	Effect size [CI]	(SMD -1.48; 95% CI -2.50 to -0.47)	(SMD -1.15; 95% CI -2.11 to -0.19)	-	-	(SMD -1.48; 95% CI -2.50 to -0.47)
09 Other treatment: ciclopirox olamine shampoo	Effect size [CI]	-	(SMD -0.07; 95% CI -0.82 to 0.68)	-	(SMD -0.11; 95% CI	(SMD -0.07; 95% CI -0.82 to 0.68)

Table 21. Analysis 18: Trial characteristics and outcomes: scalp psoriasis: placebo-controlled trials *(Continued)*

					-0.86 to 0.64)	
10 Other treatment: fluocinolone acetonide, plus occlusion	Effect size [CI]	(SMD -1.22; 95% CI -1.69 to -0.76)	(SMD -0.89; 95% CI -1.34 to -0.44)	-	-	(SMD -1.22; 95% CI -1.69 to -0.76)
11 Other treatment: salicylic acid	Effect size [CI]	(SMD -0.86; 95% CI -1.79 to 0.06)	(SMD -0.57; 95% CI -1.47 to 0.32)	-	-	(SMD -0.86; 95% CI -1.79 to 0.06)
All treatments	No. participants	2472	2897	0	1875	3011
-	Between-patient design	9	12	0	5	13
-	Within-patient design	1	0	0	0	1
-	Treatment duration	2 wks to 8 wks	2 wks to 8 wks	-	3 wks to 8 wks	2 wks to 8 wks
Sensitivity analysis: potent corticosteroids	Effect size [CI]; I^2 statistic	-	-	-	-	(SMD -1.18; 95% CI -1.40 to -0.96); I^2 statistic: 19.9%
Sensitivity analysis: very potent corticosteroids	Effect size [CI]; I^2 statistic	-	-	-	-	(SMD -1.51; 95% CI -1.70 to -1.31); I^2 statistic: 37.5%

For acronyms, see Table 1.

Table 22. Analysis 19: Trial characteristics and outcomes: scalp psoriasis: vitamin D vs. other treatment

Subcategory	Measure	01 IAGI/IGA	02 TSS	03 PASI	04 PAGI/PGA	05 Combined end point
01 Vitamin D vs. corticosteroid (potent): calcipotriol vs. BMD	Effect size [CI]	(SMD 0.48; 95% CI 0.32 to 0.64)	(SMD 0.45; 95% CI 0.28 to 0.63)	-	(SMD 0.56; 95% CI 0.31 to 0.81)	(SMD 0.48; 95% CI 0.32 to 0.64)
02 Vitamin D vs. corticosteroid (potent): calcipotriol vs. BMV	Effect size [CI]	(SMD 0.37; 95% CI 0.20 to 0.55)	(SMD 0.09; 95% CI -0.09 to 0.27)	-	(SMD 0.41; 95% CI 0.22 to 0.59)	(SMD 0.37; 95% CI 0.20 to 0.55)
03 Vitamin D vs. corticosteroid (very potent): calcipotriol vs. clobetasol propionate	Effect size [CI]	-	(SMD 0.37; 95% CI 0.05 to 0.69)	-	-	(SMD 0.37; 95% CI 0.05 to 0.69)
04 Vitamin D + corticosteroid vs. corticosteroid: calcipotriol + BMD vs. BMD	Effect size [CI]	(SMD -0.18; 95% CI -0.26 to -0.10)	(SMD -0.19; 95% CI -0.27 to -0.11)	-	(SMD -0.17; 95% CI -0.25 to -0.09)	(SMD -0.18; 95% CI -0.26 to -0.10)

Table 22. Analysis 19: Trial characteristics and outcomes: scalp psoriasis: vitamin D vs. other treatment *(Continued)*

05 Vitamin D vs. vitamin D + corticosteroid: calcipotriol vs. calcipotriol + BMD	Effect size [CI]	(SMD 0.64; 95% CI 0.44 to 0.84)	(SMD 0.70; 95% CI 0.56 to 0.84)	-	(SMD 0.84; 95% CI 0.61 to 1.08)	(SMD 0.64; 95% CI 0.44 to 0.84)
06 Vitamin D vs. other treatments: calcipotriol vs. coal tar polytherapy	Effect size [CI]	(SMD -0.24; 95% CI -0.73 to 0.25)	(SMD -0.30; 95% CI -0.84 to 0.24)	-	-	(SMD -0.45; 95% CI -0.92 to 0.02)
All treatments	No. participants	5175	4877	0	3742	5413
-	Between-patient design	10	11	0	6	12
-	Within-patient design	0	0	0	0	0
-	Treatment duration	4 wks to 52 wks	4 wks to 8 wks	0	4 wks to 8 wks	4 wks to 52 wks

For acronyms, see Table 1.

Table 23. Analysis 04: Trial characteristics and outcomes: dithranol vs. placebo

Subcategory	Measure	01 IAGI/IGA	02 TSS	03 PASI	04 PAGI/PGA	05 Combined end point
01 Dithranol	Effect size [CI], N, I^2 statistic	-	(SMD -1.06; 95% CI -1.66 to -0.46); I^2 statistic: 37.4%	-	-	(SMD -1.06; 95% CI -1.66 to -0.46); I^2 statistic: 37.4%
-	No. participants	0	47	0	0	47
-	Between-patient design	0	0	0	0	0
-	Within-patient design	0	3	0	0	3
-	Treatment duration		3 wks to 8 wks	-	-	3 wks to 8 wks
-	correlation coefficient (rho) = 0 All trials	-		-	-	(SMD -0.98; 95% CI -1.56 to -0.41) I^2 statistic: 13.9%
-	rho = 0 Btw-patient trials rho = 0.25 Within-patient trials	-	-	-	-	(SMD -1.05; 95% CI -1.67 to -0.44) I^2 statistic: 35.4%

Table 23. Analysis 04: Trial characteristics and outcomes: dithranol vs. placebo *(Continued)*

-	rho = 0 Btw-patient trials rho = 0.50 Within-patient trials	-	-	-	-	(SMD -1.12; 95% CI -1.75 to -0.48) I^2 statistic: 56.9%
-	rho = 0 Btw-patient trials rho = 0.75 Within-patient trials	-	-	-	-	(SMD -1.17; 95% CI -1.81 to -0.52) I^2 statistic: 78.5%

For acronyms, see Table 1.

Table 24. Included studies of adverse events

Study	Methods	Participants	Intervention(s)	Outcomes (AEs)	Summary findings	Notes	Allocation concealment
Andres 2006	DESIGN: between-patient patient delivery ALLOCATION: random Method of randomisation: computer-generated list Concealment: unclear BLINDING: single-blind (investigator) WITHDRAWAL/DROPOUT: described	N: 26 TD: 4 wks; FU: 4 wks LF: 0 (0%) BC: characteristics reported, but not demonstrated to be comparable (shampoo group had more severe disease and higher proportion of males) Age: 34.3 (9.5SD) Gender (per cent men): 58% Severity: DSS: 5.3 (1.3SD) % scalp affected: 63.8% INCLUSION CRITERIA: people with scalp psoriasis affecting > = 25% scalp; DSS > = 3 EXCLUSION CRITERIA: pregnancy or risk thereof; lactation; ophthalmological disorder; contact lens wearer	Clobetasol propionate 0.05% shampoo, OD. Applied to dry scalp, rinsed off after 15 minutes Clobetasol propionate 0.05% gel, OD. Applied to dry scalp and left in.	Serum cortisol atrophogenicity (ultrasound measurement of skin thickness (epidermis + dermis) (mm), averaged over 3 sites of the scalp) ocular safety (intraocular pressure) DSS (10-pt; sum of erythema, adherent desquamation, and plaque thickening; 0 (none) to 3 (severe) with half-point ratings permitted) Patient-reported ocular stinging (0 to 3) Compliance	Neither formulation had an impact on ocular safety, no report of ocular stinging. LAE: CS: 1/14; CG: 2/14 HPA suppression: CS: 0/14; CG: 2/14 Atrophy: CS: 0/14; CG: 0/14 Decrease in skin thickness from baseline: mean difference: CS: 0.04 mm CG: -0.24 mm (difference: P < = 0.025) Efficacy results of the 2 formulations were similar. Compliance with protocol was good in both groups.	Exploratory safety study Sponsored by Galderma Laboratories	Unclear
Barnes 2000	DESIGN: within-patient patient delivery ALLOCATION: non-random Method of randomisation: NA Concealment: NA BLINDING: open	N: 202 TD: 52 wks; FU: 52 wks LF: 64 (32%) BC: NA Age: 46 (14.5SD) Gender (per cent men): 60% Severity: Scalp: TSS (0 to 12): 5.9; Overall assessment (investigator): mild (31%); moderate (58%); severe (11%) Body: PASI (modified): 6.8 Overall assessment (investigator): mild	Calcipotriol scalp solution 50 mcg/ml BD plus calcipotriol cream 50 mcg/g BD (up to 70 g/wk) No control	Local AEs: number of AEs/participant % severe AEs withdrawals due to adverse events (WA) Systemic AEs: serum calcium serum PTH urinary calcium/creatinine ratio	Local AEs: the most common local AE was facial irritation (60/202 participants at wk 2), though the incidence declined rapidly over time (1/141 at wk 46). 20% of local AEs considered by investigator to be 'severe'. 14% of participants	Sponsored by Leo Pharmaceuticals	Not applicable

Table 24. Included studies of adverse events *(Continued)*

	WITHDRAWAL/DROPOUT: described	(41.5%); moderate (55%); severe (3.5%) INCLUSION CRITERIA: chronic plaque psoriasis on scalp and body; adult (≥18); outpatient EXCLUSION CRITERIA: pregnancy or risk thereof; severe (i.e. requiring additional therapy) or unstable psoriasis; hypercalcaemia; history of hypo- or hyperparathyroidism, renal/hepatic disease; systemic or phototherapies within previous 6 wks; other medication that could affect course of disease			withdrew because of adverse events Systemic AEs: no significant changes observed		
Berth-Jones 1993; Berth-Jones 1992c	DESIGN: uncontrolled study patient delivery ALLOCATION: non-random Method of randomisation: NA Concealment: NA BLINDING: open WITHDRAWAL/DROPOUT: NA	STUDY A: N: 20 TD: 52 wks; FU: 52 wks LF: 0 (0%) BC: NA Age: 43 Gender (per cent men): 65% Severity: mean PASI: 7.6 (3.5SD) STUDY B: N: intervention: 10 {32 controls} TD: 4 wks; FU: 4 wks LF: 0 (0%) BC: not demonstrated Age: 48 {42} Gender (per cent men): 50% {44%} Severity: mean PASI: 18.0 (13.9SD) {NR} INCLUSION CRITERIA: people with chronic plaque psoriasis; aged ≥18; under long-term care of investigators. Study A: compliant patients, responsive to calcipotriol. Study B: more extensive disease, failing to respond to low doses of topical agents. Controls received no calcipotriol. EXCLUSION CRITERIA: pregnancy	Study A: calcipotriol ointment 50 mcg/g BD up to 100 g/wk No control Study B: calcipotriol ointment 50 mcg/g BD, using 100 g/wk for 4 wks Control: people using alternative therapies	Local AEs: not assessed Systemic AEs: urine calcium and phosphate excretion; serum total calcium, phosphate and alkaline phosphatase	Study A: no significant trend in urine calcium excretion Study B: significant increase in urine calcium excretion (relative to controls and to baseline)	Sponsorship not reported For study B, baseline comparability of intervention and control groups not demonstrated. Berth Jones 1992 reports findings for study A at 10 mths	Not applicable

Table 24. Included studies of adverse events *(Continued)*

Bleiker 1998	DESIGN: uncontrolled study Delivery: unclear ALLOCATION: non-random Method of randomisation: NA Concealment: NA BLINDING: open WITHDRAWAL/DROPOUT: not described	N: 28 TD: 2 wks; FU: 26 wks LF: unclear BC: NA Age: 47 (range: 18 to 83) Gender (per cent men): 50% Severity: PASI: 21.4 (range: 8.2 to 53.7) INCLUSION CRITERIA: inpatients with severe chronic plaque psoriasis (> 15% BSA) EXCLUSION CRITERIA: renal impairment, pregnancy, lactation, systemic treatment, diuretics	STUDY A: 200 g calcipotriol ointment 50 mcg/g (wk 1) plus 300 g 50 mcg/g calcipotriol (wk 2) STUDY B: Calcipotriol 50 mcg/g PRN < = 360 g/wk	Local AEs: not assessed Systemic AEs: serum total adjusted calcium urinary calcium	5 participants developed hypercalcaemia during treatment, all had received a dose > 5 g/kg 9 participants became hypercalciuric during treatment; this was uncorrelated with dose	Sponsorship not reported	Not applicable
Brodell 2011b	DESIGN: uncontrolled study patient delivery ALLOCATION: non-randomised BLINDING: open WITHDRAWAL/DROPOUT: not described	N: 305 TD: 12 wks; FU: 12 LF: unclear BC: NA Age: 50.3 (13.7SD); range: 22 to 84 Gender (per cent men): 61.8% Severity: ODS: all patients scored as moderate/severe/very severe % BSA: 7.1% % white: 91.8% INCLUSION CRITERIA: people with moderate to severe plaque psoriasis; affected; aged 18 to 80 EXCLUSION CRITERIA: not stated	Clobetasol propionate 0.05% spray BD (2 to 4 wks); treatment responders (ODS < = 3) then treated with calcitriol 3 mg/g ointment (8 wks)	Pruritis, telangiectasias, burning/stinging (0 to 3), skin atrophy, folliculitis Overall disease severity (ODS) (5-pt: 0 = clear to 4 = severe/very severe) based on erythema, scaling, and plaque elevation. Treatment success (change from baseline ODS > = 1 at wk 12)	At 4 wks: skin atrophy 7/285 telangiectasias 2/285 stinging/Burning 39/285 folliculitis 11/285 At 12 wks: skin atrophy 2/235 telangiectasias 5/235 stinging/Burning 35/235 folliculitis 3/235 Any adverse event: 100/305	Sponsored by Galderma laboratories	Not applicable

Table 24. Included studies of adverse events *(Continued)*

Corbett 1976	DESIGN: within-patient patient delivery ALLOCATION: random Method of randomisation: NR Concealment: unclear BLINDING: double-blind (participant/investigator) WITHDRAWAL/DROPOUT: not described	N: 14 TD: 26 wks; FU: 26 wks LF: 2 (14.3%) BC (clinical): NR Age: 44 (18.4SD) Gender (per cent men): 64% Severity: NR INCLUSION CRITERIA: bilateral psoriasis involving < = 15% BSA; willing to participate for 6 months EXCLUSION CRITERIA: NR	Clobetasol propionate 0.05% ointment, BD Betamethasone valerate 0.1% ointment, BD	Local AEs: NR Systemic AEs: synacthen test for function of pituitary-adrenal axis at 0, 3, and 6 months	Quantities used by study participants were small (mean: 7 g/wk) No pituitary-adrenal suppression observed	Sponsorship not reported	Unclear
Gerritsen 2001; Langner 1996; van de Kerkhof 1996c	DESIGN: uncontrolled study patient delivery ALLOCATION: NA Method of randomisation: NA Concealment: NA BLINDING: open WITHDRAWAL/DROPOUT: described	N: 257 TD: < = 78 wks; FU: <= 78 wks LF: 4 (1.6%) BC: NA Age: 42 (13SD) Gender (per cent men): 61.3% Severity: BSA: 14.0% (14.2%SD); PASI: 9.7; 47% had severe disease INCLUSION CRITERIA: chronic plaque psoriasis; aged ≥18 EXCLUSION CRITERIA: non-compliant; pregnancy; use of systemic/phototherapy within previous 2 mths; use of topical therapy within previous 1 wk; concomitant disease; clinically relevant abnormality in laboratory assessments; known hypersensitivity to vitamin D/vehicle	Calcitriol 3 mcg/g BD No control	Local AEs: serious AEs reported; withdrawals due to adverse events (WA) Systemic AEs: laboratory levels for: protein albumin; calcium, phosphorus, sodium, potassium, plasma calcitriol Urinary calcium, creatinine, phosphorus; creatinine clearance; urinary calcium/creatinine ratio	Local AEs: WA: 7/253; AEs: 37/353; no serious local adverse events Systemic AEs: WA: 1/253. 4 additional participants experienced hypercalcaemia. All mean values for all parameters remained within normal levels. Mean use: 6 g/day (range: 1 to 24 g/day)	Sponsored by Solvay-Duphar BV Excludes scalp	Not applicable
Guzzo 1996	DESIGN: between-patient patient delivery	N: 78 TD: 8 wks; FU: 8 wks LF: 2 (2.6%)	Calcipotriol 50 mcg/g ointment BD, up to 120 g/wk	Local AEs: not assessed Systemic AEs: blood and urine	No adverse effects on bone metabolism or calcium	Sponsored by Bristol-Myers Squibb	Unclear

Table 24. Included studies of adverse events *(Continued)*

	ALLOCATION: random Method of randomisation: NR Concealment: unclear BLINDING: double-blind (participant/investigator) WITHDRAWAL/DROPOUT: described	BC: no (1 statistically significant difference (% BSA higher in intervention group) Age: 48 Gender (per cent men): 67% Severity: mean BSA: 9% INCLUSION CRITERIA: aged ≥18; stable plaque psoriasis; BSA: 5% to 20% EXCLUSION CRITERIA: hypercalcaemia, bone, thyroid or parathyroid disease; topical therapy within previous 2 wks; systemic/phototherapy within previous 8 wks	Placebo	chemistry analysis: parathyroid hormone, serum calcium, bone-specific alkaline phosphatase, urinary hyroxyproline, 24-hr urinary calcium excretion. Bone densitometry			
Heng 1990	DESIGN: between-patient (retrospective study) patient delivery ALLOCATION: non-random Method of randomisation: NA Concealment: NA BLINDING: NA WITHDRAWAL/DROPOUT: NA	N: 28 TD: 6 mths to 12 ys; FU: 6 mths to 12 years LF: NA BC: demographic: yes; clinical: not demonstrated Age: 49 (13SD) Gender (per cent men): 82% Severity: NR INCLUSION CRITERIA: psoriasis (any severity; types include plaque (16), generalised, seborrhoeic, guttate, erythrodermic); previous prolonged treatment with topical fluorinated steroids (range: 6 mths to 12 years). Control group matched for age and gender EXCLUSION CRITERIA: NR	Previous prolonged treatment with topical fluorinated steroids Control: 'steroid-negative' group - previous tar/UVB/sunlight or no treatment	Local AEs: light/electron microscopy for examination of basal keratinocyte herniation (BKH); layers of basement membrane Systemic AEs: NR	Local AEs: light microscopy revealed no between-group differences. Electron microscopy revealed multi-layered, fragmented and disorganised basal laminae in the steroid group, which appeared to be correlated with duration of treatment. Fragmentation was not observed in the control group	Sponsorship not reported Non-psoriatic control group also considered 16/28 participants had plaque psoriasis	Not applicable
Katz 1987b	DESIGN: between-patient patient delivery ALLOCATION: random Method of randomisation: NS	N: 40 TD: 3 wks; FU: 3 wks LF: NA BC: demographic: yes; clinical: yes (gender imbalance) Age: 44 (range: 18 to 66) Gender (per cent men): 53% Severity: 55% moderate disease; 45% severe disease INCLUSION CRITERIA:	Betamethasone dipropionate (0.05%) in optimised vehicle BD; Clobetasol 17 propionate (0.05%) ointment BD	Local AEs: not assessed Systemic AEs: morning plasma cortisol levels; 24-hr urine steroid levels; FBC, blood chemistry, urinalysis	Temporary reversible suppression of the hypothalamic-pituitary-adrenal axis in 8/40 participants	Sponsorship not reported; 1 author from Schering Corporation	Unclear

Table 24. Included studies of adverse events *(Continued)*

	Concealment: unclear BLINDING: double-blind (participant/investigator) WITHDRAWAL/DROPOUT: described	aged ≥ 18; stable or worsening, moderate or severe chronic plaque psoriasis; baseline laboratory values within normal range (5 to 25 mcg%) EXCLUSION CRITERIA: pregnancy or risk thereof; lactation; hypersensitivity to study medications; concurrent medication that could affect study outcomes; use of systemic therapies within previous 4 wks; use of topical therapies within previous 2 wks					
Katz 1989	DESIGN: within-patient patient delivery ALLOCATION: random Method of randomisation: unclear Concealment: unclear BLINDING: double-blind (participant/investigator) WITHDRAWAL/DROPOUT: described	N: 30 TD: 2 wks; FU: 4 wks LF: 0 (0%) BC: yes Age: 55 (range: 36 to 69) Gender (per cent men): 53% Severity: NR INCLUSION CRITERIA: bilateral symmetric chronic plaque psoriasis EXCLUSION CRITERIA: pregnancy or risk thereof; people with overt signs of atrophy	Betamethasone dipropionate (0.05%) in optimised vehicle BD (BMD) Clobetasol propionate (0.05%) ointment BD (CP) Uninvolved (non-psoriatic) area used as test area for each participant	Local AEs: skin surface microscopic examination with photographic documentation; oil and magnifying (8 x) lens to detect 'preatrophy' (visibility of subpapillary vascular plexus caused by thinning of epidermis and papillary dermis) Systemic AEs: NR	Local AEs: no serious adverse events observed with either treatment. Preatrophy identified in 20% of involved plaques (BMD: 11/59; CP: 12/59) and was more likely in females. In the test area (non-psoriatic skin), 5% of plaques showed preatrophy (BMD: 2/30; CP: 1/30). Preatrophy appeared to be usually reversible following treatment cessation.	Sponsored by Schering Corporation	Unclear
Kimball 2008 Phase II	DESIGN: uncontrolled patient delivery ALLOCATION: unclear BLINDING: open WITHDRAWAL/DROPOUT: described	N: 32 TD: 2 wks; FU: NS LF: 1 (3.1%) BC: NA Age: 24 to 72 Gender (per cent men): NS Severity: NS % white: 94% INCLUSION CRITERIA people with mild to moderate plaque psoriasis; aged > = 12	Clobetasol 0.05% foam BD Clobetasol 0.05% ointment BD (= 7 g/day, up to 50 g/wk)	Maximal plasma concentration of clobetasol propionate	Higher but non-significant levels of clobetasol in ointment group	Supported by Stiefel Laboratories, Inc. Review of phase II studies on AD and psoriasis (clobetasol foam)	Not applicable

Table 24. Included studies of adverse events *(Continued)*

		EXCLUSION CRITERIA: NS					
Kimball 2008 Phase III	DESIGN: between-patient patient delivery ALLOCATION: random Method of randomisation: not stated Concealment: unclear BLINDING: double-blind (participant/investigator) WITHDRAWAL/DROPOUT: described	N: 497 TD: 2 wks; FU: NS LF: 16 (3%) BC: NS Age: NS Gender (per cent men): NS Severity: most had baseline ISGA of 3 INCLUSION CRITERIA: people with mild to moderate plaque psoriasis; aged > = 12 EXCLUSION CRITERIA: NS	Clobetasol 0.05% foam BD Clobetasol 0.05% ointment BD Placebo foam BD Face, scalp, and intertriginous areas excluded from treatment	Treatment-related adverse events: • all • atrophy • burning • pruritis • folliculitis ISGA (investigator's static global assessment score) (scale NR)	Atrophy: C foam: 2% (N = 253) C ointment: NS (N = 121) Placebo foam: 1% (N = 123) Burning: C foam: 2% (N = 253) C ointment: NS (N = 121) Placebo foam: 2% (N = 123) All treatment-related adverse events: C foam: 8% (N = 253) C ointment: 2% (N = 121) Placebo foam: 7% (N = 123)	Supported by Stiefel Laboratories Inc. Review of phase III studies on AD and psoriasis (clobetasol foam).	Unclear
Kragballe 1991b	DESIGN: uncontrolled study patient delivery ALLOCATION: non-random Method of randomisation: NA Concealment: NA BLINDING: open WITHDRAWAL/DROPOUT: described	N: 15 TD: 26 wks; FU: 26 wks LF: 1(6.7%) BC: NA Age: 42 (range: 21 to 71) Gender (per cent men): 53% Severity: % BSA: 14% (range: 5% to 30%) Most 'moderate' severity INCLUSION CRITERIA: participants previously responding to calcipotriol during 8-wk clinical trial, but who had since relapsed EXCLUSION CRITERIA: hypercalcaemia, impaired renal/hepatic function, daily receiving > 400 i.u. vitamin D	Calcipotriol ointment 50 mcg/g BD (max: 100 g/wk) No control	Local AEs: patient report of adverse events Investigator report of adverse events (skin examination). Skin biopsies to determine histologic signs of epidermal and dermal atrophy. Systemic AEs: laboratory tests: FBC, serum alkaline phosphatase, aspartate aminotransferase, biliru-	Local AEs: AE(L): 3/15 (reported to be transient & mild). Cases of mild to moderate atrophy found in 4/8 participants Systemic AEs: no consistent changes in laboratory analyses, with no clinically important changes in serum calcium	Sponsorship not reported. Leo Pharmaceuticals supplied study medication Face and scalp treated with emollient or hydrocortisone cream 1% (not calcipotriol)	Not applicable

Table 24. Included studies of adverse events *(Continued)*

				bin, creatinine, total calcium, total phosphate			
Lambert 2002	DESIGN: uncontrolled study patient delivery ALLOCATION: non-random Method of randomisation: NA Concealment: NA BLINDING: open WITHDRAWAL/DROPOUT: described	N: 157 TD: 26 wks; FU: 26 wks LF: 8 (5.1%) BC: NA Age: 44.4 (14.0SD) Gender (per cent men): 57% Severity: mean BSA: 13%; mean PASI: 9.4 (5.4SD) INCLUSION CRITERIA: chronic plaque psoriasis; aged 18 to 70; BSA 7% to 20%; laboratory parameters normal at baseline EXCLUSION CRITERIA: pregnancy or risk thereof; topical antipsoriatic therapy within previous 2 wks; systemic antipsoriatic therapy within previous 6 wks; retinoids within previous 52 wks.; history of hyperparathyroidism; concomitant use of drugs affecting calcium metabolism	Tacalcitol ointment, 4 mcg/g OD. No control	Local AEs: participants asked about adverse events. Tolerability assessed by investigator (4-pt: 1 = excellent to 4 = poor). Systemic AEs: Routine haematology and biochemistry: FBC, haemoglobin, bilirubin, creatinine, alkaline phosphatase, aspartate aminotransferase, alanine aminotransferase, gamma glutamyltranspeptidase, calcium, phosphate, sodium, potassium, glucose, urea, albumin. Urinalysis: calcium, creatinine, phosphate.	Local AEs: WA: 5/157 (3.4%) (treatment-related). AE(L): 26/157 (transient skin irritation) Tolerability at least moderate in 95% of participants Systemic AEs: no serious adverse events and no hypercalcaemia	Sponsored by Hermal/BHI, Germany Scalp excluded Similar study to van de Kerkhof 2002, but unclear whether Lambert 2002 is a report of a subgroup or a distinct study	Not applicable
Lebwohl 1998b	DESIGN: between-patient patient delivery ALLOCATION: random. Method of randomisation: unclear Concealment: unclear BLINDING: double-blind (par-	N: 40 TD: 26 wks; FU: 26 wks LF: 4 (10%) BC: no (Group A had less severe disease at baseline) Age: NR Gender (per cent men): NR Severity: mild to moderate psoriasis INCLUSION CRITERIA: people with at least moderate improvement in response to initial 2-wk therapy regimen; aged ≥18; stable disease;	Initial regimen: all participants received 2 wks of calcipotriol (OM), halobetasol ointment (ON) Group A: Calcipotriol ointment 50 mcg/g (weekdays)	Local AEs: treatment-related adverse events Systemic AEs: not assessed	Local AEs: AE(L) (treatment-related; all irritant contact dermatitis): Group A: 4/17 Group B: 1/20 No cutaneous atrophy observed	Sponsored by Westwood Squibb Pharmaceuticals	Unclear

Table 24. Included studies of adverse events *(Continued)*

	ticipant/investigator) WITHDRAWAL/DROPOUT: described	BSA < = 20% (excluding face/scalp); plaque elevation at least moderate; willing to comply with study protocol EXCLUSION CRITERIA: history of sensitivity to study ingredients; topical antipsoriatics within previous 2 wks; UVB/PUVA within previous 8 wks; history of hypercalcaemia, recurrent illness	plus halobetasol 0.05% ointment BD (weekends) Group B: Placebo ointment (weekdays) plus halobetasol 0.05% ointment BD (weekends)				
Lebwohl 2001	DESIGN: between-patient patient delivery ALLOCATION: random Method of randomisation: NR Concealment: unclear BLINDING: double-blind (participant/investigator) WITHDRAWAL/DROPOUT: not described	N: 50 TD: 26 wks; FU: 26 wks LF: NR BC: NR Age: 55 Gender (per cent men): NR Severity: NR INCLUSION CRITERIA: moderate to severe plaque psoriasis; BSA < = 15%. All participants participated in an open-label treatment phase for 6 wks (tazarotene gel 0.1% OM, clobetasol propionate ointment 0.05% ON) EXCLUSION CRITERIA: topical antipsoriatic treatment within previous 2 wks; UV treatment within previous 4 wks; systemic antipsoriatic treatment within previous 8 wks	Open-label phase: tazarotene 0.1% gel plus clobetasol propionate 0.05% ointment for 6 wks. Once daily initially, then 'tapered'. Maintenance phase (20 wks): tazarotene gel, 0.1%, OM (3/7 days), plus clobetasol propionate 0.05% ointment ON (2/7days) (TC) Tazarotene gel, 0.1%, OM (3/7 days), placebo ointment OM (2/7 days), placebo ointment	Local AEs: no. steroid-specific side-effects Withdrawals due to adverse events (WA) Drug-related adverse events Systemic AEs: not assessed	Local AEs: no steroid-specific side-effects WA: 0/50 AE(L) (treatment-related): TC: 24% TP: 29% P: 0%	Sponsorship: not reported No adequate effectiveness data reported. Numbers of participants in each group NR	Unclear

Table 24. Included studies of adverse events *(Continued)*

			ON (2/7 days) (TP) Placebo gel OM (3/7 days), placebo ointment ON (2/7 days) (P)				
Menter 2007; Feldman 2007a	DESIGN: uncontrolled patient delivery ALLOCATION: NA BLINDING: open WITHDRAWAL/DROPOUT: described	N: 1423 TD: 4 wks; FU: 4 wks LF: 2 (0.1%) BC: NA Age: 49.7 (14.7SD) Gender (per cent men): NS Severity: Duration (yrs): 12.5 (13SD) BSA: 10.6% (5.75% SD) INCLUSION CRITERIA: people with moderate to severe plaque psoriasis; 3% to 20% BSA involvement EXCLUSION CRITERIA: current systemic therapy, phototherapy or topical therapy	Clobetasol 0.05% foam BD, up to 50 g/wk either as monotherapy or adjunctive to existing therapy	Erythema, peeling/scaling, dryness, stinging/burning (0 none to 3 severe). Telangiectasia, skin atrophy, pruritus, folliculitis (absent/present) Also assessed efficacy and QoL	Erythema: 23.7% peeling/scaling: 21.0% dryness: 28.3% stinging/burning: 15.1% Telangiectasia, skin atrophy, folliculitis: present in less than 1% of participants (findings not reported separately) Pruritus: 5.7%	Clobex Spray Community-Based Research Assessment (COBRA) Sponsorship not reported	Not applicable
Miyachi 2002	DESIGN: uncontrolled study patient delivery ALLOCATION: non-random Method of randomisation: NA Concealment: NA BLINDING: open WITHDRAWAL/DROPOUT: described	N: 160 TD: 54 wks; FU: 54 wks LF: 6 (3.8%) BC: NA Age: 48.2 (16.1SD) Gender (per cent men): 82% Severity: mean PASI: 22.49 (10.2SD) INCLUSION CRITERIA: inpatients and outpatients with BSA ≥10% EXCLUSION CRITERIA: pregnancy; lactation; severe liver disease, heart disease, impaired renal function, hypercalcaemia; treatment with topical, UV or systemic antipsoriatics within previous 2 wks	Tacalcitol ointment 20 mcg/g OD (max: 10 g/day) No control	Local AEs: treatment-related adverse events Systemic events: haematological tests (FBC), blood biochemical tests (calcium, inorganic phosphorus, albumin, protein, bilirubin, urea nitrogen, creatinine, GP/AST, GPT/ALT, alkaline phosphatase, LDH, intact PTH), urinalysis (glucose, protein); serum tacal-	Local AEs: AE(L): 16/154 (29 events, all mild to moderate) Systemic AEs: AE(S): 85/154 (155 events, of which 6 were considered treatment-related). Serum levels of intact PTH and tacalcitol decreased, suggesting percutaneous absorption of tacalcitol. However, mean levels of serum calcium remained within the standard	Sponsorship: not reported Scalp treated in 74/154 participants Usual dosing regimen for tacalcitol is 4 mcg/g OD	Not applicable

Table 24. Included studies of adverse events *(Continued)*

				citol and vitamin D_3 levels.	level. Data on individual responses not reported. High-dose tacalcitol affected serum calcium in participants with reduced renal function		
Poyner 1993	DESIGN: uncontrolled study patient delivery ALLOCATION: non-random Method of randomisation: NA Concealment: NA BLINDING: open WITHDRAWAL/DROPOUT: described	N: 203 TD: 48 wks; FU: 48 wks LF: 59 (29.1%) BC: NA Age: 43.8 (range: 17 to 80) Gender (per cent men): 52.7% Severity (assessment methods NR): mild (8%); moderate (63%); severe (30%) INCLUSION CRITERIA: aged ≥18; chronic plaque psoriasis ≥ 100 cm^2. EXCLUSION CRITERIA: PUVA within previous 8 wks; elevated serum calcium, unstable disease, impaired hepatic/renal function' pregnancy; concomitant oral calcium/vitamin D. topical antipsoriatics, lithium, systemic steroids	Calcipotriol 50 mcg/g ointment No control	Loca AEs: self report of adverse events. Withdrawals due to adverse events (WA) Systemic AEs: biochemical and haematological tests Compliance: self-reported usage at each visit; weighing of ointment tubes	Local AEs: WA: 8/203 AE(L): 83/203 142 events reported by 83 (41%) participants with 20.2% being lesional/perilesional irritation Systemic AEs: no significant changes in haematological values. Mean serum calcium did not change significantly over study period. Significant fall in serum urate in those treated ≥ 36 wks Compliance: median weekly use (wks 0 to 5): 16.5g; (wks 43 to 48): 11.6g	Sponsored by Leo Pharmaceuticals Face/scalp excluded	Not applicable
Ramsay 1994	DESIGN: uncontrolled open study patient delivery ALLOCATION: non-random Method of randomisation: NA Concealment: NA	N: 167 TD: 52 wks; FU: 52 wks LF: 39 (23.4%) BC: NA Age: 49 (range: 20 to 85) Gender (per cent men): 60% Severity: PASI (modified): 8.1 (6.7SD)	Calcipotriol 50 mcg/g ointment. Max dose: 100 g/wk; 2500 g/pa Face/scalp/neck excluded No control	Local AEs: self report of adverse events: mild, moderate, severe; unlikely, possibly, or probably treatment-related Systemic AEs: haematology (erythrocyte, haemo-	AE(L): 52/161 60 (46 considered to be treatment-related) events reported by 52 of 161 participants. 1 participant developed a significant rise in serum calcium. No other abnormalities in haematology or	Sponsored by Leo Pharmaceuticals	Not applicable

Table 24. Included studies of adverse events *(Continued)*

	BLINDING: open WITHDRAWAL/DROPOUT: described	INCLUSION CRITERIA: chronic plaque psoriasis; previous response to calcipotriol; managed by specialists EXCLUSION CRITERIA: pregnancy or risk thereof; abnormal serum calcium or phosphate; impaired hepatic/renal function; concomitant oral calcium/vitamin D; systemic therapy within previous 8 wks; topical therapy within previous 4 wks		globin, leukocyte, platelet counts) and biochemistry (bilirubin, AST/ALT, alkaline phosphatase, albumin, urate, creatinine, phosphate, total calcium) tests Compliance: self report of number tubes used and number daily doses	biochemistry tests. 118/161 participants reported continuous medication use and 80% to 90% used it twice daily. Mean use: 35.1 g/wk ('initially') to 23.4 g/wk during last 6 mths	
Roelofzen 2010	DESIGN: observational study using retrospective data (medical records, cancer registry) and prospective (survey) data (treatments/lifestyle). Multivariate proportional hazards regression. ALLOCATION: NA BLINDING: NA WITHDRAWAL/DROPOUT: described	N: 4315 TD: pix lithantracis (med): 4 mths (1 to 300 mths) liquor carbonis detergens (med): 6 mths (1 to 500 mths) FU: (med) 21 yrs LF: 329 (7.6%) BC: NA Age (at diagnosis): 31 (0 to 95.7) Gender (per cent men): 52% Severity: % BSA < 1%: 9% % BSA 2% to 9%: 30% % BSA 10% to 30%: 39% % BSA > 30%: 22% INCLUSION CRITERIA: people with psoriasis or eczema, diagnosed 1960 to 1990 and treated in 1 of 3 Dutch hospitals; EXCLUSION CRITERIA: people who could not be traced	All topical, phototherapy, and systemic therapies. Focus of study is on coal tar: • Liquor carbonis only (LCD) • Pix lithantiacis (PL)	Any cancer Skin cancer Internal malignancies Specific tumour groups: • haematological • breast • lung • gastrointestinal • bladder/urinary tract • prostate • female reproductive organs No statistically significant increased risk of any cancer. Hazard ratios: Any cancer: LCD: 0.85 (95% CI 0.60 to 1.19) PL: 0.64 (95% CI 0.40 to 1.03)	Analysis adjusted for smoking status, other treatments, skin type, alcohol consumption. However, data on duration of tar therapy, smoking status and alcohol consumption were missing for most participants	Not applicable-

Table 24. Included studies of adverse events *(Continued)*

				Skin cancer: LCD: 1.35 (95% CI 0.53 to 3.44) PL: 0.33 (95% CI 0.07 to 1.69)			
van de Kerkhof 1997b	DESIGN: uncontrolled study patient delivery ALLOCATION: non-random Method of randomisation: NA Concealment: NA BLINDING: open WITHDRAWAL/DROPOUT: described	N: 58 TD: < = 60 wks; FU: < = 60 wks LF: 16 (27.6%) BC: NA Age: 45 (range: 19 to 78) Gender (per cent men): 69.0% Severity: BSA: 8.6% (3.9SD); TSS (0 to 12):7.9 (2.1SD) INCLUSION CRITERIA: people with chronic plaque psoriasis participating in previous double-blind study (Van de Kerkhof 1996b); aged 25 to 80; normal serum calcium/phosphate. EXCLUSION CRITERIA: pregnancy or risk thereof; topical therapy within previous 4 wks; systemic therapy within previous 8 wks; serious disease; known allergy to study medication; concomitant medication that could interfere with study drug or systemic calcium metabolism	Part 1: double-blind study (8 wks): tacalcitol 4 mcg/g ointment OD Placebo Part 2: open follow-up study (4 wk wash-out period): tacalcitol 4 mcg/g ointment OD, < = 20 mg/day and < 2000 g per participant over study period. Participants could discontinue treatment after 12 wks No control	Local AEs: occurrence of adverse events (duration, severity, and whether treatment-related) Participant and investigator assessments of tolerability (4-pt: v. good (3) to insufficient (0)) Systemic AEs: haematology (erythrocytes, platelets, haemoglobin, haematocrit); blood chemistry (serum calcium, inorganic phosphate, creatinine, ASAT, alkaline phosphatase, LDH)	Local AEs: WA: 0/58 AE(L): 10/58 (19 events) AE(L)(treatment-related): 8/58 Tolerability: investigator assessment: 2.60 (0.53SD, N = 58); participant assessment: 2.53 (0.63SD, N = 58) Systemic AEs: AE(S): 0/58 No case of hypercalcaemia	Sponsorship not reported Follow-up study to Van de Kerkhof 1996b - 3 of 15 centres participated Scalp excluded	Not applicable
van de Kerkhof 2002c (see also Lambert 2002)	DESIGN: uncontrolled study patient delivery ALLOCATION: non-random Method of randomisation: NA	Part 1: N: 304 TD: 13 wks; FU: 13 wks LF: 47 (15.5%) BC: NA Age: 44 (range: 15 to 76) Gender (per cent men): 57% Severity: median PASI (modified to exclude head): 9.5 (range: 2.2 to 24.4); TSS (0 to 12): 6.0	Tacalcitol 4 mcg/g OD. Treatment discontinued during remission and restarted if relapse No control	Local AEs: number treatment-related adverse events; withdrawals due to adverse events (WA); investigator assessment of tolerability; participant assessment of tolerability	Local AEs: WA: 18/304 AE(L): 65/304 Tolerability excellent/good in 76% (patient assessment) to 92% (investigator assessment) of participants at final assessment.	Sponsored by Hermal/BHI, Germany Scalp excluded	Not applicable

Table 24. Included studies of adverse events *(Continued)*

	Concealment: NA BLINDING: open WITHDRAWAL/DROPOUT: described	Part 2: n: 197 TD: 65 wks; FU: 65 wks LF: 83 (42.1%) BC: NA Age: NR Gender (per cent men): NR Severity: NR INCLUSION CRITERIA: chronic plaque psoriasis; BSA 7% to 20% (excluding scalp); aged 18 to 70; normal baseline laboratory values Part 2 of study: responders to part 1 (≥ 30% reduction in sum score (TSS) from baseline) EXCLUSION CRITERIA: topical steroids in previous 2 wks; systemic antipsoriatics within previous 6 wks; retinoids within previous 52 wks; known hypersensitivity to vitamin D_3 analogues; serious concomitant disease; disease that might interfere with study assessments; concomitant use of oral calcium/vitamin D; pregnancy or risk thereof		Systemic AEs: Haematology: serum calcium, parathyroid hormone (PTH), calcitonin, calcitriol Urine: calcium, creatinine, calcium/creatinine ratio. Compliance with medication	Systemic AEs: No clinically significant changes in routine haematology, urinalysis or serum chemistry. Compliance with treatment regimen varied between 82% and 92%. However, 54% of those with BSA 10% to 20% exceeded recommended daily dose of 5 g (up to 13 g daily), but there was no effect on calcium homeostasis. Duration of excess dosing not reported		
Vazquez-Lopez 2004	DESIGN: uncontrolled study patient delivery ALLOCATION: non-random Method of randomisation: NA Concealment: NA BLINDING: open WITHDRAWAL/DROPOUT: described	N: 20 TD: 26 wks; FU: 34 wks LF: 0 (0%) BC: NA Age: 28.2 (range: 20 to 55) Gender (per cent men): 40% Severity: NR INCLUSION CRITERIA: absence of visible or dermascopic red lines (linear telangiectasias) EXCLUSION CRITERIA: use of topical steroids in previous 2 mths	Clobetasol propionate 0.05% cream, OD (weekends) plus calcipotriol 50 mcg/g ointment BD (weekdays) No control	Local AEs: clinical (naked eye) examination of psoriatic plaque and surrounding area Dermoscopic examination of psoriatic plaque and surrounding area Systemic AEs: NR Compliance: quantity and frequency of study drug use (tubes weighed)	Overuse of topical steroids resulted in appearance of clinically unapparent but dermoscopically apparent linear telangiectasias. 7/20 participants failed to adhere to recommended steroid dosing schedules. Dermoscopic red lines not apparent in 15/20 participants. Dermoscopic red lines apparent in 5/20 participants, of whom 4 had overused top-	Links compliance with adverse events Study received no funding	Not applicable

Table 24. Included studies of adverse events *(Continued)*

					ical steroid cream. Steroid discontinued in participants with red lines and there was complete resolution within 2 mths		
Veraldi 2006	DESIGN: uncontrolled study patient delivery ALLOCATION: sequential recruitment BLINDING: open WITHDRAWAL/DROPOUT: described	N: 48 TD: 45 dys; FU: 45 dys LF: 5 (10.4%) BC: NA Age: 48.9 (range: 21 to 71) Gender (per cent men): 62.5% Severity: NR INCLUSION CRITERIA: people with chronic stable plaque psoriasis; % BSA < = 20% EXCLUSION CRITERIA: use of antipsoriatic therapy within previous 2 wks; concurrent use of other topical, photo or systemic therapies	0.1% tazarotene gel, short contact therapy (applied OD for 20 minutes then rinsed off with water)	Pruritis (4-pt: 0 = absent to 3 = severe) Burning (4-pt: 0 = absent to 3 = severe)	At day 45: pruritis (0 to 3): 0.17 (0.38SD) 14/43 had mild pruritis Burning (0 to 3) 0.17 (0.38SD) 14/43 14/43 had mild burning No participant withdrew because of irritation on treated lesion	Sponsorship not reported	Not applicable
Wishart 1994	DESIGN: uncontrolled study patient delivery ALLOCATION: groups determined according to BSA affected. BLINDING: open WITHDRAWAL/DROPOUT: described	N: 30 TD: 6 wks; FU: 6 wks LF: 1 (3%) BC: NA Age: 42.5 (13.2SD) Gender (per cent men): 47% Severity: Duration (mths): 202 (176SD) INCLUSION CRITERIA: people aged >18 with severe chronic plaque psoriasis; lesion severity > = 3 (GSS 0 to 4) EXCLUSION CRITERIA: pregnancy, other type of psoriasis, concurrent use of medicines containing calcium or vitamin D, antacids or digitalis	Calcitriol 15 mcg/g ointment OD Quantity of study drug varied by group: Group 1 (N =12): 4% to 8% BSA treated (300 to 600 cm^2) Group 2 (N = 10): 8% to 15% BSA	IAGI (6-pt) ECG Haematology, biochemistry, urine protein and glucose. Serum calcium, phosphorus, plasma PTH, serum 25-hydroxyvitaim D, 1-alpha,25dihydroxy-vitaim D, 24 hr urine tests for calcium, creatinine and phosphorus.	Mean daily usage: 74.0 to 306.1 mcg. No systemic adverse events, no skin irritation. No clinically relevant changes in vital signs, haematology, biochemistry, urine or ECGs. IAGI (0 to 5): -3.57 (1.01SD, N = 30)	Usual dose is 3 mcg/g BD, max. 30 g daily Sponsored by Solvay Duphar	Not applicable

Table 24. Included studies of adverse events *(Continued)*

		treated (600 to 1200 cm^2) Group 3 (N = 8): 15% to 30% BSA treated (1200 to 2400 cm^2)	Compliance also assessed (medication weight)

per cent men: per cent male; AE(L): number local adverse events/number participants; AE(S): number systemic adverse events/number participants; AE: adverse events; BC: baseline comparability; BD: twice daily; BSA: body surface area; FU: follow up (includes TD); N: number enrolled; NA: not applicable; NR: not reported; OD: once daily; PASI: Psoriasis Area and Severity Index; PRN: as required; TD: treatment duration; TSS: Total Severity Score; WA: withdrawal due to adverse events

Table 25. Excluded studies of adverse events

Study	Reason for exclusion
Aste 2004	Follow-up under 12 wks and not focused on adverse events
Bos 2002	Not psoriasis, short review (letter)
Breneman 2007	Not a product included in our review (bexarotene gel 1%)
Carboni 2005	Not focused on adverse events
Feldman 2007a	Evaluated add-on clobetasol for participants treated concurrently with topical or systemic therapy
Floden 1975	Inadequate reporting of adverse events
Franssen 1999	Small (N = 54) retrospective study using participant questionnaires - aimed to identify teratogenetic effects of tar, but many women unable to recall whether tar used in pregnancy
Hong 2010; Hong 2011	Not chronic plaque psoriasis: paediatric dermatology participants had eczema or "eczema–psoriasis overlap (atopic dermatitis with associated features of psoriasis)"
Jacobi 2008	Small uncontrolled short-term and already reflected in results from main review
Kang 1998	Short-term and already reflected in results from main review
Lebwohl 1996	Follow-up under 12 wks and not focused on adverse events
Park 2002	Case study
Senter 1983	Adverse events not reported
Singh 2000	Short-term (4 weeks) and brief mention of adverse events
Stevanovic 1977	Short-term, unclear if psoriasis, small numbers (N = 6)
Traulsen 2003	Participants were healthy volunteers
Uhoda 2003	Not about adverse events
Vissers 2004	Not about adverse events

Table 26. Included studies of compliance

Study	Methods	Participants	Interventions	Outcomes (compliance	Summary findings	Notes	Allocation concealment
Balkrishnan 2003	DESIGN: uncontrolled study patient delivery ALLOCATION: nonrandom Method of randomisation: NA Concealment: NA BLINDING: single-blind (participants unaware of electronic compliance assessment) WITHDRAWAL/DROPOUT: described	N: 10 TD: 1 wk; FU: 1 wk LF: 0 (0%) BC: NA Age: NR Gender (per cent men): NR Severity: NR INCLUSION CRITERIA: participants with psoriasis who already enrolling in a study with salicylic acid and topical tacrolimus ointment (Protopic) combination therapy. EXCLUSION CRITERIA: NR	Topical salicylic acid 6% No control	Medication adherence: (1) MEMS cap: medication bottle cap with microprocessor to record time/date of every opening of the bottle. (2) Patient log (self report) of compliance Mean adherence rate: method 1: 67% (32% SD); method 2: 92% (7% SD)	Medication adherence measured by method 1 (electronic) much lower than by method 2 (patient log)	Sponsorship not reported	D
Carroll 2004a; Carroll 2004b; Carroll 2005	DESIGN: within-patient patient delivery ALLOCATION: random Method of randomisation: NR Concealment: unclear BLINDING: Single-blind (participants unaware of electronic compliance assessment) WITHDRAWAL/DROPOUT: described	N: 30 TD: 8 wks; FU: 12 wks LF: 6 (20%) BC: Yes Age: 43.6 (range 18 to 70) Gender (per cent men): 50% Severity: TSS (0 to 8): 5.3 INCLUSION CRITERIA: participants aged ≥18; symmetrical plaque-type psoriasis; BSA < = 10%; symmetrical target plaque 1cm^2 with each with a score of at least 1 for erythema, thickness, and scale EXCLUSION CRITERIA: pregnancy or risk thereof; topical treatment within previous 2 wks; phototherapy or systemic therapy within previous 4 wks	Topical salicylic acid 6% plus 0.1% tacrolimus ointment BD Topical salicylic acid 6% plus placebo BD	Medication adherence: (1) MEMS cap: medication bottle cap with microprocessor to record time/date of every opening of the bottle. (2) Patient log (self report) of compliance (3) medication weights	Adherence decreased over time. On the intervention side, a decrease in adherence rate of 10% was associated with a 1-point increase in severity (P < 0.05). For the placebo-treated side, adherence was not significantly correlated with changes in severity. Poor compliance appears to have an impact on treatment outcomes in psoriasis Mean adherence (method 1): % (doses taken/doses expected): 55%;	Sponsored by Fujisawa Healthcare, Inc. and by Wake Forest University School of Medicine. Excluded from effectiveness review (comparator is not placebo)	B

Table 26. Included studies of compliance *(Continued)*

					% (days with twice-daily dose/total days): 39.1% Higher adherence rate for women and older participants		
Feldman 2007	DESIGN: uncontrolled study patient delivery ALLOCATION: non-random Method of randomisation: NA Concealment: NA BLINDING: single-blind (participants unaware of electronic compliance assessment) WITHDRAWAL/DROPOUT: described	N: 29 TD: 8 wks; FU: 8 wks LF: NR BC: NA Age: 43.5 Gender (per cent men): NR Severity: NR INCLUSION CRITERIA: NR EXCLUSION CRITERIA: NR	6% salicylic acid gel BD No control	Impact of office visits on participants' adherence to topical treatment. Adherence assessed using MEMS cap: medication bottle cap	Adherence statistically significantly higher at time of office visit. Mean adherence over the study duration was 55%. Mean applications/day: 1.1 (range: 0.72 to 1.4)	Sponsored in part by Astellas Pharma US, Inc. The Center for Dermatology Research is funded by a grant from GaldermaLaboratories, LP. (see also Balkrishnan 2003; Carroll 2004a, 2004b, 2005)	D
Ferrandiz 1998	DESIGN: between-patient patient delivery (therapy) Clinician delivery (programme) ALLOCATION: random Method of randomisation: NR Concealment: unclear BLINDING: open WITHDRAWAL/DROPOUT: described	N: 881 TD: 16 wks; FU: 16 wks LF: 127 (12.6%) BC: Yes Age: 43.3 (16.9SD) Gender (per cent men): NR Severity: mean PASI: 7.0 INCLUSION CRITERIA: moderately severe chronic plaque psoriasis; BSA < = 30%; aged 18 to 70; under specialist supervision EXCLUSION CRITERIA: pregnancy or lactation; history of intolerance to calcipotriol/excipients; concurrent vitamin D (> 400 units/day) or calcium tablets; psoriasis mainly on face or hirsute areas	Calcipotriol plus reinforcement programme Calcipotriol without reinforcement programme	Reinforcement therapeutic programme to enhance adherence: dermatologist provided participant education with explanation of disease characteristics and treatment efficacy and application, plus written information card	The reinforcement programme had no effect on treatment efficacy	Sponsorship not reported	B

Table 26. Included studies of compliance *(Continued)*

Fouere 2005	DESIGN: questionnaire survey (observational cross-sectional study) ALLOCATION: non-random Method of randomisation: NA Concealment: NA BLINDING: open WITHDRAWAL/DROPOUT: response rate not reported	N: 1281 TD: NA; FU: NA LF: NA BC: NA Age: 51.9 (SD 14.8) Gender (per cent men): 48% Severity: 74% considered their psoriasis as at least moderately severe INCLUSION CRITERIA: members of the national psoriasis patient associations in France, UK, Belgium, Germany, and the Netherlands. EXCLUSION CRITERIA: not stated	Any antipsoriatic therapy	Compliance measured against PMAQ-3w scale (patient medication adherence questionnaire): strict adherence to prescribed regimen over previous 3 days and last weekend Reasons for non-compliance Perceived necessary measures to increase compliance	73% reported non-compliance with current treatment Main reasons for non-compliance: lack of efficacy, messiness, and time constraints To improve compliance, patients suggested improved efficacy, less greasy, sticky and smelly treatment, and fewer side-effects.	Sponsorship not reported. 70% of responders used topical therapy	D
Gokdemir 2008	DESIGN: open uncontrolled study patient delivery ALLOCATION: non-random Method of randomisation: NA Concealment: NA BLINDING: open WITHDRAWAL/DROPOUT: described	N: 109 TD: 8 wks; FU: 8 wks LF: 6 (6%) BC: NA Age: 40 (range: 16 to 70) Gender (per cent men): 43% Severity: PASI: 9.1 (range: 1.2 to 35) INCLUSION CRITERIA: chronic plaque psoriasis; received prescribed antipsoriatic therapy; aged ≥16; attending outpatient clinic in Istanbul. EXCLUSION CRITERIA: other types of psoriasis; hospitalised; pregnancy	Any prescribed antipsoriatic therapy	Medication adherence: number prescribed doses taken/number prescribed doses prescribed (see Zaghloul 2004).	Mean adherence for topical therapy: 72% (31%SD) Adherence rate was correlated with being unmarried, more highly educated, and being satisfied with treatment Main reasons for non-adherence were busyness and 'being fed up'	Findings relate to any treatment for psoriasis (not just topical therapy) Sponsorship not reported	D
Richards 1999	DESIGN: questionnaire survey (cross-sectional uncontrolled study)	N: 120 TD: NA; FU: NA LF: NA BC: NA	Any antipsoriatic therapy	Per cent complying with treatment (self	39 per cent reported non-compliance (sometimes/never complying) with prescribed treat-	Sponsorship not reported	D

Table 26. Included studies of compliance *(Continued)*

	patient delivery ALLOCATION: non-random Method of randomisation: NA Concealment: NA BLINDING: open WITHDRAWAL/DROPOUT: Response rate not reported	Age: 49 (18 to 84) Gender (per cent men): 54% Severity: Duration: range: 1 to 63 yrs INCLUSION CRITERIA: consecutive participants attending tertiary psoriasis specialty clinic; psoriasis. EXCLUSION CRITERIA: not stated		report): scale not reported	ment. The non-compliant group had a higher self-rated disease severity, were younger, and had a younger age at onset. The non-compliant group reported that psoriasis had a greater impact on daily life Factors affecting compliance included the doctor-participant relationship; optimism with the treatment prescribed; and a limited 'nuisance' value of treatment in terms of side-effects and hassle of use	55% of participants were using topical therapies	
van de Kerkhof 1998	DESIGN: questionnaire survey (uncontrolled study) patient delivery ALLOCATION: non-random Method of randomisation: NA Concealment: NA BLINDING: NA WITHDRAWAL/DROPOUT: Response rate reported	N: 972 TD: NA; FU: NA Response rate: 13% BC: NA Age: 45.8 (range: 5 to 87) Gender (per cent men): 43% Severity: duration of psoriasis > 10 yrs in 67% of responders INCLUSION CRITERIA: subscribers to 'Psoriasis', the journal of the Dutch Psoriasis Patient Organisation EXCLUSION CRITERIA: none stated	Any topical antipsoriatic therapy	Per cent complying with frequency of application of prescribed topical therapies Reason for non-compliance	29% of responders reported that the prescriber did not specify dosage frequency. Where dosage frequency was specified, 33% (39%) complied with twice (once) daily regimens Main reasons for non-adherence were preference for less frequent dosage; greasiness; lack of efficacy; and higher-than expected efficacy	Sponsorship not reported. 14-item questionnaire mailed in 1996 to 6100 subscribers of Psoriasis, the Journal of the Dutch Psoriasis Patient Organisation Responders asked to report on compliance over past 6 mths	D
van de Kerkhof 2000	DESIGN: questionnaire survey (uncontrolled study)	N: 839 TD: NA; FU: NA LF: NA Response rate: 14%	Any antipsoriatic therapy including topical treat-	Per cent complying with duration of prescribed treat-	Per cent complying with duration of prescribed treatment (topical therapies): 71%	Sponsorship not reported	D

Table 26. Included studies of compliance *(Continued)*

	ALLOCATION: non-random Method of randomisation: NA Concealment: NA BLINDING: single-blind WITHDRAWAL/DROPOUT: response rate reported	BC: NA Age: 48.5 (range: 4 to 91) Gender (per cent men): 46% Severity: duration of psoriasis ≥ 11 years in 62% of responders INCLUSION CRITERIA: subscribers to 'Psoriasis', the Journal of the Dutch Psoriasis Patient Organisation EXCLUSION CRITERIA: none stated	ments, photo(chemo)therapy and systemic therapy	ment (topical therapies) Per cent complying with frequency of application of prescribed treatment (topical therapies) Reason for non-compliance	Per cent complying with frequency of application of prescribed treatment (topical therapies): 51% Main reasons for non-adherence were preference for minimum dosage; time constraints; and lack of confidence in efficacy	41-item questionnaire mailed to 6100 subscribers of Psoriasis, the Journal of the Dutch Psoriasis Patient Organisation Responders asked to report on compliance over past 6 mths	
van de Kerkhof 2001	DESIGN: within-patient (see Notes) patient delivery ALLOCATION: non-random Method of randomisation: NA concealment: NA BLINDING: open WITHDRAWAL/DROPOUT: described	N: 976 TD: 8 wks; FU: 8 wks LF: 93 (9.5%) BC: NR Age: 45.6 (range: 7.4 to 88.4) Gender (per cent men): 52% Severity: BSA ≥ 10% in 51% of participants INCLUSION CRITERIA: psoriasis (type NR); eligible for treatment with calcipotriol EXCLUSION CRITERIA: concomitant topical or systemic antipsoriatic therapy; co-existing skin disorder other than psoriasis	Calcipotriol cream OM plus calcipotriol ointment ON Calcipotriol ointment BD	Compliance: self-reported number of days cream/ointment regimen applied	At wk 3, 72% of participants applied the regimen on most days. By wk 8, this statistic had fallen to 61% 51% of the 309 participants with previous experience of calcipotriol ointment monotherapy reported that their compliance with the cream/ointment regimen was higher	Sponsorship not reported Control group comprised retrospective self-reported experience of calcipotriol ointment monotherapy by 35% of participants in the intervention group	D
Zaghloul 2004	DESIGN: uncontrolled study patient delivery ALLOCATION: non-random Method of randomisation: NA Concealment: NA	N: 294 TD: 12 wks; FU: 12 wks LF: 93 (31.6%) BC: NA Age: 45.1 (range: 20 to 65) Gender (per cent men): 44.3% Severity: NR INCLUSION CRITERIA: psoriasis (unclear if chronic plaque only);	Topical, oral, or combined antipsoriatic medication No control	Medication adherence: (1) number prescribed doses taken/number prescribed doses prescribed (2) patient self-report	Medication adherence measured by method 1 (objective) much lower than by method 2 (patient self report). Mean rate: 60.6% (33.0%SD); (range: 0% to169%)	Authors report no relevant financial interests	D

Table 26. Included studies of compliance *(Continued)*

	BLINDING: single-blind (participants unaware that study focused on compliance) WITHDRAWAL/DROPOUT: described	aged 18 to 65; prescribed oral, topical or combined treatment EXCLUSION CRITERIA: pregnancy, lactation, concomitant disease	Quality of Life (DLQI) (0 to 30; higher score implies lower quality of life)	Direct correlation observed between medication adherence and quality of life Adherence rate higher for participants who were women, married, employed, or not paying for prescriptions Adherence greater for topical (vs. systemic) therapy, once daily, or first-time use

per cent men: per cent male; AE(L): number local adverse events/number participants; AE(S): number systemic adverse events/number participants; AE: adverse events; BC: baseline comparability; BD: twice daily; BSA: body surface area; FU: follow up (includes TD); N: number enrolled; NA: not applicable; NR: not reported; OD: once daily; PASI: Psoriasis Area and Severity Index; PRN: as required; TD: treatment duration; TSS: Total Severity Score; WA: withdrawal due to adverse events

Table 27. Excluded studies of compliance

Study	Reason for exclusion
Atkinson 2004	Adherence not assessed
Chu 2000	Treatment guideline (not primary study)
Gupta 2007	Review/think piece
Lee 2006	Review
Osborne 2002	Study focused on non-responsive participants rather than those that are specifically non-compliant
Richards 2006	Review
Szeimies 2004	Think piece (not primary study)

APPENDICES

Appendix 1. Specialised Register search strategy (RCTs)

Searched 04/12/04
Search updated on 17/11/2008: from January 2005 to date
Search updated on 3/02/2011: from November 2008 to date. One additional term added to 1st part: 'taclonex'.
Search updated 29/08/12: from February 2011 to date.

1st part

(*psorias* or *psoriat*) AND (*tar* or *gel* or alphosyl or carbodome or exorex or balneum or cocois or capasal or ceanel or ionil or meted or pentrax or anthralin or dithr* or micanol or psorin or psoriderm or salicylic or (vitamin and D) or calcipo* or dovo* or *calcit* or curatoderm or tazarotene or zorac or silkis or acitretin or neotigason or ciclosporin or cyclosporin or methotrexate or tacrolimus or pimecrolimus or protopic or elidel or retinoid* or macrolactam* or immunosuppressant* or taclonex) AND topical*

2nd part

(*psorias* or *psoriat*) AND ((adrenal and cortex and hormone*) or *steroid* or hydrocort* or cobadex or efcortelan or *derm or *dermal or *movate or mildison or calmurid or locoid or alclometasone or modrasone or beclo* or betametha* or betacap or betnovate or bettamousse or dipro* or clobetaso* or desox* or stiedex or diflucortolone or nerisone or fluocino* or synalar or metosyn or fluocortolone or ultralanum or flurandrenolone or fludroxycortide or haelan or fluticasone or cutivate or halci* or mometasone or elocon or triamcinolone or *cort or *cortyl)

Appendix 2. CENTRAL (Cochrane Library CD-ROM) and National Research Register (NRR) (CD-ROM interface) search strategies (RCTs)

CENTRAL (Cochrane Library CD-ROM 2005 issue 1): publication years 2001 to 2005-02-24
Searched on 17/11/08: CENTRAL (The Cochrane Library: http://www.thecochranelibrary.com/)
Searched on 02/02/11: CENTRAL (The Cochrane Library: http://www.thecochranelibrary.com/)
Searched on 23/08/12: CENTRAL (The Cochrane Library: http://www.thecochranelibrary.com/)

National Research Register (CD-ROM interface, issue 2004/4): all projects with a start date of 2001 to 2005
Website browsed on 20/11/08: UK Clinical Research Network Study Portfolio (http://public.ukcrn.org.uk/search/)
Website browsed on 22/02/11: UK Clinical Research Network Study Portfolio (http://public.ukcrn.org.uk/search/)
Website browsed on 10/09/12: UK Clinical Research Network Study Portfolio (http://public.ukcrn.org.uk/search/)

#1 MeSH descriptor Psoriasis explode all trees
#2 (Psorias* or psoriat* or antipsoria*)
#3 MeSH descriptor Coal Tar, this term only

#4 "coal tar"
#5 (alphosyl)
#6 "carbo dome"
#7 (clinitar or exorex or gelcosal or gelcotar)
#8 (pragmatar or psorigel or balneum or polytar)
#9 (psoriderm or tarcortin or cocois)
#10 "T gel"
#11 (capasal or ceanel or clinitar or ionil)
#12 (meted or pentrax)
#13 MeSH descriptor Anthralin, this term only
#14 (Dithranol or dithrocream or micanol or psorin)
#15 (salicylic next acid*)
#16 (vitamin next d next analogue*)
#17 (vitamin next d next derivative*)
#18 (calcipotriol or calcipotriene or dovonex or dovobet)
#19 (tacalcitol or curatoderm or tazarotene or zorac)
#20 MeSH descriptor Calcitriol, this term only
#21 (silkis or maxacalcitol)
#22 (#3 OR #4 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14 OR #15 OR #16 OR #17 OR #18 OR #19 OR #20 OR #21)
#23 MeSH descriptor Acitretin, this term only
#24 MeSH descriptor Cyclosporins explode all trees
#25 MeSH descriptor Methotrexate, this term only
#26 MeSH descriptor Tacrolimus, this term only
#27 (methotrexate or tacrolimus)
#28 (pimecrolimus or elidel or protopic)
#29 (acitretin or neotigason or cyclosporin or ciclosporin)
#30 (#23 OR #24 OR #25 OR #26 OR #27 OR #28 OR #29)
#31 (topical)
#32 (#30 AND #31)
#33 (topical next retinoid*)
#34 (topical next macrolactam*)
#35 (topical next immunosuppressant*)
#36 MeSH descriptor Dermatologic Agents, this term only
#37 MeSH descriptor Adrenal Cortex Hormones explode all trees
#38 (corticosteroid* or (cortico next steroid*))
#39 MeSH descriptor Hydrocortisone explode all trees
#40 (hydrocortisone or cobadex or dioderm or efcortelan or hydrocortisyl mildison or alphaderm or calmurid)
#41 "hydrocortisone butyrate"
#42 "alclometasone dipropionate"
#43 (modrasone or locoid or propaderm)
#44 MeSH descriptor Beclomethasone, this term only
#45 "beclomethasone dipropionate"
#46 MeSH descriptor Betamethasone explode all trees
#47 "betamethasone esters"
#48 (betamethasone or betacap or betnovate or diprosone)
#49 (diprosalic or bettamousse)
#50 "clobetasol propionate"
#51 "clobetasone butyrate"
#52 (eumovate or trimovate or dermovate)
#53 MeSH descriptor Desoximetasone, this term only
#54 (desoxymethasone or desoximetasone or stiedex)
#55 MeSH descriptor Diflucortolone, this term only
#56 "diflucortolone valerate"
#57 MeSH descriptor Fluocinolone Acetonide explode all trees
#58 "fluocinolone acetonide"
#59 (synalar or fluocinonide or metosyn or nerisone or elocon)
#60 MeSH descriptor Fluocortolone explode all trees
#61 (fluocortolone or ultralanum or flurandrenolone or haelan)
#62 MeSH descriptor Flurandrenolone, this term only
#63 (fludroxycortide)
#64 (fluticasone next propionate)

#65 (cutivate or halcinonide or halciderm)
#66 "mometasone furoate"
#67 MeSH descriptor Triamcinolone explode all trees
#68 "triamcinolone acetonide"
#69 (adcortyl or aureocort or nystadermal or triadcortyl)
#70 MeSH descriptor Steroids explode all trees
#71 (steroid*)
#72 (#33 OR #34 OR #35 OR #36 OR #37 OR #38 OR #39 OR #40)
#73 (#41 OR #42 OR #43 OR #44 OR #45 OR #46 OR #47 OR #48)
#74 (#49 OR #50 OR #51 OR #52 OR #53 OR #54 OR #55 OR #56)
#75 (#57 OR #58 OR #59 OR #60 OR #61 OR #62 OR #63 OR #64)
#76 (#65 OR #66 OR #67 OR #68 OR #69 OR #70 OR #71)
#77 (#22 OR #32 OR #72 OR #73 OR #74 OR #75 OR #76)
#78 ((#1 OR #2) AND #77), from 2008 to 2011

Appendix 3. MEDLINE (OVID) search strategy (RCTs)

MEDLINE (OvidSP Online http://www.ovid.com/): database updates 2002/07 to 2005/02 week 2
Search updated on 17/11/2008: 1950 to November Week 1 2008
Search updated on 22/02/2011: 1948 to January Week 3 2011
Search updated on 23/08/2012: 1946 to Present

1 randomized controlled trial.pt.
2 randomized controlled trial/
3 Random Allocation/
4 Double-Blind Method/
5 single-blind method/
6 clinical trial.pt.
7 exp clinical trial/
8 ((clinical$ or intervention$) adj5 (trial$ or study or studies)).tw.
9 ((singl$ or doubl$ or trebl$ or tripl$) adj5 (blind$ or mask$)).tw.
10 Placebos/
11 (placebo$ or random$).tw.
12 Research Design/
13 Comparative Study/
14 exp evaluation studies as topic/
15 Follow-Up Studies/
16 Prospective Studies/
17 (control$ or prospectiv$ or volunteer$).tw.
18 Animals/
19 Humans/
20 or/1-17
21 18 not (18 and 19)
22 20 not 21
23 exp Psoriasis/
24 psorias$.tw.
25 psoriat$.tw.
26 or/23-25
27 coal tar/
28 coal tar.tw.
29 alphosyl.tw.
30 carbo dome.tw.
31 clinitar.tw.
32 exorex.tw.
33 gelcosal.tw.
34 gelcotar.tw.
35 pragmatar.tw.
36 psorigel.tw.
37 balneum.tw.
38 polytar.tw.
39 psoriderm.tw.
40 tarcortin.tw.

41 cocois.tw.
42 (T adj gel).tw.
43 capasal.tw.
44 ceanel.tw.
45 clinitar.tw.
46 ionil.tw.
47 meted.tw.
48 pentrax.tw.
49 Anthralin/
50 dithranol.tw.
51 dithrocream.tw.
52 micanol.tw.
53 psorin.tw.
54 salicylic acid$.tw.
55 (vitamin adj d adj2 analogue$).tw.
56 (vitamin adj d adj2 derivative$).tw.
57 calcipotriol.tw.
58 calcipotriene.tw.
59 dovonex.tw.
60 dovobet.tw.
61 tacalcitol.tw.
62 curatoderm.tw.
63 tazarotene.tw.
64 zorac.tw.
65 Calcitriol/
66 silkis.tw.
67 maxacalcitol.tw.
68 or/27-67
69 Acitretin/
70 acitretin.tw.
71 neotigason.tw.
72 exp Cyclosporins/
73 cyclosporin.tw.
74 ciclosporin.tw.
75 Methotrexate/
76 methotrexate.tw.
77 Tacrolimus/
78 tacrolimus.tw.
79 protopic.tw.
80 pimecrolimus.tw.
81 elidel.tw.
82 or/69-81
83 topical.tw.
84 82 and 83
85 topical retinoid$.tw.
86 topical macrolactam$.tw.
87 topical immunosuppressant$.tw.
88 or/84-87
89 68 or 88
90 antipsoriat$.tw.
91 antipsorias$.tw.
92 26 or 90 or 91
93 exp Psoriasis/th, pc, dt [Therapy, Prevention & Control, Drug Therapy]
94 Dermatologic Agents/
95 92 and 22
96 93 and 22
97 94 and 92 and 22
98 or/95-97
99 exp Adrenal Cortex Hormones/
100 corticosteroid$.tw.
101 cortico steroid$.tw.
102 exp Hydrocortisone/

103 hydrocortisone.tw.
104 cobadex.tw.
105 dioderm.tw.
106 efcortelan.tw.
107 hydrocortisyl.tw.
108 mildison.tw.
109 alphaderm.tw.
110 calmurid.tw.
111 hydrocortisone butyrate.tw.
112 locoid.tw.
113 alclometasone dipropionate.tw.
114 modrasone.tw.
115 Beclomethasone/
116 beclomet$asone dipropionate.tw.
117 propaderm.tw.
118 exp Betamethasone/
119 betamethasone esters.tw.
120 betamethasone.tw.
121 betacap.tw.
122 betnovate.tw.
123 diprosone.tw.
124 diprosalic.tw.
125 bettamousse.tw.
126 clobetasol propionate.tw.
127 dermovate.tw.
128 clobetasone butyrate.tw.
129 eumovate.tw.
130 trimovate.tw.
131 Desoximetasone/
132 desoxymethasone.tw.
133 desoximetasone.tw.
134 stiedex.tw.
135 Diflucortolone/
136 diflucortolone valerate.tw.
137 nerisone.tw.
138 exp Fluocinolone Acetonide/
139 fluocinolone acetonide.tw.
140 synalar.tw.
141 fluocinonide.tw.
142 metosyn.tw.
143 exp Fluocortolone/
144 fluocortolone.tw.
145 ultralanum.tw.
146 Flurandrenolone/
147 flurandrenolone.tw.
148 fludroxycortid$.tw.
149 haelan.tw.
150 fluticasone propionate.tw.
151 cutivate.tw.
152 halcinonide.tw.
153 halciderm.tw.
154 mometasone furoate.tw.
155 elocon.tw.
156 exp Triamcinolone/
157 triamcinolone acetonide.tw.
158 adcortyl.tw.
159 aureocort.tw.
160 nystadermal.tw.
161 tri-adcortyl.tw.
162 exp Steroids/
163 steroid$.tw.
164 or/99-163

165 22 and 92 and 164
166 22 and 92 and 89
167 98 or 165 or 166
168 (200811$ or 200812$).ed.
169 (2009$ or 2010$ or 2011$).ed.
170 168 or 169
171 167 and 170

Appendix 4. EMBASE (OVID) search strategy (RCTs)

EMBASE (OvidSP Online http://www.ovid.com/): database updates 2002/08 to 2005/08
Search updated on 17/11/2008: 1980 to 2008 Week 46
Search updated on 31/01/2011: 1980 to 2011 Week 04
Search updated on 23/08/2012: 1996 to 2012 Week 33

1 Coal Tar/
2 dithranol/ or tazarotene/ or 22 Oxacalcitriol/
3 (coal tar or alphosyl or carbo dome or clinitar or exorex or cocois or T gel or capasal or ceanel or ionil or meted or pentrax).ti,ab.
4 (gelcosal or gelcotar or pragmatar or psoriderm or psorigel or balneum or polytar or tarcortin or dithranol or dithrocream).ti,ab.
5 (anthralin or micanol or psorin or salicylic acid$ or vitamin d analogue$ or vitamin d derivative$).ti,ab.
6 (calcipotriol or calcipotriene or dovonex or dovobet or tacalcitol or curatoderm or tazarotene or zorac or silkis or maxacalcitol).ti,ab.
7 vitamin d derivative/ or calcipotriol/ or calcitriol/ or tacalcitol/ or Salicylic Acid/
8 or/1-7
9 Etretin/ or Immunosuppressive Agent/ or Tacrolimus/
10 Cyclosporin/ or Retinoid/ or Pimecrolimus/
11 Methotrexate/
12 ((immunosuppressant$ or acitretin or neotigason or cyclosporin$ or ciclosporin$ or methotrexate or retinoid$ or macrolactam) adj5 topical$).ti,ab.
13 ((tacrolimus or protopic or pimecrolimus or elidel) adj5 topical$).ti,ab.
14 or/9-11
15 topical.ti,ab. or topical treatment/ or topical drug administration/
16 (14 and 15) or 12 or 13
17 exp Corticosteroid/
18 Hydrocortisone/
19 (corticosteroid$ or cortico steroid$ or hydrocortisone or cobadex or dioderm or efcortelan).ti,ab.
20 (hydrocortisyl or mildison or alphaderm or calmurid).ti,ab.
21 (locoid or modrasone or beclomethasone dipropionate).ti,ab.
22 (alclometasone diproprionate or propaderm or betamethasone or betacap or betnovate or diprosone).ti,ab.
23 (diprosalic or bettamousse or clobetasol propionate or dermovate or clobetasone butyrate).ti,ab.
24 (eumovate or trimovate or desoxymethasone or desoxymetasone or desoximethasone or desoximetasone or stiedex).ti,ab.
25 (diflucortolone valerate or nerisone or fluocinolone acetonide or synalar or fluocinonide or metosyn).ti,ab.
26 (ultralanum or flurandrenolone or haelan or fluticasone propionate or cutivate or halcinonide or halciderm).ti,ab.
27 (mometasone furoate or elocon or adcortyl or aureocort or nystadermal or tri adcortyl or steroid$).ti,ab.
28 beclometasone/ or psoralon/ or psoraderm/ or psoradexan/ or psorin/
29 Beclometasone Dipropionate/ or Urea/ or hydrocortisone butyrate/ or hydrocortisone plus urea/
30 alclometasone dipropionate/ or betamethasone dipropionate/ or betamethasone valerate/ or diflucortolone/
31 clobetasol propionate/ or clobetasone butyrate/ or desoximetasone/ or diflucortolone valerate/ or fluocinonide/ or Fluticasone Propionate/
32 fluocinolone/ or halcinonide/ or mometasone furoate.mp. or triamcinolone acetonide/
33 Fluocortolone/
34 Fludroxycortide/
35 Triamcinolone/
36 exp Steroid/
37 exp Steroid Hormone/
38 or/17-37
39 exp Antipsoriasis Agent/
40 8 or 16 or 38 or 39
41 exp Psoriasis/
42 (psorias$ or psoriat$ or antipsorias$ or antipsoriat$).ti,ab.
43 or/41-42
44 40 and 43
45 randomization/

46 Single Blind Procedure/
47 Double Blind Procedure/
48 exp clinical trial/
49 Placebo/
50 Methodology/
51 comparative study/
52 exp drug comparison/
53 evaluation/
54 Follow Up/
55 Prospective Study/
56 Crossover Procedure/
57 (clinical$ adj3 (trial$ or study or studies)).ti,ab.
58 (intervention$ adj3 (trial$ or study or studies)).ti,ab.
59 ((single$ or doubl$ or trebl$ or tripl$) adj3 blind$).ti,ab.
60 ((single$ or doubl$ or trebl$ or tripl$) adj3 mask$).ti,ab.
61 (placebo or placebos or random$ or control$ or prospectiv$ or volunteer$).ti,ab.
62 or/45-61
63 44 and 62
64 (2008$ or 2009$ or 2010$ or 2011$).em.
65 63 and 64
66 from 65 keep 1-2041

Appendix 5. Science Citation Index (ISI web of Knowledge interface) and Conference Proceedings Citation Index - Science (ISI web of Knowledge interface) search strategies (RCTs)

Science Citation Index (SCI Web Of Knowledge http://wos.mimas.ac.uk/): publication years 2000 to 2005
Search updated on 17/11/2008: All lines linted as follows: DocType=All document types; Language=All languages; Database=SCI EXPANDED; Timespan=2005-2008
Search updated on 02/02/2011: All lines linted as follows: Databases=SCI-EXPANDED Timespan=2008-2011
Search updated on 23/08/12: (limited to 2011-01-01 - 2012-08-23)

Conference Proceedings Citation Index - Science (SCI Web Of Knowledge http://wos.mimas.ac.uk/)
Search updated on 02/02/2011: All lines linted as follows: Databases=CPCI-S Timespan=2008-2011
Search updated on 23/08/12: (limited to 2011-01-01 - 2012-08-23)

1 Topic=((psoria* OR antipsoria*) AND (trial* OR random* OR control OR controls OR double blind OR doubleblind or single blind OR singleblind OR placebo* or evaluation*))
2 Topic=(coaltar or coal tar or alphosyl or carbo dome or clinitar or exorex or gelcosal or gelcotar or pragmatar)
3 Topic=(psorigel or balneum or polytar or psoriderm or tarcortin or cocois or t gel or tgel or capasal or ceanel or clinitar or ionil or meted or pentrax)
4 Topic=(eumovate or trimovate or desoxime$asone or desoxyme$asone or stiedex or diflucortolone or nerisone or fluocinolone or synalar)
5 Topic=(anthralin OR dithranol or dithrocream or micanol or psorin or salicylic acid or salicylic acids or vitamin d or calcipotriol or calcipotriene or dovonex or dovobet or tacalcitol or curatoderm or tazarotene or zorac)
6 Topic=(fluocinonide or metosyn or fluocortolone or ultralanum or flurandrenolone or fludroxycortide or haelan or fluticasone propionate)
7 Topic=(calcitriol or silkis or maxacalcitol)
8 Topic=(cutivate or halcinonide or halciderm or mometasone furoate or elocon or triamcinolone or adcortyl or aureocort or nystadermal or triadcortyl or steroid or steroids or steroidal)
9 Topic=((acitretin or neotigason or cyclosporin* or ciclosporin* or methotrexate or tacrolimus or protopic or pimecrolimus or elidel or retinoid* or macrolactam* or immunosuppressant*) same topical)
10 Topic=(adrenal cortex hormone* or corticosteroid* or cortico steroid* or hydrocortisone or cobadex or dioderm or efcortelan or hydrocortisyl or mildison)
11 Topic=(alphaderm or calmurid or locoid or alclometasone dipropionate or modrasone or beclomet$asone or propaderm)
12 Topic=(betamethasone or betacap or betnovate or diprosone or diprosalic or bettamousse or clobetasol propionate or dermovate or clobetasone butyrate)
13 #12 OR #11 OR #10 OR #9 OR #8 OR #7 OR #6 OR #5 OR #4 OR #3 OR #2
14 #13 AND #1

Appendix 6. BIOSIS (EDINAinterface) search strategy (RCTs)

BIOSIS (EDINAinterface): publication years 2001 to 2005

((((((((((((((al: betamethasone or betacap or betnovate or diprosone or diprosalic or bettamousse or "clobetasol propionate" or dermovate or "clobetasone butyrate") and (sy: 2001-2005)) or ((al: alphaderm or calmurid or locoid or "alclometasone dipropionate" or modrasone or beclomethasone beclometasone or propaderm) and (sy: 2001-2005))) or ((al: "adrenal cortex hormone*" or corticosteroid* or "cortico steroid*" or hydrocortisone or cobadex or dioderm or efcortelan or hydrocortisyl or mildison) and (sy: 2001-2005))) or ((al: (acitretin or neotigason or cyclosporin* or ciclosporin* or methotrexate or tacrolimus or protopic or pimecrolimus or elidel or retinoid* or macrolactam* or immunosuppressant*)) and (sy: 2001-2005))) or ((al: cutivate or halcinonide or halciderm or "mometasone furoate" or elocon or triamcinolone or adcortyl or aureocort or nystadermal or triadcortyl or steroid or steroids or steroidal) and (sy: 2001-2005))) or ((al: (calcitriol or silkis or maxacalcitol)) and (sy: 2001-2005))) or ((al: fluocinonide or metosyn or fluocortolone or ultralanum or flurandrenolone or fludroxycortide or haelan or "fluticasone propionate") and (sy: 2001-2005))) or ((al: anthralin OR dithranol or dithrocream or micanol or psorin or "salicylic acid" or "salicylic acids" or "vitamin d" or calcipotriol or calcipotriene or dovonex or dovobet or tacalcitol or curatoderm or tazarotene or zorac) and (sy: 2001-2005))) or ((al: (eumovate or trimovate or desoxime$asone or desoxyme$asone or stiedex or diflucortolone or nerisone or fluocinolone or synalar)) and (sy: 2001-2005))) or (al: (psorigel or balneum or polytar or psoriderm or tarcortin or cocois or t gel or tgel or capasal or ceanel or clinitar or ionil or meted or pentrax))) or (al: (coaltar or coal tar or alphosyl or carbo dome or clinitar or exorex or gelcosal or gelcotar or pragmatar)))) and ((((al: trial* or random* or "double blind" or doubleblind or "single blind" or singleblind or evaluation* or placebo* or control or controls) and (sy: 2001-2005)) and ((al: (psoria* or antipsoria*)) and (sy: 2001-2005)))))

Appendix 7. Dissertation Abstracts (Dialog Classic interface) and Inside Conferences (Dialog Classic interface) search strategies (RCTs)

Dissertation Abstracts (Dialog Classic interface): all publication years
Inside Conferences (Dialog Classic interface): all publication years
Biosis (Dialog Classic interface): all publication years

Search updated 17/11/2008: 1993-2008/Nov W2
Search updated 01/02/2011: 1993-2011/Jan W4
Search updated on 24/08/2012: 1993-2012/Aug W3

1 s (coal()tar or coaltar or alphosyl or carbo()dome or clinitar or exorex or cocois)/ti,ab,de
2 s (t()gel or tgel or capasal or ceanel or clinitar or ionil or meted or pentrax)/ti,ab,de
3 s (dithranol or gelcosal or gelcotar or pragmatar or psoriderm or psorigel or balneum or 4. polytar or tarcortin or dithrocream)/ti,ab,de
4 s (micanol or psorin or salicylic()acid? ? or vitamin()d()analogue? or vitamin()d()derivative?)/ti,ab,de
5 s (calcipotriol or calcipotriene or dovonex or dovobet or tacalcitol or curatoderm or tazarotene or zorac)/ti,ab,de
6 s (calcitriol or silkis or maxacalcitol or adrenal()cortex()hormone? ?)/ti,ab,de
7 s ((cyclosporin or ciclosporin or methotrexate or acitretin or neotigason)(4w)topical?)/ti,ab,de
8 s ((retinoid? ? or immunosuppressant? ? or tacrolimus or protopic or pimecrolimus or macorlactam? ?)(4w)topical?)/ti,ab,de
9 s (corticosteroid? ? or cortico()steroid? ? or hydrocortisone or cobadex or dioderm or efcortelan)/ti,ab,de
10 s (hydrocortisyl or mildison or alphaderm or calmurid)/ti,ab,de
11 s (locoid or alclometasone()dipropionate or modrasone or beclomethasone()dipropionate)/ti,ab,de
12 s (propaderm or betamethasone or betacap or betnovate or diprosone)/ti,ab,de
13 s (diprosalic or bettamousse or clobetasol()propionate or dermovate or clobetasone()butyrate)/ti,ab,de
14 s (eumovate or trimovate or desoxymethasone or desoxymetasone or desoximetasone or desoximethasone or stiedex)/ti,ab,de
15 s (diflucortolone()valerate or nerisone or fluocinolone()acetonide or synalar or fluocinonide or metosyn)/ti,ab,de
16 s (fluocortolone or ultralanum or haelan or fluticasone()propionate or cutivate or halcinonide or halciderm or flurandrenolone or triamcinolone)/ti,ab,de
17 s (mometasone()furoate or elocon or adcortyl or aureocort or nystadermal or triadcortyl or steroid? ? or steroidal)/ti,ab,de
18 s (beclometasone()dipropionate or fludroxycortide or triamcinolone)/ti,ab,de
19 s s1:s18
20 s (psoria? or antipsoria?)/ti,ab,de
21 s (random? or single()blind or singleblind or double()blind or doubleblind)/ti,ab,de
22 s (placebo or comparative()study or evaluation or prospective()study or crossover or trial or trials or triallist? ?)/ti,ab,de
23 s (control or controls? or prospectiv?)/ti,ab,de
24 s s21:s23
25 s s19 and s20 and s24
26 s UD=200812:201102
27 s s25 and s26
28 s rd s27

Appendix 8. SIGLE (WebSPIRS interface) search strategy (RCTs)

SIGLE (WebSPIRS interface): publication years 2001 to 2005 (database issue 2004/12)
SIGLE has not been updated since 2005, so searches were not rerun.

#1 psoriat* or psorias*(83 records)
#2 (2002 in PY) or (2003 in PY) or (2004 in PY) or (2005 in PY)(49881 records)
#3 ((2002 in PY) or (2003 in PY) or (2004 in PY) or (2005 in PY)) and (psoriat* or psorias*)(5 records)

Appendix 9. MEDLINE (OVID) search strategy (adverse events)

MEDLINE (OvidSP Online http://www.ovid.com/): database updates 1990 to 2005/02 week 2
Search updated on 17/11/08: 1950 to November Week 1 2008
Search updated on 02/02/11: 1948 to January Week 3 2011
Search updated on 23/08/12: 1946 to present

1 (coal adj tar).tw.
2 alphosyl.tw.
3 (carbo adj dome).tw.
4 clinitar.tw.
5 exorex.tw.
6 gelcosal.tw.
7 gelcotar.tw.
8 pragmatar.tw.
9 psorigel.tw.
10 balneum.tw.
11 polytar.tw.
12 psoriderm.tw.
13 tarcortin.tw.
14 cocois.tw.
15 (T adj gel).tw.
16 capasal.tw.
17 ceanel.tw.
18 ionil.tw.
19 meted.tw.
20 pentrax.tw.
21 dithranol.tw.
22 dithrocream.tw.
23 micanol.tw.
24 psorin.tw.
25 (salicylic adj acid$).tw.
26 (vitamin adj d adj2 analogue$).tw.
27 (vitamin adj d adj2 derivative$).tw.
28 calcipotriol.tw.
29 calcipotriene.tw.
30 dovonex.tw.
31 dovobet.tw.
32 tacalcitol.tw.
33 curatoderm.tw.
34 tazarotene.tw.
35 zorac.tw.
36 silkis.tw.
37 maxacalcitol.tw.
38 antipsoriat$.tw.
39 antipsorias$.tw.
40 corticosteroid$.tw.
41 (cortico adj steroid$).tw.
42 hydrocortisone.tw.
43 cobadex.tw.
44 dioderm.tw.
45 efcortelan.tw.
46 hydrocortisyl.tw.
47 mildison.tw.
48 alphaderm.tw.
49 calmurid.tw.
50 (hydrocortisone adj butyrate).tw.
51 locoid.tw.

52 (alclometasone adj dipropionate).tw.
53 modrasone.tw.
54 (beclomet$asone adj dipropionate).tw.
55 propaderm.tw.
56 (betamethasone adj esters).tw.
57 betamethasone.tw.
58 betacap.tw.
59 betnovate.tw.
60 diprosone.tw.
61 diprosalic.tw.
62 bettamousse.tw.
63 (clobetasol adj propionate).tw.
64 dermovate.tw.
65 (clobetasone adj butyrate).tw.
66 eumovate.tw.
67 trimovate.tw.
68 desoxymethasone.tw.
69 desoximetasone.tw.
70 stiedex.tw.
71 (diflucortolone adj valerate).tw.
72 nerisone.tw.
73 (fluocinolone adj acetonide).tw.
74 synalar.tw.
75 fluocinonide.tw.
76 metosyn.tw.
77 fluocortolone.tw.
78 ultralanum.tw.
79 flurandrenolone.tw.
80 haelan.tw.
81 (fluticasone adj propionate).tw.
82 cutivate.tw.
83 halcinonide.tw.
84 halciderm.tw.
85 (mometasone adj furoate).tw.
86 elocon.tw.
87 (triamcinolone adj acetonide).tw.
88 adcortyl.tw.
89 aureocort.tw.
90 nystadermal.tw.
91 tri-adcortyl.tw.
92 steroid$.tw.
93 Coal Tar/
94 Anthralin/
95 Calcitriol/
96 exp Cyclosporins/
97 Tacrolimus/
98 Dermatologic Agents/
99 exp Adrenal Cortex Hormones/
100 exp Hydrocortisone/
101 Beclomethasone/
102 exp Betamethasone/
103 Desoximetasone/
104 Diflucortolone/
105 exp Fluocinolone Acetonide/
106 Fluocortolone/
107 Flurandrenolone/
108 Flurandrenolone/
109 exp Triamcinolone/
110 exp Steroids/
111 or/1-110
112 Acitretin/
113 Immunosuppressive Agents/

114 Cyclosporine/
115 Retinoids/
116 Methotrexate/
117 or/112-116
118 topical.ti,ab. or topical treatment/ or topical drug administration/
119 117 and 118
120 ((tacrolimus or protopic or pimecrolimus or elidel or immunosuppressant$ or acitretin or neotigason or cyclosporin$ or ciclosporin $ or methotrexate or retinoid$ or macrolactam) adj5 topical$).tw.
121 119 or 120 or 111
122 (safe or safety).tw.
123 side effect$.tw.
124 treatment emergent.tw.
125 undesirable effect$.tw.
126 tolerability.tw.
127 toxicity.tw.
128 adrs.tw.
129 (adverse adj3 (effect or effects or reaction or reactions or event or events or outcome or outcomes)).tw.
130 Adverse Drug Reaction Reporting Systems/
131 drug hypersensitivity/
132 hypersensit$.tw.
133 harm$.tw.
134 exp Substance Withdrawal Syndrome/ci [Chemically Induced]
135 rebound.tw.
136 Hypercalcemia/ci [Chemically Induced]
137 exp Urinary Calculi/ci [Chemically Induced]
138 Tachyphylaxis/ci, de [Chemically Induced, Drug Effects]
139 exp Substance Withdrawal Syndrome/ci [Chemically Induced]
140 exp Atrophy/ci [Chemically Induced]
141 exp Telangiectasis/ci [Chemically Induced]
142 cutaneous atrophy.tw.
143 striae.tw.
144 skin atrophy.tw.
145 exp Abnormalities, Drug-Induced/
146 exp Drug Toxicity/
147 or/122-146
148 Coal Tar/ae [Adverse Effects]
149 Anthralin/ae [Adverse Effects]
150 Calcitriol/ae [Adverse Effects]
151 Acitretin/ae [Adverse Effects]
152 exp Cyclosporins/de, ae [Drug Effects, Adverse Effects]
153 Methotrexate/ae [Adverse Effects]
154 Tacrolimus/ae [Adverse Effects]
155 Dermatologic Agents/ae [Adverse Effects]
156 exp Adrenal Cortex Hormones/ae, de [Adverse Effects, Drug Effects]
157 exp Hydrocortisone/ae [Adverse Effects]
158 Beclomethasone/ae [Adverse Effects]
159 exp Betamethasone/ae [Adverse Effects]
160 Desoximetasone/ae [Adverse Effects]
161 Diflucortolone/ae [Adverse Effects]
162 exp Fluocinolone Acetonide/ae [Adverse Effects]
163 Fluocortolone/ae [Adverse Effects]
164 Flurandrenolone/ae [Adverse Effects]
165 exp Triamcinolone/ae [Adverse Effects]
166 exp Steroids/ae [Adverse Effects]
167 or/148-166
168 147 or 167
169 (psorias$ or psoriat$).tw.
170 exp psoriasis/
171 or/169-170
172 121 and 168 and 171
173 exp animals/ not (exp animals/ and humans/)
174 172 not 173

175 (comment or editorial).pt.
176 174 not 175
177 (2008$ or 2009$ or 2010$ or 2011$).ed.
178 176 and 177

Appendix 10. EMBASE (OVID) search strategy (adverse events)

EMBASE (OvidSP Online http://www.ovid.com/): 1990 to 2005/08

Search updated on 11/12/08: 1980 to 2008 Week 49
Search updated on 02/02/11: 1980 to 2011 week 4
Search updated on 23/08/12: 1996 to 2012 Week 34

Note: A pragmatic approach was taken to reduce irrelevant records and to negate the over indexing of records in EMBASE; EMTREE terms were focused in this strategy

1 (coal adj tar).ti,ab.
2 alphosyl.ti,ab.
3 (carbo adj dome).ti,ab.
4 clinitar.ti,ab.
5 exorex.ti,ab.
6 gelcosal.ti,ab.
7 gelcotar.ti,ab.
8 pragmatar.ti,ab.
9 psorigel.ti,ab.
10 balneum.ti,ab.
11 polytar.ti,ab.
12 psoriderm.ti,ab.
13 tarcortin.ti,ab.
14 cocois.ti,ab.
15 (T adj gel).ti,ab.
16 capasal.ti,ab.
17 ceanel.ti,ab.
18 ionil.ti,ab.
19 meted.ti,ab.
20 pentrax.ti,ab.
21 dithranol.ti,ab.
22 dithrocream.ti,ab.
23 micanol.ti,ab.
24 psorin.ti,ab.
25 (salicylic adj acid$).ti,ab.
26 (vitamin adj d adj2 analogue$).ti,ab.
27 (vitamin adj d adj2 derivative$).ti,ab.
28 calcipotriol.ti,ab.
29 calcipotriene.ti,ab.
30 dovonex.ti,ab.
31 dovobet.ti,ab.
32 tacalcitol.ti,ab.
33 curatoderm.ti,ab.
34 tazarotene.ti,ab.
35 zorac.ti,ab.
36 silkis.ti,ab.
37 maxacalcitol.ti,ab.
38 antipsoriat$.ti,ab.
39 antipsorias$.ti,ab.
40 corticosteroid$.ti,ab.
41 (cortico adj steroid$).ti,ab.
42 hydrocortisone.ti,ab.
43 cobadex.ti,ab.
44 dioderm.ti,ab.
45 efcortelan.ti,ab.
46 hydrocortisyl.ti,ab.
47 mildison.ti,ab.

48 alphaderm.ti,ab.
49 calmurid.ti,ab.
50 (hydrocortisone adj butyrate).ti,ab.
51 locoid.ti,ab.
52 (alclometasone adj dipropionate).ti,ab.
53 modrasone.ti,ab.
54 (beclomet$asone adj dipropionate).ti,ab.
55 propaderm.ti,ab.
56 (betamethasone adj esters).ti,ab.
57 betamethasone.ti,ab.
58 betacap.ti,ab.
59 betnovate.ti,ab.
60 diprosone.ti,ab.
61 diprosalic.ti,ab.
62 bettamousse.ti,ab.
63 (clobetasol adj propionate).ti,ab.
64 dermovate.ti,ab.
65 (clobetasone adj butyrate).ti,ab.
66 eumovate.ti,ab.
67 trimovate.ti,ab.
68 desoxymethasone.ti,ab.
69 desoximetasone.ti,ab.
70 stiedex.ti,ab.
71 (diflucortolone adj valerate).ti,ab.
72 nerisone.ti,ab.
73 (fluocinolone adj acetonide).ti,ab.
74 synalar.ti,ab.
75 fluocinonide.ti,ab.
76 metosyn.ti,ab.
77 fluocortolone.ti,ab.
78 ultralanum.ti,ab.
79 flurandrenolone.ti,ab.
80 haelan.ti,ab.
81 (fluticasone adj propionate).ti,ab.
82 cutivate.ti,ab.
83 halcinonide.ti,ab.
84 halciderm.ti,ab.
85 (mometasone adj furoate).ti,ab.
86 elocon.ti,ab.
87 (triamcinolone adj acetonide).ti,ab.
88 adcortyl.ti,ab.
89 aureocort.ti,ab.
90 nystadermal.ti,ab.
91 tri-adcortyl.ti,ab.
92 steroid$.ti,ab.
93 *Coal Tar/
94 *alphosyl/
95 *carbo dome/
96 *Salicylic Acid/
97 *capasal/
98 *meted/
99 *Dithranol/
100 *Psorin/
101 *Vitamin d Derivative/
102 *Calcipotriol/
103 *Betamethasone Dipropionate Plus Calcipotriol/
104 *Tacalcitol/
105 *Tazarotene/
106 *Calcitriol/
107 *22 Oxacalcitriol/
108 *Corticosteroid/
109 *Hydrocortisone/

110 *Urea/
111 *Hydrocortisone Butyrate/
112 *Alclometasone Dipropionate/
113 *Beclometasone Dipropionate/
114 *Betamethasone/
115 *Betamethasone Valerate/
116 *Betamethasone Dipropionate/
117 *Clobetasol Propionate/
118 *Clobetasone Butyrate/
119 *trimovate/
120 *Desoximetasone/
121 *Diflucortolone Valerate/
122 *Fluocinolone Acetonide/
123 *Fluocinonide/
124 *Fluocortolone/
125 *Fludroxycortide/
126 *Fluticasone Propionate/
127 *Halcinonide/
128 *Mometasone Furoate/
129 *Triamcinolone Acetonide/
130 *Triamcinolone/
131 *Mycolog/
132 *exp Steroid/
133 *Cyclosporin Derivative/ or *Cyclosporin/
134 *Tacrolimus/
135 *Dermatological Agent/
136 or/1-135
137 *Tacrolimus/
138 *Pimecrolimus/
139 *Immunosuppressive Agent/
140 *Etretin/
141 *Cyclosporin/
142 *Cyclosporin A/
143 *Methotrexate/
144 *Retinoid/
145 or/137-144
146 topical.ti,ab. or topical treatment/ or topical drug administration/
147 145 and 146
148 ((tacrolimus or protopic or pimecrolimus or elidel or immunosuppressant$ or acitretin or neotigason or cyclosporin$ or ciclosporin $ or methotrexate or retinoid$ or macrolactam) adj5 topical$).ti,ab.
149 136 or 147 or 148
150 (safe or safety).ti,ab.
151 side effect$.ti,ab.
152 treatment emergent.ti,ab.
153 undesirable effect$.ti,ab.
154 tolerability.ti,ab.
155 toxicity.ti,ab.
156 adrs.ti,ab.
157 (adverse adj3 (effect or effects or reaction or reactions or event or events or outcome or outcomes)).ti,ab.
158 *Safety/ or *Drug Safety/
159 *Side Effect/
160 *Adverse Drug Reaction/
161 *Drug Tolerability/
162 *Toxicity/ or *Drug Toxicity/
163 *Drug Surveillance Program/
164 *Adverse Outcome/
165 hypersensit$.ti,ab.
166 harm$.ti,ab.
167 rebound.ti,ab.
168 *Drug Hypersensitivity/
169 *Rebound/
170 *Withdrawal Syndrome/

171 *Hypercalcemia/
172 *Urolithiasis/
173 *Tachyphylaxis/
174 *Drug Withdrawal/
175 *Atrophy/
176 *Telangiectasia/
177 cutaneous atrophy.ti,ab.
178 striae.ti,ab.
179 skin atrophy.ti,ab.
180 *Skin Atrophy/
181 *Stria/
182 or/150-181
183 *Coal Tar/ae, to [Adverse Drug Reaction, Drug Toxicity]
184 *alphosyl/ae [Adverse Drug Reaction]
185 *Salicylic Acid/ae, to [Adverse Drug Reaction, Drug Toxicity]
186 *Dithranol/ae, to [Adverse Drug Reaction, Drug Toxicity]
187 *Psorin/ae [Adverse Drug Reaction]
188 *Vitamin d Derivative/ae, to [Adverse Drug Reaction, Drug Toxicity]
189 *Calcipotriol/ae, to [Adverse Drug Reaction, Drug Toxicity]
190 *Betamethasone Dipropionate Plus Calcipotriol/to, ae [Drug Toxicity, Adverse Drug Reaction]
191 *Tacalcitol/ae, to [Adverse Drug Reaction, Drug Toxicity]
192 *Tazarotene/ae, to [Adverse Drug Reaction, Drug Toxicity]
193 *Calcitriol/ae, to [Adverse Drug Reaction, Drug Toxicity]
194 *22 Oxacalcitriol/ae, to [Adverse Drug Reaction, Drug Toxicity]
195 *Corticosteroid/ae, to [Adverse Drug Reaction, Drug Toxicity]
196 *Hydrocortisone/ae, to [Adverse Drug Reaction, Drug Toxicity]
197 *Urea/ae, to [Adverse Drug Reaction, Drug Toxicity]
198 *Hydrocortisone Butyrate/ae, to [Adverse Drug Reaction, Drug Toxicity]
199 *Alclometasone Dipropionate/ae, to [Adverse Drug Reaction, Drug Toxicity]
200 *Beclometasone Dipropionate/ae, to [Adverse Drug Reaction, Drug Toxicity]
201 *Betamethasone/ae, to [Adverse Drug Reaction, Drug Toxicity]
202 *Betamethasone Valerate/ae, to [Adverse Drug Reaction, Drug Toxicity]
203 *Betamethasone Dipropionate/ae, to [Adverse Drug Reaction, Drug Toxicity]
204 *Clobetasol Propionate/ae, to [Adverse Drug Reaction, Drug Toxicity]
205 *Clobetasone Butyrate/ae [Adverse Drug Reaction]
206 *trimovate/ae [Adverse Drug Reaction]
207 *Desoximetasone/ae, to [Adverse Drug Reaction, Drug Toxicity]
208 *Diflucortolone Valerate/to, ae [Drug Toxicity, Adverse Drug Reaction]
209 *Fluocinolone Acetonide/ae, to [Adverse Drug Reaction, Drug Toxicity]
210 *Fluocinonide/ae, to [Adverse Drug Reaction, Drug Toxicity]
211 *Fluocortolone/ae, to [Adverse Drug Reaction, Drug Toxicity]
212 *Fludroxycortide/ae [Adverse Drug Reaction]
213 *Fluticasone Propionate/ae, to [Adverse Drug Reaction, Drug Toxicity]
214 *Halcinonide/ae [Adverse Drug Reaction]
215 *Mometasone Furoate/ae, to [Adverse Drug Reaction, Drug Toxicity]
216 *Triamcinolone Acetonide/ae, to [Adverse Drug Reaction, Drug Toxicity]
217 *Triamcinolone/ae, to [Adverse Drug Reaction, Drug Toxicity]
218 *Mycolog/ae [Adverse Drug Reaction]
219 *exp Steroid/ae, to [Adverse Drug Reaction, Drug Toxicity]
220 *Cyclosporin Derivative/ae, to [Adverse Drug Reaction, Drug Toxicity]
221 *Cyclosporin/ae, to [Adverse Drug Reaction, Drug Toxicity]
222 *Tacrolimus/ae, to [Adverse Drug Reaction, Drug Toxicity]
223 *Dermatological Agent/ae, to [Adverse Drug Reaction, Drug Toxicity]
224 *Pimecrolimus/ae, to [Adverse Drug Reaction, Drug Toxicity]
225 *Immunosuppressive Agent/ae, to [Adverse Drug Reaction, Drug Toxicity]
226 *Etretin/ae, to [Adverse Drug Reaction, Drug Toxicity]
227 *Cyclosporin A/ae, to [Adverse Drug Reaction, Drug Toxicity]
228 *Methotrexate/ae, to [Adverse Drug Reaction, Drug Toxicity]
229 *Retinoid/ae, to [Adverse Drug Reaction, Drug Toxicity]
230 or/183-229
231 182 or 230
232 (psorias$ or psoriat$).ti,ab.

233 *exp Psoriasis/
234 232 or 233
235 149 and 231 and 234
236 animal/ not (animal/ and human/)
237 235 not 236
238 ("200800" or "200900").em.
239 (2010$ or 2011$).em.
240 238 or 239
241 237 and 240

Appendix 11. EMBASE (OVID) search strategy (compliance)

EMBASE (OvidSP Online http://www.ovid.com/): 1980 to 2007 Week 49
Not updated in 2011

1 compliance$.ti,ab. (46694)
2 complied.ti,ab. (1455)
3 compliance/ (1674)
4 comply.ti,ab. (3613)
5 (medicat$ adj4 adher$).ti,ab. (1732)
6 (drug$ adj4 adher$).ti,ab. (777)
7 (medicine$ adj4 adher$).ti,ab. (62)
8 (treatment adj4 adher$).ti,ab. (3072)
9 concordance$.ti,ab. (12825)
10 or/1-9 (68155)
11 psor$.ti,ab. (20549)
12 10 and 11 (171)
13 from 12 keep 1-171 (171)

Appendix 12. MEDLINE (OVID) search strategy (compliance)

MEDLINE(OvidSP Online http://www.ovid.com/): 1950 to November Week 2 2007
Not updated in 2011

1. compliance$.ti,ab. (52891)
2. complied.ti,ab. (1748)
3. compliance/ (2982)
4. comply.ti,ab. (4307)
5. (medicat$ adj4 adher$).ti,ab. (2047)
6. (drug$ adj4 adher$).ti,ab. (878)
7. (medicine$ adj4 adher$).ti,ab. (76)
8. (treatment adj4 adher$).ti,ab. (3442)
9. concordance$.ti,ab. (14973)
10. or/1-9 (78297)
11. psor$.ti,ab. (25210)
12. 10 and 11 (162)

WHAT'S NEW

Date	Event	Description
9 December 2015	Amended	Author information (affiliation) updated

HISTORY

Protocol first published: Issue 4, 2004
Review first published: Issue 2, 2009

Date	Event	Description
2 April 2013	Amended	'Declarations of interest' section updated.
25 February 2013	New citation required but conclusions have not changed	This review was updated, but there was no change to the conclusions.
25 February 2013	New search has been performed	48 new RCTs added. Comparisons revised to reflect new evidence. Scalp trials moved to separate comparison groups ready for removal at next update (#18; #19). Inverse psoriasis trials also moved to separate comparison groups (#16; #17). Nail trials removed, as now part of separate Cochrane review.
15 December 2008	Amended	Review amended to reflect peer review comments
25 June 2008	Amended	Converted to new review format.
29 September 2003	New citation required and conclusions have changed	Substantive amendment

CONTRIBUTIONS OF AUTHORS

The following contributions were made by the authors stated.
Link with editorial base and co-ordinate contributions from co-authors (AM).
Draft protocol (AM with contributions from MC, GD, GE, and JM).
Run searches (adherence) (AM).
Identify relevant titles and abstracts from searches, i.e. broad screen (AM and JM).
Obtain copies of trials (AM).
Select which trials to include (AM, JM, and MC as arbitrator when necessary).
Extract data from trials (AM, JM, and HH).
Enter data into RevMan (AM).
Carry out analysis (AM and JM)
Interpret analysis (AM, JM, and HH).
Draft final review (AM with contribution from MC, GD, HH, and JM).
Update review (AM, JM, HH, and MC).

DECLARATIONS OF INTEREST

Mike Cork: "I gave a lecture for Leo Pharmaceuticals about psoriasis and atopic eczema in 2012."

Anne R Mason: none declared

Gordon Dooley: none declared

James Mason: none declared

Helen Hancock: none declared

The clinical referee for this review, Dr Phyllis Spuls, stated the following potential conflict of interest on her comments form: "I have participated in an advisory board of LEO Pharma to give guidance to general practitioners regarding what to do if patients used calcipotriol, which has been removed from the market. I am involved as a Principal Investigator in many clinical trials with systemic agents for psoriasis and now in one for the improvement of adherence to Dovobet."

SOURCES OF SUPPORT

Internal sources

- Funding from Centre for Reviews and Dissemination to update review (2002) for UK products only, UK.

- Award from University of York Fund for Staff on Fixed-Term Contracts, UK.

External sources

- Grant from Crookes Healthcare Ltd. to do original systematic review (1999), UK.
- Grant from the Psoriasis Association to update review (2011), Other.

DIFFERENCES BETWEEN PROTOCOL AND REVIEW

There are some differences between the protocol and the review.

1. In our protocol, we stated our intention to adjust for the precision of findings from within-patient studies for within-patient correlation. However, we were unsuccessful in our attempts to identify estimates of this correlation from published or unpublished sources. We therefore undertook sensitivity analysis to investigate differences between within-patient and between-patient studies.

2. In our protocol, we listed three primary outcome measures for data extraction. In the review, we also included the Patient Assessment of Global Improvement.

3. In our protocol, we stated that there would be no language restrictions when searching for publications. However, the search for longer-term studies of adverse events included a restriction to publications in English.

4. In our protocol, we stated our intention that studies meeting only some of the inclusion criteria stated above would be listed as excluded studies. However, as large numbers of studies would need to be listed, this was not feasible. Therefore, we listed as excluded studies only those studies that we deemed potentially eligible for inclusion *and* for which we retrieved full papers, but which we subsequently found to fail to meet the inclusion criteria.

5. Throughout the text, we replaced all references to vitamin D3 with 'vitamin D analogues'.

6. Under Types of studies, we relaxed the condition that studies were of at least two weeks duration. In the same section, we added the following sentence: "If no useful effectiveness, withdrawal or adverse events data were available, either from the published paper or from sponsors or trialists, we excluded the study."

7. Under Types of interventions, we added the sentence "The potency of topical corticosteroids was based on classifications from a previous review (Mason 2002b)".

8. Under Methods, Selection of studies, and our explanations of the studies excluded, we added the searches for studies exploring adverse events and compliance studies.

9. Under Methods/Data extraction and management, we added the phrase 'between-patient design'.

10. Under Methods/Assessment of risk of bias in included studies, we removed the phrase 'in each arm'.

11. Under Methods/Unit of analysis issues/'Summarising primary outcomes with standardised mean differences', we revised the text in this section to include the PAGI outcome and to provide a fuller explanation of our analytic approach.

12. Under Methods/Unit of analysis issues/Secondary outcomes, we gave an explanation regarding the different method of analysis used.

13 Under Methods/Data collection and analysis/Sensitivity analysis, we added text to describe the different types of sensitivity analysis undertaken.

14 We replaced 'standardised weighted mean difference' with 'standardised mean difference' throughout the text to reflect Cochrane terminology.

15. Under Methods/Data and analyses/Subgroup analysis and investigation of heterogeneity, we inserted two paragraphs to explain our approach to statistical heterogeneity.

INDEX TERMS

Medical Subject Headings (MeSH)

Administration, Topical; Adrenal Cortex Hormones [adverse effects] [*therapeutic use]; Bone Density Conservation Agents [adverse effects] [*therapeutic use]; Chronic Disease; Facial Dermatoses [drug therapy]; Psoriasis [*drug therapy]; Randomized Controlled Trials as Topic; Scalp Dermatoses [drug therapy]; Vitamin D [adverse effects] [analogs & derivatives] [*therapeutic use]

MeSH check words

Humans