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Topical anti-inflammatory agents for seborrhoeic dermatitis of the face or scalp (Review)

Kastarinen H, Oksanen T, Okokon EO, Kiviniemi VV, Airola K, Jyrkkä J, Oravilahti T, Rannanheimo PK, Verbeek JH

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[Intervention Review]

Topical anti-inflammatory agents for seborrhoeic dermatitis of the face or scalp

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ABSTRACT

Background

Seborrhoeic dermatitis is a chronic inflammatory skin disorder affecting primarily the skin of the scalp, face, chest, and intertriginous areas, causing scaling and redness of the skin. Current treatment options include antifungal, anti-inflammatory, and keratolytic agents, as well as phototherapy.

Objectives

To assess the effects of topical pharmacological interventions with established anti-inflammatory action for seborrhoeic dermatitis occurring in adolescents and adults.

Search methods

We searched the following databases up to September 2013: the Cochrane Skin Group Specialised Register, CENTRAL in *The Cochrane Library* (2013, Issue 9), MEDLINE (from 1946), Embase (from 1974), LILACS (from 1982), and the GREAT database. We searched five trials databases and checked the reference lists of included studies for further references to relevant randomised controlled trials (RCTs).

Selection criteria

We included RCTs in adults or adolescents (> 16 years) with diagnosed seborrhoeic dermatitis of the scalp or face, comparing topical anti-inflammatory treatments (steroids, calcineurin inhibitors, and lithium salts) with other treatments.

Data collection and analysis

Pairs of authors independently assessed eligibility for inclusion, extracted data, and evaluated the risk of bias. We performed meta-analyses if feasible.

Main results

We included 36 RCTs (2706 participants), of which 31 examined topical steroids; seven, calcineurin inhibitors; and three, lithium salts. The comparative interventions included placebo, azoles, calcipotriol, a non-steroidal anti-inflammatory compound, and zinc, as well as different anti-inflammatory treatments compared against each other. Our outcomes of interest were total clearance of symptoms,

erythema, scaling or pruritus scores, and adverse effects. The risk of bias in studies was most frequently classified as unclear, due to unclear reporting of methods.

Steroid treatment resulted in total clearance more often than placebo in short-term trials (four weeks or less) (relative risk (RR) 3.76, 95% confidence interval (CI) 1.22 to 11.56, three RCTs, 313 participants) and in one long-term trial (lasting 12 weeks). Steroids were also more effective in reducing erythema, scaling, and pruritus. Adverse effects were similar in both groups.

There may be no difference between steroids and calcineurin inhibitors in total clearance in the short-term (RR 1.08, 95% 0.88 to 1.32, two RCTs, 60 participants, low-quality evidence). Steroids and calcineurin inhibitors were found comparable in all other assessed efficacy outcomes as well (five RCTs, 237 participants). Adverse events were less common in the steroid group compared with the calcineurin group in the short-term (RR 0.22, 95% CI 0.05 to 0.89, two RCTs, 60 participants).

There were comparable rates of total clearance in the steroid and azole groups (RR 1.11, 95% CI 0.94 to 1.32, eight RCTs, 464 participants, moderate-quality evidence) as well as of adverse effects in the short-term, but less erythema or scaling with steroids.

We found mild (class I and II) and strong (class III and IV) steroids comparable in the assessed outcomes, including adverse events. The only exception was total clearance in long-term use, which occurred more often with a mild steroid (RR 0.79, 95% CI 0.63 to 0.98, one RCT, 117 participants, low-quality evidence).

In one study, calcineurin inhibitor was more effective than placebo in reducing erythema and scaling, but there were similar rates in total clearance or adverse events for short-term treatment. In another study, calcineurin inhibitor was comparable with azole when erythema, scaling, or adverse effects were measured for longer-term treatment.

Lithium was more effective than placebo with regard to total clearance (RR 8.59, 95% CI 2.08 to 35.52, one RCT, 129 participants) with a comparable safety profile. Compared with azole, lithium resulted in total clearance more often (RR 1.79, 95% CI 1.10 to 2.90 in short-term treatment, one RCT, 288 participants, low-quality evidence).

Authors' conclusions

Topical steroids are an effective treatment for seborrhoeic dermatitis of the face and scalp in adolescents and adults, with no differences between mild and strong steroids in the short-term. There is some evidence of the benefit of topical calcineurin inhibitor or lithium salt treatment. Treatment with azoles seems as effective as steroids concerning short-term total clearance, but in other outcomes, strong steroids were more effective. Calcineurin inhibitor and azole treatment appeared comparable. Lithium salts were more effective than azoles in producing total clearance.

Steroids are similarly effective to calcineurin inhibitors but with less adverse effects.

Most of the included studies were small and short, lasting four weeks or less. Future trials should be appropriately blinded; include more than 200 to 300 participants; and compare steroids to calcineurin inhibitors or lithium salts, and calcineurin inhibitors to azoles or lithium salts. The follow-up time should be at least one year, and quality of life should be addressed. There is also a need for the development of well-validated outcome measures.

PLAIN LANGUAGE SUMMARY

Topical anti-inflammatory agents for seborrhoeic dermatitis of the face or scalp

Seborrhoeic dermatitis is an inflammation of the skin that most often affects areas of the body that have a lot of sebaceous glands. These include the skin of the scalp; face; chest; and flexure areas such as the armpits, groin, and abdominal folds. The most typical symptoms of seborrhoeic dermatitis are scaling of the skin and reddish patches. Seborrhoeic dermatitis is fairly common: one to three in 100 people have seborrhoeic dermatitis. The disease is more common in men than in women. Anti-inflammatory, antifungal, and antikeratolytic treatments can be used to treat seborrhoeic dermatitis. The treatment does not cure the disease but relieves the symptoms.

We included 36 randomised controlled trials with 2706 participants, examining the effect of anti-inflammatory treatments on seborrhoeic dermatitis. These trials were short-term; most of them lasting four weeks or less.

Topical steroid treatment (such as hydrocortisone and betamethasone), topical calcineurin inhibitor treatment (such as tacrolimus and pimecrolimus), and topical lithium salts all reduced the symptoms of seborrhoeic dermatitis when compared with placebo treatment. Mild (such as hydrocortisone 1%) and strong (such as betamethasone) steroid compounds were comparable in short-term follow up. Short-term total clearance was achieved with antifungal azole treatment (such as ketoconazole and miconazole), as well as with steroids. Strong steroids were better than azole treatment in reducing erythema, scaling, and pruritus, and were comparable in terms of safety. Steroids were also as effective as calcineurin inhibitors, but side-effects occurred more often with calcineurin inhibitors. We found no differences between calcineurin inhibitors and azole treatments in effectiveness or side-effects. Lithium was more effective than azoles but had a similar frequency of side-effects (one study).

The most common side-effects were burning, itching, erythema, and dryness in all treatment groups.

Topical anti-inflammatory agents are useful in treating seborrhoeic dermatitis. Steroids are the most investigated anti-inflammatories. We still do not know the effects and safety of topical anti-inflammatory treatments in long-term or continuous use. This is regrettable as the disease is chronic in nature. Furthermore, there are no data concerning the effects of different treatments on quality of life.

SUMMARY OF FINDINGS

Summary of findings for the main comparison. Calcineurin inhibitor compared with steroid for seborrhoeic dermatitis of the scalp or face

Steroid compared with calcineurin inhibitor for seborrhoeic dermatitis of the scalp or face

Patient or population: people with seborrhoeic dermatitis
Settings: community setting implied from context but not stated
Intervention: steroid
Comparison: calcineurin inhibitor

Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	No of participants (studies)	Quality of the evidence (GRADE)	Comments
	Assumed risk	Corresponding risk				
	Calcineurin inhibitor	Steroid				
Total clearance (at 4 weeks or less) Investigator's assessment Follow up: ≦ 2 weeks	**839 per 1000**	**906 per 1000** (738 to 1000)	**RR 1.08** (0.88 to 1.32)	60 (2 studies)	⊕⊕⊖⊖ **low**[1],[2]	-

*The basis for the **assumed risk** is the risk in the control groups of the relevant trials. The **corresponding risk** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).
CI: Confidence interval; **RR:** Risk ratio

GRADE Working Group grades of evidence
High quality: Further research is very unlikely to change our confidence in the estimate of effect.
Moderate quality: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.
Low quality: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.
Very low quality: We are very uncertain about the estimate.

[1]Participants were not blinded.
[2]Small number of participants in studies.

Summary of findings 2. Steroid compared with azole for seborrhoeic dermatitis of the scalp or face

Steroid compared with azole for seborrhoeic dermatitis of the scalp or face

Patient or population: people with seborrhoeic dermatitis of the scalp or face
Settings: community setting implied from context but not stated
Intervention: steroid
Comparison: azole

Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	No of participants (studies)	Quality of the evidence (GRADE)	Comments
	Assumed risk	Corresponding risk				
	Azole	Steroid				
Total clearance (at 4 weeks or less) Investigator's assessment Follow up: 3 to 4 weeks	**474 per 1000**	**526 per 1000** (445 to 625)	**RR 1.11** (0.94 to 1.32)	464 (8 studies)	⊕⊕⊕⊖ **moderate**[1]	-

*The basis for the **assumed risk** (e.g. the median control group risk across studies) is provided in footnotes. The **corresponding risk** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).
CI: Confidence interval; **RR:** Risk ratio

GRADE Working Group grades of evidence
High quality: Further research is very unlikely to change our confidence in the estimate of effect.
Moderate quality: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.
Low quality: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.
Very low quality: We are very uncertain about the estimate.

[1]Risk of bias considerable in all studies.

Summary of findings 3. Strong steroid (class III or IV) compared with mild steroid (class I or II) for seborrhoeic dermatitis of the scalp or face

Strong steroid (class III or IV) compared with mild steroid (class I or II) for seborrhoeic dermatitis

Patient or population: people with seborrhoeic dermatitis
Settings: community setting implied from context but not stated
Intervention: strong steroid (class III or IV)
Comparison: mild steroid (class I or II)

Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	No of participants (studies)	Quality of the evidence (GRADE)	Comments
	Assumed risk	Corresponding risk				
	Mild steroid (class I or II)	Strong steroid (class III or IV)				
Total clearance (at 4 weeks or less) Investigator's assessment Follow up: 3 to 4 weeks	**413 per 1000**	**397 per 1000** (268 to 578)	**RR 0.96** (0.65 to 1.4)	93 (2 studies)	⊕⊕⊕⊖ **moderate**[1]	-
Total clearance (more than 4 weeks)	**644 per 1000**	**509 per 1000**	**RR 0.79**	117	⊕⊕⊖⊖	-

Investigator's assessment Follow up: 6 weeks		(406 to 631)	(0.63 to 0.98)	(1 study)	**low**[2]

*The basis for the **assumed risk** (e.g. the median control group risk across studies) is provided in footnotes. The **corresponding risk** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).
CI: Confidence interval; **RR:** Risk ratio

GRADE Working Group grades of evidence
High quality: Further research is very unlikely to change our confidence in the estimate of effect.
Moderate quality: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.
Low quality: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.
Very low quality: We are very uncertain about the estimate.

[1]Imprecision (two small studies).
[2]One study that was not blinded (patient and care provider not blinded; blinding of outcome assessment not reported).

Summary of findings 4. Lithium compared with azole for seborrhoeic dermatitis of the scalp or face

Lithium compared with azole for seborrhoeic dermatitis

Patient or population: people with seborrhoeic dermatitis
Settings: community setting
Intervention: lithium
Comparison: azole

Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	No of participants (studies)	Quality of the evidence (GRADE)	Comments
	Assumed risk	Corresponding risk				
	Azole	Lithium				
Total clearance Investigator's assessment Follow up: 4 weeks	**147 per 1000**	**263 per 1000** (162 to 426)	**RR 1.79** (1.1 to 2.9)	288 (1 study)	⊕⊕⊝⊝ **low**[1]	-

*The basis for the **assumed risk** (e.g. the median control group risk across studies) is provided in footnotes. The **corresponding risk** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).
CI: Confidence interval; **RR:** Risk ratio

GRADE Working Group grades of evidence
High quality: Further research is very unlikely to change our confidence in the estimate of effect.
Moderate quality: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.
Low quality: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.

Very low quality: We are very uncertain about the estimate.

[1]One study in which participants were not blinded and blinding of others was not reported.

BACKGROUND

Seborrhoeic dermatitis or eczema is a chronic inflammatory skin disorder primarily affecting areas rich in sebaceous glands (Kim 2010). Such areas include, for example, skin of the scalp, face, chest, and intertriginous areas (areas where folds of skin are touching each other, such as the armpits, groin, and abdominal folds). These areas are liable to irritation from sweating and infection (Naldi 2009). Typical symptoms of the disease are scaling of the skin and erythematous (reddish) patches (Schwartz 2006).

Description of the condition

The specific cause of seborrhoeic dermatitis (SeD) is not known in detail. Despite its name and affected areas, this disease is not always associated with excessive sebum secretion (Burton 1983). It has been suggested that many endogenous and exogenous factors are associated with the course and severity of this disorder. These include hormonal factors; comorbidities (associated diseases); individual immunological features; and nutritional, environmental, and lifestyle factors (Gupta 2004; Schwartz 2006), but the mechanism of action of each of these factors has not been determined. A causative role has been suggested for *Malassezia* yeasts because SeD responds to antifungal treatments when a concurrent decrease of the number of the yeasts on the skin is seen (Gupta 2004). However, the overall evidence is still somewhat unclear.

The diagnosis of this disease is largely clinical and based on affected areas and the type of rash. Ill-defined erythematous patches with fine scaling on the sides of the nose, eyebrows, and scalp are seen most often in adult patients. Pruritus (itch) is often present in an affected scalp (Del Rosso 2011). In dark-skinned people, SeD can present as postinflammatory changes, such as hypopigmentation (Halder 2003). A skin biopsy is rarely needed for diagnosis, but it can be useful for excluding other less common conditions, such as lupus (Naldi 2009; Schwartz 2006). Dandruff is a commonly used term for any scalp condition that produces fine scales, but it has also been used in the context of mild SeD (Naldi 2009; Schwartz 2006). The disease has a chronic nature with occasional relapses. The severity of SeD varies from mild flaking to severe oily scaling. The distribution of lesions is generally symmetrical (Gupta 2004). Although the disease affects the skin of the scalp, it does not normally cause baldness.

Seborrhoeic dermatitis is a fairly common skin disorder. The prevalence is not known precisely as there are no validated criteria for diagnosis of the condition (Naldi 2009). An infantile form (cradle cap) has been reported to affect as many as 70% of newborns during the first three months of life, but this quickly resolves (Foley 2003). So, the overall prevalence of seborrhoeic dermatitis is 10% in children five years of age or younger (Foley 2003). In the adult population, prevalence is between 1% to 3%, and occurrence is more common in adolescents and young adults than those in middle age (Gupta 2004). The incidence increases again in people over 50 years of age (Gupta 2004). Seborrhoeic dermatitis affects men more frequently than women, and some diseases, such as Parkinson's disease and HIV (human immunodeficiency virus)/AIDS, are known to increase the risk of the disease (Naldi 2009).

Description of the intervention

The standard treatments for seborrhoeic dermatitis include topical anti-inflammatory (immunomodulatory) agents, such as corticosteroids and calcineurin inhibitors, to reduce inflammation; topical antifungals, such as azoles, ciclopirox olamine, and zinc pyrithione, to reduce *Malassezia*; and topical keratolytic agents, such as salicylic acid, tar, selenium sulphide, and zinc pyrithione, to soften and remove thick hardened crusts. Many agents have multiple mechanisms of action, and in some, the exact mechanism is not known (Gupta 2004; Naldi 2009; Schwartz 2006).

How the intervention might work

Topical corticosteroids (e.g. hydrocortisone, betamethasone, clobetasol, and desonide) have traditionally been used in the treatment of SeD. They reduce inflammation and relieve erythema and itching. Calcineurin inhibitors (e.g. pimecrolimus and tacrolimus) have also been used for their anti-inflammatory effects. It has been suggested that lithium salts, lithium succinate (often in combination with zinc sulphate), and lithium gluconate have anti-inflammatory effects, but they may also have antifungal properties (Gupta 2004; Naldi 2009; Schwartz 2006).

Why it is important to do this review

Seborrhoeic dermatitis is a fairly common skin disorder that affects a considerable number of children and adults. There are many available treatment options, but it is unclear which should be preferred. It is important to evaluate the efficacy of these options in order to improve the outcome of the therapy. This review is one of two Cochrane systematic reviews on this topic and will focus on treatment options with an established anti-inflammatory mechanism. The other Cochrane review is focused on drugs with an antifungal mechanism (Okokon 2011).

OBJECTIVES

To assess the effects of topical pharmacological interventions with established anti-inflammatory action for seborrhoeic dermatitis occurring in adolescents and adults.

METHODS

Criteria for considering studies for this review

Types of studies

We included randomised controlled trials and cross-over randomised controlled trials (including within-patient studies).

We excluded cluster randomised trials.

Types of participants

We included studies of adults or adolescents (> 16 years) with diagnosed seborrhoeic dermatitis of the scalp or face. At least 75% of the study participants had to be over 10 years of age to fulfil the age criterion.

We excluded studies of people having other skin diseases or seborrhoeic dermatitis occurring solely in areas other than the scalp or face.

Types of interventions

We included the following topically administered drugs with an established anti-inflammatory mechanism of action: corticosteroids and calcineurin inhibitors. We also included lithium salts in the review as it has been suggested that their effect is based on anti-inflammatory properties.

We excluded studies in which the anti-inflammatory intervention had been combined with a non-anti-inflammatory agent in preparation. We examined all clinically relevant comparisons between treatments.

Types of outcome measures

Primary outcomes

1. Percentage of treated persons with total resolution of symptoms as evaluated by the outcome assessor (total clearance).
2. Disease severity scores for scaling, pruritus, or erythema at the end of treatment as evaluated by participant self-report, outcome assessor, or both.
3. Percentage of persons treated who develop side-effects or intolerance to treatment.

Secondary outcomes

1. Improvement in quality of life.

Timing of outcomes

We defined the timing of outcomes using the following categories:

1. When the treatment period lasted for four weeks or less, we defined these outcomes as short-term effects.
2. When the treatment period lasted for more than four weeks, we defined these outcomes as long-term effects.

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

We searched the following databases up to 18 September 2013:

- the Cochrane Skin Group Specialised Register using the following terms: "seborrh* dermatitis" or "scalp dermatos*" or "scalp dermatitis" or "scalp eczema" or "cradle cap" or dandruff or malassezia or "seborrh* eczema";
- the Cochrane Central Register of Controlled Trials (CENTRAL) in *The Cochrane Library* using the search strategy in Appendix 1;
- MEDLINE via OVID (from 1946) using the strategy in Appendix 2;
- Embase via OVID (from 1974) using the strategy in Appendix 3;
- the Global Resource of EczemA Trials (GREAT, Centre of Evidence Based Dermatology, accessed at http://www.greatdatabase.org.uk on 18 September 2013) using the same search terms as for the Skin Group Specialised Register above; and
- LILACS (Latin American and Caribbean Health Science Information database, from 1982) using the strategy in Appendix 4.

Trials databases

We searched the following trials registers on 22 October 2013, using the following search terms: seborrheic dermatitis or seborrhoeic or dandruff or cradle cap or malassezia or scalp dermatoses.

- The metaRegister of Controlled Trials (www.controlled-trials.com).
- The US National Institutes of Health Ongoing Trials Register (www.clinicaltrials.gov).
- The Australian New Zealand Clinical Trials Registry (www.anzctr.org.au).
- The World Health Organization International Clinical Trials Registry platform (www.who.int/trialsearch).
- The EU Clinical Trials Register (www.clinicaltrialsregister.eu).

Searching other resources

References from included studies

We checked the bibliographies of included studies for further references to relevant trials.

Adverse effects

We did not perform a separate search for adverse effects of the target interventions. We examined data on adverse effects from the included studies we identified.

Data collection and analysis

Selection of studies

Three authors (TOk, HK, and JJ) independently identified relevant articles retrieved from the literature searches by assessing their titles and abstracts. Where we had differing views, we retained the article for full-text assessment.

The same three authors and one additional author (TOr) independently assessed the full-text papers using study eligibility forms in order to determine which studies satisfied the inclusion criteria. Where there were differing views that could not be resolved between the review authors, a third author (PP) made the decision of inclusion or exclusion.

Data extraction and management

The same authors (TOk, HK, and JJ) carried out data extraction independently using data extraction forms. A third researcher (PP) resolved discrepancies if consensus could not be found between the primary authors. TOk and HK managed the data including entering it into Review Manager (RevMan). HK checked the entered data for accuracy. We requested any further information needed from the original authors by email and included any relevant information obtained in this manner in the review.

Assessment of risk of bias in included studies

The assessment of the risk of bias included an evaluation of the following components for each included study using the criteria outlined in the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011):

(a) selection bias - we considered whether the methods of randomisation were adequate and whether the treatment allocation was concealed in the included studies. As there was

some overlap between the clinical spectrum of seborrhoeic eczema and dandruff, we paid attention to the presence of the diagnosis of seborrhoeic dermatitis in participants and to the baseline severity of the disease in study groups;
(b) performance bias - we assessed whether the participants and the caregivers were blinded to the interventions and whether cointerventions and other treatments were similar in study groups;
(c) detection bias - we evaluated whether the outcome assessors were blinded to the interventions;
(d) attrition bias - we assessed whether the trial described dropout rates and whether they were acceptable, whether compliance was acceptable in all groups, and whether the study reports used intention-to-treat analysis (we used the number of randomised participants in our analyses, where available);
(e) reporting bias - we evaluated whether there were signs of selective reporting in the studies; and
(f) other bias - we evaluated whether there might have been other sources of bias, for example, relating to particular study designs.

We assessed the study quality without blinding to authorship or journal.

We have summarised the information in the 'Risk of bias' table for each included study.

Measures of treatment effect

For dichotomous outcomes, we expressed the combined estimate of effects as risk ratios (RR) and their 95% confidence intervals (CI). For the main outcome (total clearance), we expressed summary estimates also as number needed to treat (NNT) for statistically significant findings, with a 95% CI and the baseline risk to which it applies.

For continuous outcomes, we used the mean difference with a 95% CI for summarising results. Where similar outcomes were measured differently across studies but measured the same concept, we used the standardised mean difference and a 95% confidence interval.

Unit of analysis issues

When there was intrapatient correlation in studies that had randomised body parts of the same participant and the study authors had not adjusted for this clustering effect, we did this adjustment according to the methods described in the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011).

We analysed studies with multiple treatment groups using pair-wise comparisons. We avoided counting the control group of multiple treatment studies twice, by dividing the number of control participants over the number of comparisons in the same meta-analysis, excluding the outcome of any adverse effects.

Dealing with missing data

We applied the intention-to-treat (ITT) principle by considering dropouts as non-responders (conservative approach). If data necessary for meta-analysis (such as standard deviations) were missing in the trial reports, we asked study authors for additional information. If they could not be reached, we calculated the necessary data from other statistics, if such information was available, or approximated them from information (e.g. graphics) given in the reports.

Assessment of heterogeneity

We assessed clinical heterogeneity by examining types of participants, interventions, and outcomes in each study. We assessed statistical heterogeneity using the I^2 statistic. We interpreted heterogeneity in effect estimates as considerable when the I^2 statistic was greater than 50%.

Assessment of reporting biases

We assessed reporting bias as within-study reporting bias (selective outcome reporting) and as publication bias. We did not perform funnel plot analyses as the number of studies was small in our meta-analyses. To avoid language bias, we imposed no language restrictions.

Data synthesis

For studies judged to be clinically and statistically homogenous with an I^2 statistic < 50%, we pooled the measures of treatment effect using their weighted average for the treatment effect (using a fixed-effect meta-analysis method, as implemented in Review Manager). For studies deemed to be heterogeneous (I^2 statistic ≥ 50%), we performed a random-effects meta-analysis. For studies with I^2 statistics more than 80%, we did not perform a meta-analysis, but described the results individually.

Subgroup analysis and investigation of heterogeneity

We planned to explore heterogeneity by examining age (less than 65 or over 65 years), gender (male or female), and dose (frequency) distributions of the studies. We aimed to conduct subgroup analyses if significant heterogeneity between the studies for the primary outcomes in a comparison appeared. The number of studies was small in most comparisons; therefore, performing subgroup analyses was not reasonable with the exception of comparison between mild and strong steroids.

Sensitivity analysis

We aimed to but did not perform sensitivity analyses to examine the effects of risk of bias as there were few studies in each comparison. Furthermore, the overall risk of bias was at least moderate in most studies.

RESULTS

Description of studies

Results of the search

The database searches yielded 1019 records. We identified a further seven records:

- five from handsearching the references of our included studies;
- one from a related Cochrane review (Okokon 2011); and
- one published study from a trials register (Ortonne 2011).

We screened 1026 records, of which we excluded 912 based on the title and abstract or because they were duplicates.

We screened 114 full-text articles. We excluded 76 records (see the 'Characteristics of excluded studies' tables).

Altogether, we included 36 studies (see the 'Characteristics of included studies' tables). We assigned two studies to the Studies

awaiting classification section on the grounds that it was unclear whether they measured the outcomes of interest.

We present our screening process in Figure 1.

Figure 1. Study flow diagram

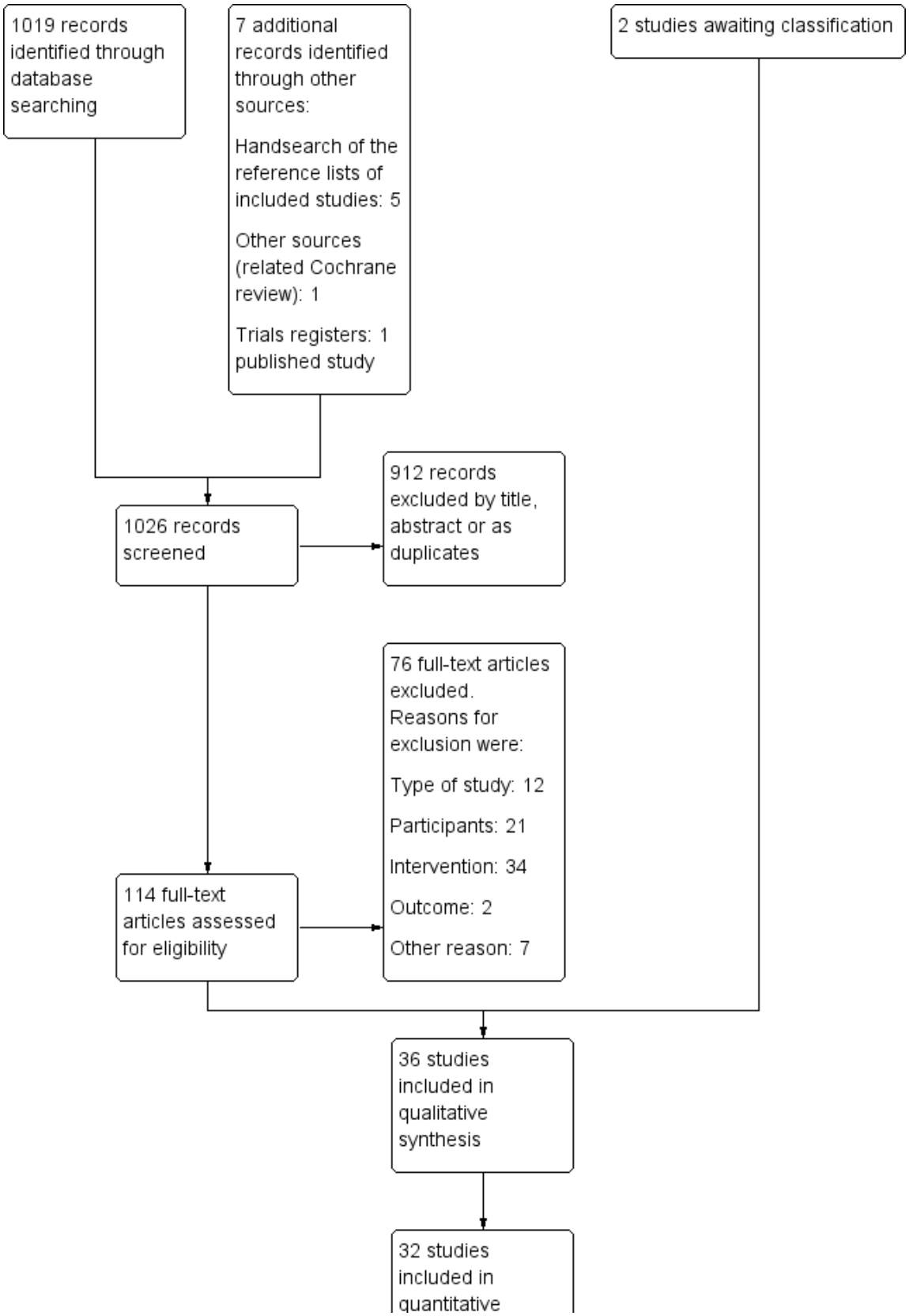
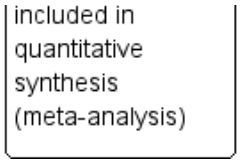


Figure 1. (Continued)



Included studies

Study design

All 36 included studies, with 2706 participants, were reported as randomised controlled trials, with three comparing body parts.

Year of study

The 36 included studies were carried out between 1970 and 2012 with 13 studies before the year 1990, 10 studies between 1990 and 2000, and 13 studies after the year 2000.

Participants

In seven studies, a physician explicitly diagnosed participants with seborrhoeic dermatitis (SeD), and in 29 studies, this was unclear (implied from context but not clearly stated). The definition of SeD was given in one study only (Cicek 2009). The studied area was the scalp only in 16 reports; the face only in 10 reports; the face and scalp in one report; and the face, scalp, or both with other areas in seven reports. Two studies did not specify the affected and investigated areas, but it could be concluded that they included facial or scalp involvement based on the assessed body areas.

Six studies included participants under 18 years of age (from ages 12, 14, or 15 upwards). Four reports did not state the age of the participants. In three studies, there was an upper limit of age (65 years in two and 55 years in one study). All studies but one included both men and women (Langtry 1997 included only homosexual men with HIV). Frequent exclusion criteria were pregnancy, lactation state, other dermatoses or interventions, too severe or mild disease, or HIV. The older studies often did not report the exclusion criteria.

The number of participants in individual studies varied between 12 and 303, resulting in a median of 64.

Geography

The geographical variation of studies was as follows: USA (10 studies), France (four studies), Greece (four studies), Sweden (four studies), Turkey (three studies), Finland (two studies), UK (two studies), Iran (one study), Denmark (one study), Korea (one study), India (one study), Canada (one study), and Netherlands (one study). One study was multicentre (Belgium, France, Germany, Mexico, and South Korea).

Interventions

The included studies used the following drugs (doses and mode of delivery) for seborrhoeic dermatitis.

- Mild steroids (class I or class II, classification according to the ATC (Anatomical Therapeutic Chemical) classification by the World Health Organization (WHO))
  - hydrocortisone (cream 1%, liniment 1%, lotion 0.1%, ointment 1.0%, and solution 1%)
  - alclometasone (ointment 0.05%)
  - desonide (cream 0.05%)
- Strong steroids (class III or class IV, classification according to ATC classification by the WHO)
- ○ methylprednisolone (cream 1%)
  - ○ betamethasone (lotion 0.1%, lotion 0.05%, cream 0.1%, and solution 1 mg/ml)
  - ○ clobetasol (shampoo 0.05% and cream 0.05%)
  - ○ amcinonide (lotion 0.1%)
  - ○ mometasone (solution 0.1% or cream 0.1%)
  - ○ fluocinolone acetonide (solution 0.01%, shampoo 0.01%)
- Calcineurin inhibitors
- ○ pimecrolimus (cream 1%)
  - ○ tacrolimus (ointment 0.1%)
- Azoles
- ○ ketoconazole (cream 2%, foaming gel 2%, shampoo 2%, shampoo 1%, and hydrogel 20 mg/g)
  - ○ metronidazole (gel 0.75%)
  - ○ miconazole (base 2%)
- Lithium (gluconate ointment 8% and succinate ointment 8%)
- Zinc pyrithione (shampoo 1%)
- Calcipotriol (solution 50 µg/ml)
- Promiseb® (cream)
- Placebo or propylene glycol

We decided to pool together all steroid studies as there were so many different steroidal compounds studied and often only one study on one compound. We also decided to pool together all calcineurin inhibitors and all azoles as the number of studies was limited. This enabled us to make the following direct comparisons.

1. Steroids compared with placebo (six trials)
2. Steroids compared with calcineurin inhibitors (five trials)
3. Steroids compared with azoles (12 trials)
4. Steroids compared with other compounds (calcipotriol, zinc pyrithione, Promiseb®) (three trials)
5. Mild steroids compared with strong steroids (five trials)
6. Calcineurin inhibitors compared with placebo (one trial)
7. Calcineurin inhibitors compared with azoles (two trials)
8. Calcineurin inhibitors compared with other compounds (zinc pyrithione) (one trial)
9. Lithium salts compared with placebo (two trials)
10. Lithium salts compared with azoles (one trial)

We also identified two studies comparing a mild steroid with another mild steroid (Cornell 1986; Cornell 1993) and one study comparing a strong steroid with another strong steroid (Cornell 1989). We do not display the results for these comparisons,

however, as the focus of this review is to compare anti-inflammatory treatments with placebo and comparisons between different anti-inflammatory treatment classes.

We contacted three authors for additional data, which we received from two.

Outcomes

Twenty-three of the 36 included studies used total clearance as a measure of outcome. Resolution of symptoms was measured either on scale or as resolution of that specific symptom as follows: scaling in 19 studies, erythema in 17 studies, pruritus in 15 studies. The validation of the scales used was not reported in any of the articles. In four studies, adverse events were the only outcome we could use in this review (Cicek 2009; Ortonne 1992; Ortonne 2011). Seven studies (19%) did not report the side-effects.

Excluded studies

We excluded 76 studies. The most frequent reason for exclusion was that the intervention in the study was not anti-inflammatory or it was a combination of two drugs. Another common reason for excluding a study was that the proportion of people with SeD was unclear or that the proportion of them was too small. We identified two studies that did not report outcomes relevant for this review or did not report them in numerical form. We excluded them as they had no useful data to add to the analyses (Kim 2012; Marks 1974).

We present detailed reasons for exclusions in the 'Characteristics of excluded studies' tables.

Studies awaiting classification and ongoing studies

We assigned two studies to the Studies awaiting classification section as we had no evidence that they measured the outcomes of interest. We will reconsider these studies in the next update of the review. See the 'Characteristics of studies awaiting classification' tables for details. We identified seven studies from trials registers that are either ongoing or not yet published. See the 'Characteristics of ongoing studies' tables for details.

Risk of bias in included studies

We assessed the risk of bias in the included studies as described above (Assessment of risk of bias in included studies). The most frequent classification of risk of bias in studies was unclear. This was especially because of unclear reporting of methods, such as reporting studies to be double-blind without specifying who was blinded. Figure 2 displays the overall percentages of risk of bias for the studies included in the review. Figure 3 displays the risk of bias judged for each included study.

Figure 2. 'Risk of bias' graph: review authors' judgements about each 'Risk of bias' item presented as percentages across all included studies

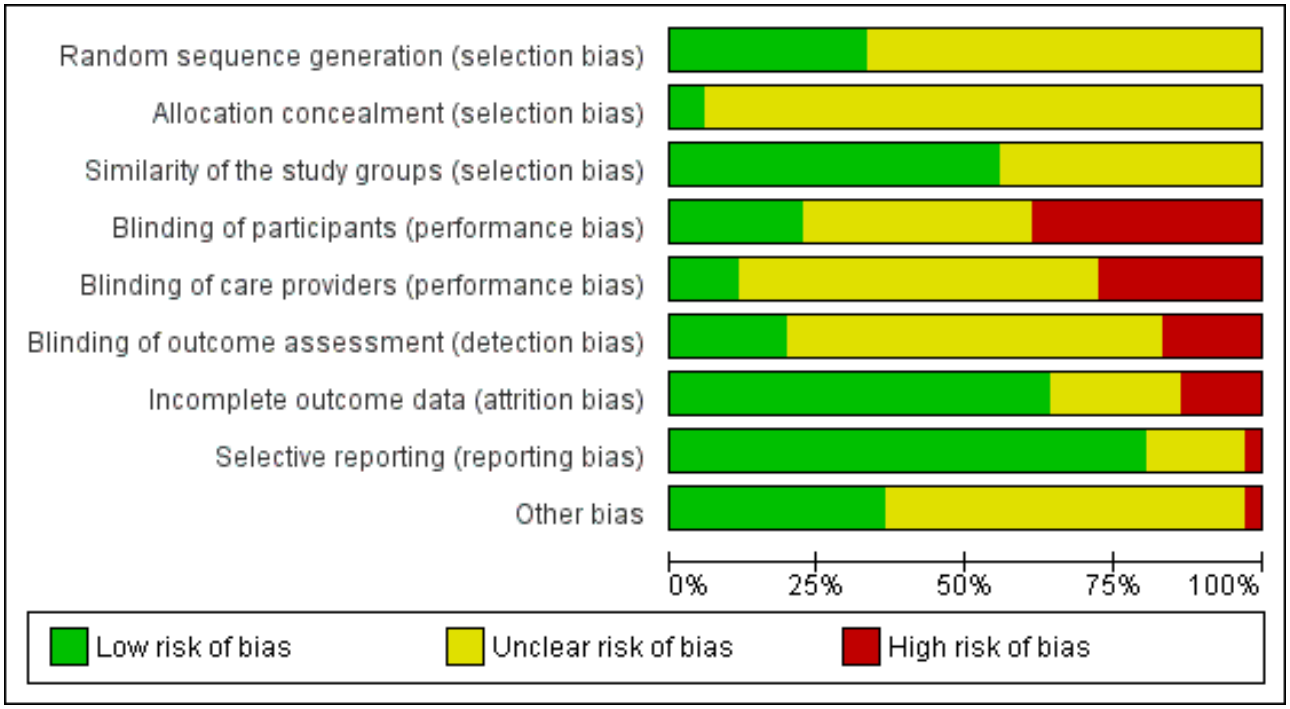


Figure 3. 'Risk of bias' summary: review authors' judgements about each 'Risk of bias' item for each included study

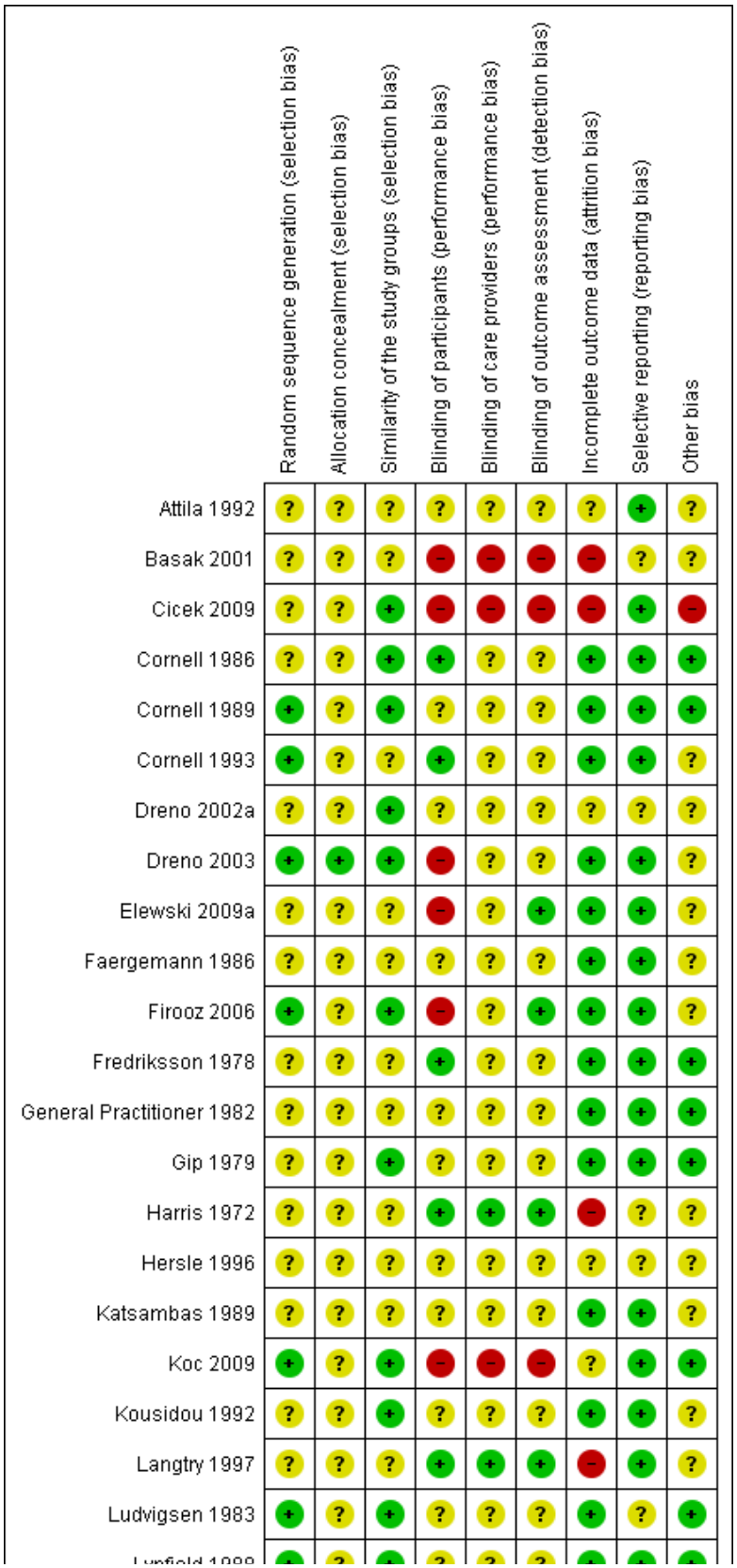
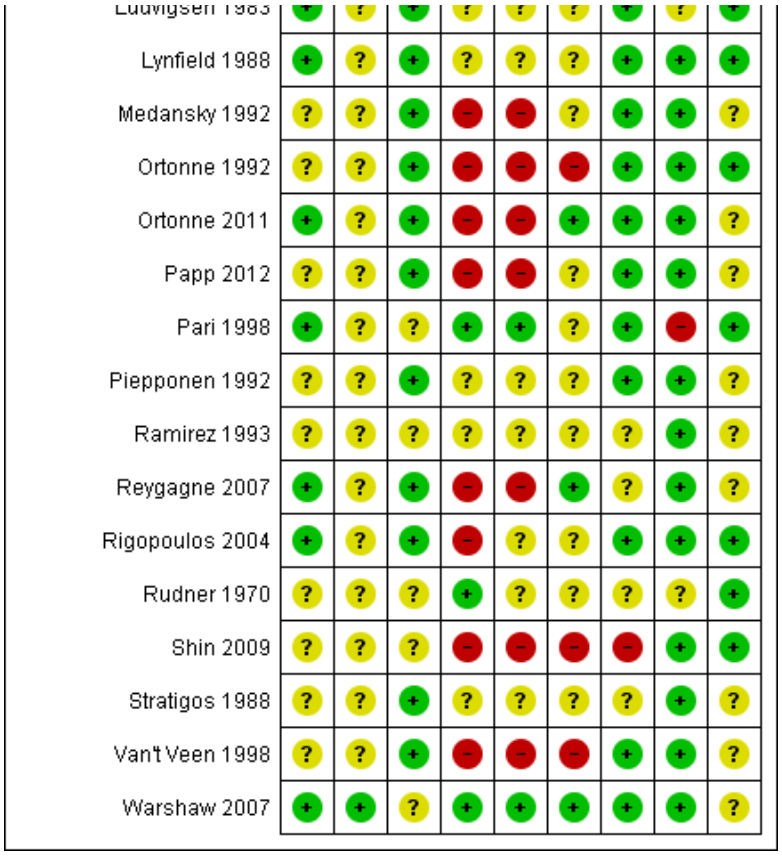


Figure 3. (Continued)



Allocation

Most reports classified selection bias as unclear. They often stated that participants were randomly allocated but did not report the methods of randomisation or allocation sequence concealment in detail. Twelve studies reported the generation of the randomisation sequence, and most commonly, it was computer-based. Only two studies described the allocation concealment method; otherwise, the studies did not mention it at all, and therefore we classified them as unclear risk.

Blinding

Most often the studies were reported to be double-blind, but it was not clear which two of the three parties (the participants, the caregivers, or the outcome assessors) were blinded. In these cases, we evaluated the risk of bias as unclear. Seven reports stated that the whole study was outcome assessor blinded. Six of the included studies were completely open-label or did not mention blinding, which we rated as at high risk of detection bias.

Incomplete outcome data

We evaluated attrition bias to be low in 23 of the studies. The reason we classified a study with a high risk for attrition bias was most often because of a considerable dropout rate (over 20%). We evaluated attrition bias to be unclear in eight studies when it was unclear whether the results given in percentages were calculated using the randomised or the completed participant numbers.

Selective reporting

We classified the risk for reporting bias as low in 29 of the studies. One study did not prespecify the outcomes in the report, but the outcomes reported were those commonly used in SeD studies. In seven studies, there was no mention of side-effects at all, which we consider a serious omission. However, we did not assess the lack of information concerning side-effects as a reporting bias unless the measurement of adverse effects was part of the predefined outcome measures, but had not been reported.

Other potential sources of bias

We sought other potential sources of bias. One study (Cicek 2009) evaluated both the efficacy outcome and side-effects using the same symptoms (erythema and pruritus were both an efficacy outcome and a side-effect); therefore, it was impossible for a reader to evaluate when or why these symptoms were classified as an outcome or a side-effect. Therefore, we classified the risk of bias as high for this trial. One study (Koc 2009) did not report the affected area (although we could conclude from the report that facial involvement was an inclusion criterion); therefore, we were not sure that the efficacy or the intervention on facial or scalp SeD was the same as reported in the article. We judged the risk of bias as low regarding this study. One study (Langtry 1997) only included male HIV participants, which may limit the ability to generalise the results into other populations. (We judged risk of bias as unclear.)

The most common circumstance in studies classified as having unclear risk was author affiliation to the pharmaceutical industry or interventions sponsored or provided by the pharmaceutical

industry (N = 21 for studies having some kind of affiliations to the pharmaceutical industry). This classification was done categorically, and it does not imply that in the opinion of the review authors, these studies have increased risk of bias. In 13 studies, we were unable to identify other potential sources of bias, so we classed these at low risk of bias.

Similarity of study groups (selection bias)

Most of the included studies described adequately the similarity of study groups, and the risk of bias was low in 20 studies.

Effects of interventions

See: **Summary of findings for the main comparison** Calcineurin inhibitor compared with steroid for seborrhoeic dermatitis of the scalp or face; **Summary of findings 2** Steroid compared with azole for seborrhoeic dermatitis of the scalp or face; **Summary of findings 3** Strong steroid (class III or IV) compared with mild steroid (class I or II) for seborrhoeic dermatitis of the scalp or face; **Summary of findings 4** Lithium compared with azole for seborrhoeic dermatitis of the scalp or face

We have addressed the comparisons under the following headings.

- Steroids versus comparators
  - Steroids versus placebo
  - Steroids versus calcineurin inhibitors
  - Steroids versus azoles
  - Mild steroids versus strong steroids
  - Other comparisons for steroids
- Calcineurin inhibitors versus comparators
  - Calcineurin inhibitors versus placebo
  - Calcineurin inhibitors versus azoles
  - Calcineurin inhibitors versus zinc pyrithione
- Lithium versus comparators
  - Lithium salts versus placebo
  - Lithium salts versus azoles

For each of these comparisons, we addressed our prespecified outcomes. Our primary outcomes were as follows.

1. Percentage of treated persons with total resolution of symptoms as evaluated by the outcome assessor (total clearance).
2. Disease severity scores for scaling, pruritus, or erythema at the end of treatment as evaluated by participant self-report, outcome assessor, or both.
3. Percentage of persons treated who develop side-effects or intolerance to treatment.

With regard to our primary outcome 'Total clearance', we considered this to be present where the terms "complete" or "total" resolution of symptoms or cure or clearance were used, whereas we did not accept as total clearance the term "excellent" without any definition of its meaning. Total clearance was the investigator's assessment unless otherwise stated. The included studies reported our other primary outcomes 'Disease severity' and 'Adverse events'.

None of the included studies assessed our secondary outcome 'Quality of life'.

Steroids versus comparators

We identified six studies comparing steroids with placebo or vehicle, five studies comparing steroids with calcineurin inhibitors, and 12 studies comparing steroids with azoles. Of these studies, one compared steroid with placebo and azole, one compared steroid with calcineurin inhibitor and azole, and one compared steroid with calcineurin inhibitor and zinc pyrithione. Additionally, we identified one study that compared steroid with Promiseb®, which is a non-steroidal compound, and one study that compared steroid with calcipotriol (vitamin D).

We performed subgroup analyses using the strength of the steroid compound as classification criterion. We classified class I and II steroids as mild steroids, and we classified class III and IV steroids as strong steroids. Five identified studies compared strong steroids with mild steroids. Furthermore, we identified two studies comparing a mild steroid with another mild steroid (Cornell 1986; Cornell 1993), and one study comparing a strong steroid with another strong steroid (Cornell 1989). We did not display the results for these three comparisons, as the focus of this review is to compare anti-inflammatory treatments with placebo and comparisons between different anti-inflammatory treatment classes. We also included analyses comparing mild steroids with strong steroids. We consider these comparisons to be most important from the clinical decision-making point of view.

Steroids versus placebo

In our analyses, steroids displayed a stronger effect on the studied outcomes than placebo with a comparable safety profile.

Total clearance (at four weeks or less of treatment)

Three studies, with a total of 303 participants, investigated this outcome. Participants achieved 'Total clearance' with steroids more often than with placebo (risk ratio (RR) 3.76, 95% confidence interval (CI) 1.22 to 11.56) when pooling steroids together (Analysis 1.1) (number needed to treat (NNT) 4, 95% CI 3 to 6). Two studies not included in this meta-analysis (Harris 1972; Reygagne 2007; Table 1) further supported this finding. However, there were indications that only a strong steroid is more effective than placebo (RR 5.92, 95% CI 0.99 to 35.52) in Analysis 1.1.

Total clearance (at four weeks or more)

One study with 43 participants examined the effect of a strong steroid on total clearance compared with placebo and found that participants achieved total clearance more often with the steroid than with placebo (RR 2.24, 95% CI 1.10 to 4.56) (Analysis 1.2) (NNT 3, 95% 1 to 11).

Erythema (at four weeks or less of treatment)

One study with 134 participants examined the mean change in erythema scores. There was a greater reduction in erythema score with a strong steroid (in favour of steroid) than with placebo (mean difference (MD) 0.53, 95% CI 0.27 to 0.79) (Analysis 1.3).

This finding is furthermore supported by another study (44 participants) (Reygagne 2007; Table 1). A study with 98 participants examined the level of erythema scores at the end of treatment and found that with strong steroid the erythema score was lower (in favour of steroid) when compared with placebo (MD -0.79, 95% CI -1.07 to -0.51) (Analysis 1.4).

Scaling (at four weeks or less of treatment)

One study with 136 participants examined the mean change in scaling scores. There was a greater reduction in scaling score with strong steroid (in favour of steroid) than with placebo (MD 0.77, 95% CI 0.49 to 1.05) (Analysis 1.5). Another study with 98 participants reported the level of scaling scores at the end of treatment, and here also, a strong steroid was more effective than placebo because the scaling score was lower with steroid (MD -0.80, 95% CI -1.10 to -0.50) (Analysis 1.6).

One study with 44 participants (Reygagne 2007; Table 1) further supported this finding.

Pruritus (at four weeks or less of treatment)

One study with 116 participants examined the mean change in pruritus scores and found that there were no statistically significant differences between a strong steroid and placebo (MD 0.27, 95% CI -0.04 to 0.58) (Analysis 1.7). Another study with 98 participants reported the level of pruritus scores at the end of treatment. In this study, a strong steroid proved to be more effective than placebo (MD -0.41, 95% CI -0.69 to -0.13) (Analysis 1.8).

Another study with 44 participants found a strong steroid to be more effective in this outcome when compared with placebo (Reygagne 2007; Table 1).

Any adverse effects

One study compared a mild steroid and placebo, and three studies compared a strong steroid and placebo. As a whole, there were 606 participants in these trials. We found no statistically significant differences between steroid treatment and placebo regardless of the strength of the steroid (pooled RR 0.89, 95% CI 0.29 to 2.72) (Analysis 1.9). One study with 44 participants (Reygagne 2007; Table 1) supported this finding. We could not use in meta-analysis one study with 100 randomised participants, which reported that there were no adverse effects (Ramirez 1993), as the effect estimate was inestimable.

The most commonly reported adverse effects were burning and itching in both steroid and placebo treatment. The proportion of participants experiencing any adverse effect was mostly low, approximately two to three per cent of the total study population.

Steroids versus calcineurin inhibitors

In our analyses, there were no statistically significant differences between steroids and calcineurin inhibitors in terms of the assessed outcomes in three studies. In two studies, only the adverse events outcomes were of relevance to this review (Cicek 2009; Papp 2012). There were implications that adverse events may be more common in calcineurin inhibitor treatment when compared with steroids.

Total clearance (at four weeks or less of treatment)

There was no statistically significant difference between steroids and calcineurin inhibitors for this outcome in two studies with a combined total of 60 participants (RR 1.08, 95% CI 0.88 to 1.32) (Analysis 2.1), and there were no conclusive statistical differences between a strong and a mild steroid when compared with calcineurin inhibitor. We rated the quality of the evidence as low (Summary of findings for the main comparison).

Erythema (at four weeks or less of treatment)

One study with 37 participants examined the erythema scores at the end of treatment and found that there was no statistically significant difference between a mild steroid and calcineurin inhibitor (MD -0.05, 95% CI -0.22 to 0.12) (Analysis 2.2).

Scaling (at four weeks or less of treatment)

One study with 38 participants examined the scaling scores at the end of treatment and found that there were no statistically significant differences between steroids and calcineurin inhibitors (MD 0.00, 95% CI -0.24 to 0.24) (Analysis 2.3). Another study with 32 participants examined the mean change in dandruff scores, and the findings of this study were similar (MD -0.20, 95% CI -0.73 to 0.33) (Analysis 2.4).

Pruritus (at four weeks or less of treatment)

One study with 37 participants examined pruritus scores and found that there were no statistically significant differences between a mild steroid and calcineurin inhibitor (Firooz 2006). We could not use the results of the trial in analyses for statistical reasons. (The standard deviations were 0.00 in the other treatment arm.)

Any adverse effects

Two studies with a combined total of 60 participants examined the incidence of adverse events when comparing calcineurin inhibitors with steroids for short-term treatment. Adverse events were found to be less common with steroid treatment (RR 0.22, 95% CI 0.05 to 0.89) (Analysis 2.5). The most commonly reported adverse effects were erythema, burning, and prickling sensations.

Two studies with a combined total of 72 participants examined the incidence of adverse effects for long-term treatment. There was no statistically significant difference between steroid and calcineurin-inhibitor treatment (RR 0.62, 95% CI 0.26 to 1.47) (Analysis 2.6). One study with 54 participants (Shin 2009) did not report adverse effects with sufficient detail.

Steroids versus azoles

No statistically significant differences were found between steroids and azoles in their efficacy in producing total clearance when evaluated by the investigator for short-term treatment, whereas when evaluated by the participant, azole treatment was found to be more effective than a mild steroid. For short-term treatment, the effect of azoles was milder than that of (at least strong) steroids on erythema, scaling, or pruritus. When long-term treatment was given, an azole compound was found to be more effective than a steroid compound in producing total clearance. There seemed to be no differences between steroids and azoles for adverse effects; however, in one study of long-term use, there were more adverse effects with a strong steroid than with an azole compound.

Total clearance (at four weeks or less of treatment)

A total of eight studies with a combined number of 464 participants assessed the comparative effectiveness of steroids and azoles in producing total clearance and found that there were no statistically significant differences between them (RR 1.11, 95% CI 0.94 to 1.32) when judged by the investigator (Analysis 3.1). The finding was similar in studies investigating mild and strong steroids. We rated the quality of the evidence as moderate (Summary of findings 2).

One study with 44 participants, which we did not include in the meta-analysis, reached inconclusive results (Reygagne 2007; Table 1). There was also one study (62 participants) with conflicting results where azole treatment was more effective than steroid treatment in producing an excellent (this trial did not use total clearance as an outcome) response (Ortonne 1992).

Two studies assessed the comparative effectiveness of steroids and azoles in producing total clearance when judged by the participant. In one study with 101 participants, azole treatment was more effective in producing total clearance when compared with a mild steroid (RR 1.55, 95% CI 1.09 to 2.21) (Piepponen 1992), whereas in another study with 69 participants, there were no statistically significant differences between a strong steroid and an azole treatment (RR 0.99, 95% CI 0.80 to 1.23) (Van't Veen 1998) (Analysis 3.2).

Erythema (at four weeks or less of treatment)

Three studies with a combined total of 160 participants addressed the effect of steroids and azoles on erythema evaluated by erythema scores at the end of treatment. One study (49 participants) comparing a strong steroid with azole found steroid to be more effective (MD -0.19, 95% CI -0.26 to -0.12) (Analysis 3.3). In two studies comparing mild steroids with azoles (111 participants), the results were inconsistent (Kousidou 1992; Stratigos 1988). We could not use these trials in the analysis because of missing statistical data.

One study (101 participants, mild steroid) assessed the mean change in erythema scores. There was no statistically significant difference between the two treatments (MD 0.12, 95% CI -0.27 to 0.51) (Analysis 3.4).

Scaling (at four weeks or less of treatment)

Two studies with a combined total of 118 participants addressed the effect of steroids when compared with azoles on scaling evaluated by scaling scores at the end of treatment. Strong steroids were associated with statistically significantly lower scaling scores (in favour of steroids) at the end of treatment (standardised mean difference (SMD) -2.72, 95% CI -3.24 to -2.21 for strong steroids, two studies) (Analysis 3.5).

By contrast, there was a high degree of heterogeneity (I^2 statistic of 90%) between the results for the two trials comparing mild steroids with azoles (Kousidou 1992; Stratigos 1988, altogether 111 participants). The first mentioned trial found azole treatment to be more effective when compared with steroid (MD 0.92, 95% CI 0.26 to 1.59, 39 participants), whereas the results of the latter trial displayed no statistically significant difference between steroid and azole treatment (MD -0.38, 95% CI -0.85 to 0.08, 72 participants).

One study with 101 participants addressed the mean change in scaling scores and found that the treatments were equally effective (MD -0.05, 95% CI -0.40 to 0.30) (Analysis 3.6).

Pruritus (at four weeks or less of treatment)

Five studies with a combined total of 260 participants assessed the effect of steroids and azoles on pruritus evaluated by pruritus scores at the end of treatment. One trial with mild steroids (Stratigos 1988, 72 participants) noted no statistically significant difference in pruritus at four weeks (72 participants). We could not use the results of this trial in the meta-analysis because of lack of statistical data. In the other trial with mild steroids, the treatments seemed comparable as well (MD 0.06, 95% CI -0.02 to 0.14, 39 participants) (Analysis 3.7).

The results of three studies with strong steroids displayed a high degree of heterogeneity (I^2 statistic of 83%), and therefore we could not pool them together in a meta-analysis. However, in two of these trials, there were indications that strong steroids are more effective than azoles in reducing pruritus (MD -1.52, 95% CI -2.17 to -0.88, 49 participants in Hersle 1996) (MD -1.81, 95% CI -2.38 to -1.25, 69 participants in Van't Veen 1998), whereas in the third study, there were no statistically significant differences between a strong steroid and azole treatment (MD -0.28, 95% CI -0.99 to 0.43, 31 participants) (Pari 1998).

One study with 101 participants evaluated the mean change in pruritus scores and found that the treatments were equally effective (MD 0.03, 95% CI -0.36 to 0.42) (Analysis 3.8).

Total clearance (at more than four weeks of treatment)

Only one study (Ortonne 1992), with 62 participants lasting four months, assessed clearance as a long-term outcome. However, this trial did not measure total clearance; instead, it evaluated excellent clearance. We did not predefine excellent clearance as an outcome of interest.

Any adverse effects

Three studies did not report adverse effects at all (Faergemann 1986; Fredriksson 1978; Pari 1998).

Altogether, six studies with a combined total of 381 participants reported the occurrence of any adverse effects at four weeks or less of treatment, and there was no statistically significant difference between steroid and azole treatment (RR 1.45, 95% CI 0.74 to 2.85) (Analysis 3.9). Adverse effects most often reported were dryness of skin, burning, and dandruff. Dryness of skin was more often associated with steroid treatment than with azole treatment.

In the long-term studies (four weeks or more of treatment) comparing steroid and azole treatment, strong steroids seemed to produce adverse effects more often than azoles (RR 3.20, 95% CI 1.34 to 7.65, one study with 62 participants), whereas there were no statistically significant differences between mild steroid and azole treatment in one study with 43 participants (RR 0.48, 95% CI 0.22 to 1.04) (Analysis 3.10).

Mild steroids versus strong steroids

We compared mild steroids (class I and II steroids) with strong steroids (class III or IV) in three studies. In general, there were no differences between mild and strong steroids with regard to the assessed outcomes including adverse effects.

Total clearance (at four weeks or less of treatment)

Two studies lasting four weeks or less, with 93 participants, assessed total clearance. We found that there were no statistically significant differences between mild or strong steroids whether total clearance was evaluated by the investigator (RR 0.96, 95% CI 0.65 to 1.40) (Analysis 4.1; Summary of findings 3) or by the participant (one study, 29 participants) (RR 1.03, 95% CI 0.65 to 1.61) (Analysis 4.2). We rated the quality of the evidence as moderate.

Total clearance (at more than four weeks of treatment)

One study with 117 participants assessed total clearance at four weeks or more. In this study, we found a mild steroid to be more effective than a strong steroid (RR 0.79, 95% CI 0.63 to 0.98) (NNT 6, 95% CI 3 to 59) (Analysis 4.3). We rated the quality of the evidence as low (Summary of findings 4).

Erythema (at four weeks or less of treatment)

Two studies with a combined total of 55 participants assessed the effect of mild or strong steroids on erythema evaluated with erythema scores. We found that there was no statistically significant difference between mild and strong steroids (MD 0.10, 95% CI -0.34 to 0.54, one study, 35 participants) (Analysis 4.4). Another trial (Ludvigsen 1983) with 20 participants supported this finding. We could not use the results of the latter trial in the analysis because of a lack of statistical data.

Scaling (at four weeks or less of treatment)

Two studies with a combined total of 63 participants assessed the effect of mild or strong steroids on scaling evaluated with scaling scores, and we found that there was no statistically significant difference (SMD -0.05, 95% CI -0.55 to 0.45) (Analysis 4.5).

Pruritus (at four weeks or less of treatment)

Three studies with a combined total of 114 participants assessed the effect of mild or strong steroids on pruritus evaluated with pruritus scores, and we found that there was no statistically significant difference (SMD 0.13, 95% CI -0.24 to 0.50) (Analysis 4.6).

Any adverse effects

When used in the short-term, there was no statistically significant difference between mild and strong steroids with regard to rate of adverse effects (RR 1.37, 95% CI 0.32 to 5.93) in three studies with a combined total of 118 participants (Analysis 4.7), and in long-term use, the finding was similar (RR 5.90, 95% CI 0.73 to 47.49) in one study with 117 participants (Analysis 4.8). The reported adverse effects were scalp dryness or appearance of papules or other kinds of rash.

Other comparisons for steroids

There were two additional studies that compared a mild steroid with another mild steroid (Cornell 1986; Cornell 1993), and one study compared a strong steroid with another strong steroid (Cornell 1989). We did not perform analyses on these studies as we were focusing on differences between different classes of drugs.

One study with 56 participants compared a strong steroid (betamethasone) with zinc pyrithione, and we found no statistically significant differences in their effect on scaling (MD -0.40, 95% CI -0.92 to 0.12) (Analysis 5.1), but this study (Shin 2009) did not report adverse effects.

One study with 77 participants compared a mild steroid (desonide) with non-steroidal cream, Promiseb® (Elewski 2009a). There was no statistically significant difference in the effect on total clearance (RR 1.83, 95% CI 0.88 to 3.80) (Analysis 6.1). In the same study, there were no statistically significant differences between the two drugs with regard to their ability to reduce erythema, scaling, or pruritus or to produce adverse effects.

One study with 60 participants compared steroid with calcipotriol (vitamin D compound) (Basak 2001). In this study, steroid proved to be more effective in accomplishing total clearance when compared with calcipotriol (RR 2.86, 95% CI 1.42 to 5.73) (Analysis 7.1). Furthermore, the incidence of adverse effects was lower with steroid treatment than with calcipotriol treatment (RR 0.12, 95% CI 0.03 to 0.47) (Analysis 7.2).

Calcineurin inhibitors versus comparators

We identified four studies comparing calcineurin inhibitors to steroids as described above. Of these, one study compared calcineurin inhibitor with azole and steroid, one compared calcineurin inhibitor with steroid and zinc pyrithione, one compared calcineurin inhibitor with placebo, and one compared calcineurin inhibitor with azole only.

Calcineurin inhibitors versus placebo

One study with 96 participants found calcineurin inhibitors to be more effective in reducing erythema and scaling when compared with placebo. There were no differences in total clearance or adverse effects between calcineurin inhibitors and placebo.

Total clearance (at four weeks or less of treatment)

We identified only one study (96 participants) assessing the effect of calcineurin inhibitors on total clearance when compared with placebo; there was no statistically significant difference in the effect on total clearance (RR 1.41, 95% CI 0.81 to 2.48) (Analysis 8.1).

Erythema (at four weeks or less of treatment)

This study (results available for 86 participants) compared the effect of calcineurin inhibitors on erythema with placebo, and we found that calcineurin inhibitor was more effective in reducing erythema when evaluated by mean change in erythema scores (MD 0.40, 95% CI 0.06 to 0.74) (Analysis 8.2).

Scaling (at four weeks or less of treatment)

This study (results available for 86 participants) compared the effect of calcineurin inhibitor on scaling with placebo. We found that calcineurin inhibitor was more effective in reducing scaling as evaluated by mean change in scaling scores (MD 0.30, 95% CI 0.00 to 0.60) (Analysis 8.3).

Any adverse effects

In this study (results available for 86 participants), the proportion of participants experiencing adverse effects (at four weeks or less of treatment) was not statistically significantly different between the calcineurin inhibitor group and the placebo group (RR 1.43, 95% CI 0.87 to 2.37) (Analysis 8.4). The nature of these adverse events was not reported.

Calcineurin inhibitors versus azoles

We identified two studies with a combined total of 90 participants assessing the effect of calcineurin inhibitors when compared with azoles. Of these, in one study, there were data concerning adverse effects relevant for this review. These two studies did not assess total clearance. With regard to efficacy outcomes, we identified no statistically significant differences between calcineurin inhibitors and azoles. Evidence concerning adverse effects was not conclusive.

Erythema (at four weeks or more of treatment)

In one study with 38 participants, we found no statistically significant differences between a calcineurin inhibitor and an azole in their effect on erythema evaluated with erythema scores at the end of treatment (MD 0.17, 95% CI -0.24 to 0.58) (Analysis 9.1).

Scaling (at four weeks or more of treatment)

In the same study, we found the calcineurin inhibitor to be comparable to azole treatment in its effect on scaling evaluated with scaling scores at the end of treatment (MD -0.02, 95% CI -0.33 to 0.29) (Analysis 9.2).

Any adverse effects

Two studies with a combined total of 90 participants addressed the incidence of adverse effects (at four weeks or more of treatment) (Analysis 9.3). Their results were conflicting with a heterogeneity (I^2 statistic) of over 80%; therefore, we did not use their results in a meta-analysis. In a study with 42 participants, there were no statistically significant differences in adverse effect rate between calcineurin inhibitor treatment and azole treatment (Cicek 2009). In another trial with 58 participants, there were more adverse events in calcineurin inhibitor treatment when compared with azole treatment (Koc 2009). The trial reported burning, pruritus, and irritation as adverse effects.

Calcineurin inhibitors versus zinc pyrithione

One study compared calcineurin inhibitor (tacrolimus) with zinc pyrithione. It also included a comparison with a steroid. We found that when compared with zinc pyrithione, calcineurin inhibitor was more effective in reducing the dandruff scores (MD -0.60, 95% CI -1.01 to -0.19) (Analysis 10.1). The study did not report adverse effects in sufficient detail (Shin 2009).

Lithium versus comparators

We identified two studies comparing lithium salts with placebo (Dreno 2002a; Langtry 1997) and one study comparing lithium salt with azole treatment (Dreno 2003). Lithium seemed to be more effective than placebo with regard to total clearance, but concerning erythema or scaling, there were no statistically significant differences between lithium and placebo. Lithium was also more effective when compared with azole with regard to total clearance. The differences between lithium and its comparators were ambiguous with regard to adverse effects, which were most often burning, erythema, dryness, and pruritus.

Lithium salts versus placebo

Lithium seems to be more effective when compared with placebo with regard to total clearance, with a comparable safety profile.

Total clearance (at four weeks or more of treatment)

Only one study with 129 participants assessed total clearance. We found that lithium was more effective than placebo (RR 8.59, 95% CI 2.08 to 35.52) (NNT 4, 95% CI 3 to 9) (Analysis 11.1).

Erythema (at four weeks or less of treatment)

One study with 12 participants assessed the effect of lithium salts on erythema, comparing it to placebo (Langtry 1997). This study was a body-part study on HIV-positive male participants. At two weeks of treatment, It was found that there were no statistically significant differences in the percentage change in erythema scores between the lithium compound (30.7% of the baseline value) and placebo treatment (47.1% of the baseline value) (P = 0.055). However, at this point, 50% of the participants had already dropped out.

Scaling (at four weeks or less of treatment)

One study assessed the effect of lithium salts on scaling, comparing it to placebo. This study was a body-part randomisation study on 12 HIV-positive male participants (Langtry 1997). At two weeks of treatment, it was found that there were no statistically significant differences in the percentage change in erythema scores between the lithium compound (19.5% of the baseline value) and the placebo treatment (33.8% of the baseline value) (P = 0.76). However, at this point, 50% of the participants had already dropped out.

Any adverse effects

In one study lasting for eight weeks, there was no statistically significant difference between lithium and placebo in the occurrence of adverse effects (RR 0.72, 95% CI 0.31 to 1.66, 123 participants) (Analysis 11.2). In this study, the adverse effects reported most often were burning, erythema, and pruritus. The report of the other study (Langtry 1997) comparing lithium to placebo was imprecise regarding adverse effects.

Lithium salts versus azoles

Total clearance (at four weeks or less of treatment)

One study with 288 participants compared the effect of lithium salt with azole on total clearance of SeD. In this study, we found that lithium salt was more effective (RR 1.79, 95% CI 1.10 to 2.90) (Analysis 12.1) in terms of short-term results (four weeks). We rated the quality of the evidence as low (Summary of findings 4).

Total clearance (at four weeks or more of treatment)

The results were similar at eight weeks (RR 1.79, 95% CI 1.32 to 2.43) (Analysis 12.2).

Any adverse effects

This study reported adverse events in 26% of participants using topical lithium and in 25% of participants using topical azole treatment. Most commonly reported adverse events included erythema, burning, and dryness.

DISCUSSION

Summary of main results

We located 36 studies, of which 31 studies examined steroid as one intervention; seven examined calcineurin inhibitor as one intervention; and three examined lithium as one intervention.

Based on four studies, steroids increased the total clearance of all symptoms when compared with placebo, but with a similar safety profile both at four weeks and 12 weeks of follow-up. Steroids and calcineurin inhibitors had similar effects, but there were more often adverse effects with calcineurin inhibitor treatment than with steroid treatment. Compared with azoles, the effect varied between different outcomes. There were no differences between azole and steroid treatment regarding short-term total clearance. The effect of azoles on erythema, scaling, and pruritus was weaker than that of strong steroids. The rate of adverse effects was similar,

at least in short-term use. In general, for short-term use, there were no differences between mild and strong steroids for outcomes including adverse effects.

Calcineurin inhibitors were more effective in reducing erythema and scaling when compared with placebo. Calcineurin inhibitors and azoles had similar effects and a similar rate of adverse effects.

Lithium was more effective than placebo with regard to total clearance, but there were no differences in erythema or scaling. The safety of these two was comparable. Lithium was also more effective than azoles with regard to total clearance with a similar safety profile.

The median rate of adverse effects was 7% in active treatment groups. Across treatments, the most commonly reported adverse effects were burning, itching, erythema, and dandruff. Some of these symptoms are similar to the symptoms of seborrhoeic dermatitis itself.

Overall completeness and applicability of evidence

We performed the literature searches without language restrictions up until September 2013. These searches provide assurance that we located the majority of studies on topical anti-inflammatory treatments for seborrhoeic dermatitis. Most studies included both men and women, and the age range was wide. Therefore, we consider the results to be applicable to both adult men and women. However, as pregnancy was a widely used exclusion criterion, it is unclear whether those who have seborrhoeic dermatitis when they are pregnant should use anti-inflammatory treatments. The studies rarely reported compliance rates. There were also multiple modes of delivering the interventions, which may account for some variation in the results. The trials covered several races including Caucasian and Asian participants, but not many people of African origin. This is important as seborrhoeic dermatitis may have a different pattern of symptoms in those with dark skin.

We only included trials investigating face or scalp involvement, and therefore the results of this review may not be applicable to people with seborrhoeic dermatitis affecting other parts of the body. It is also questionable whether the results can be generalised to people with dandruff but without the diagnosis of seborrhoeic dermatitis, as in most of the trials, the diagnosis of seborrhoeic dermatitis was an inclusion criteria. The available evidence does not allow us to determine whether there are differences in the effects of the assessed agents in different areas of the body or to make comparisons between the treatments in this regard.

The overwhelming majority of the trials were of short duration, whereas the disease itself is chronic in nature. Relapses often occur, sometimes triggered by environmental or individual stimuli. The available evidence does not cover the treatment effects (including side-effects) of repeated, long-term, or continuous use of anti-inflammatory agents. Seborrhoeic dermatitis cannot be cured, but the symptoms can be relieved.

This review did not include combination treatments in which an anti-inflammatory agent had been combined with an agent having another mechanism of action, such as an antimycotic or antiproliferative effect. There are also other topical treatments that may have anti-inflammatory effects (such as coal tar, selenium sulfide, and zinc). We did not include these treatments in the review however as their suggested modes of action have been classified as unclear or included additional mechanisms, such as antiproliferative, bacteriostatic, or fungistatic properties.

Quality of the evidence

For the main outcome (total clearance) and for the main comparisons, we assessed the quality of the evidence using the Grade Profiler software (Summary of findings for the main comparison; Summary of findings 2; Summary of findings 4). For this outcome, the quality of the evidence was low to moderate.

For other outcomes, we also considered the quality of evidence as low to moderate on the basis of small sample sizes; short follow up; limitations in study design and reporting; and uncertainties in, or lack of blinding of, the participants, caregivers, or outcome assessors. In general, the level of evidence remains limited, and it is possible that further research may change the effect estimates substantially. The pharmaceutical industry sponsored most (21 trials, 58%) of the trials, or the study authors had considerable affiliations.

Potential biases in the review process

Two independent assessors assured the eligibility of the identified articles based on title or abstract. If either author regarded an article as possibly relevant, they retained the article for full-text assignment. Two independent authors also assessed the eligibility of the identified articles based on full text. We consider that the literature search was adequate and comprehensive.

We excluded reports that did not contain enough data (e.g. posters) if they gave results in a form not eligible for the purposes of the review (e.g. symptom scores were given as pooled, not separate, for each symptom), or if they only stated outcomes not relevant for this review (e.g. microbial growth indicators). We considered that this approach did not introduce bias.

If there were insufficient data in the included reports, we excluded the studies from the meta-analyses. Nevertheless, we described the results qualitatively when the reports used prespecified outcomes.

Agreements and disagreements with other studies or reviews

We identified a recently published systematic review on pimecrolimus cream for the treatment of seborrhoeic dermatitis (Ang-Tiu 2012). We have considered all the trials included in that review (Cicek 2009; Firooz 2006; Koc 2009; Warshaw 2007) in our Cochrane review as well. The conclusions of the authors concerning clinical efficacy are consistent with our conclusions.

AUTHORS' CONCLUSIONS

Implications for practice

Topical steroids and lithium salts are more effective than placebo in achieving total clearance in seborrhoeic dermatitis of the face or scalp. Calcineurin inhibitors show benefit over placebo in reducing erythema and scaling. Azoles may be comparable to steroids in achieving total clearance, but there are implications that strong steroids are more efficient with symptoms like erythema, scaling, and pruritus. Furthermore, adverse effects occur at a similar rate at four weeks' follow-up. Calcineurin inhibitors seem to be comparable with azoles and steroids concerning efficacy. Lithium is more effective than azole with regard to total clearance. Mild and

strong steroids seemed to be comparable with regard to efficacy and adverse effects in up to six weeks' follow-up. However, there are no data regarding the efficacy or safety of repeated, long-term (such as more than one year), or continuous use of any of the assessed medicines.

The median rate of achieving total clearance was 53% with anti-inflammatory treatments across studies. This is an indication of the need for further research to identify optimal treatment agents, possibly treatment combinations, regimens, and length.

Implications for research

To prevent reporting bias, authors should first publish a protocol of their study and register this in a trials registration database. To further increase the quality of evidence of topical anti-inflammatory treatments for seborrhoeic dermatitis, future trials should deal with the following issues.

- Quality of methods: Trials should properly conduct and report random sequence allocation, as well as allocation concealment and the method of blinding.
- Quality of reporting: Trials should report results in numbers, preferably in tables, instead of graphs, as well as reporting standard deviations and exact P values.
- Outcomes: There is an urgent need for one or more validated outcome measures for seborrhoeic dermatitis that should at least cover erythema, scaling, pruritis, and the area of the body and the amount of skin affected. Trials should also examine patient-centered outcomes, such as quality-adjusted life measures, as well as compliance. Trials should measure outcomes at long-term follow up, such as one year after starting treatment, in order to assess the relapse rate or the efficacy in long-term use. For adverse effects, we need measurements at several years of follow up.
- Economic evaluations: Trials should put the therapeutic value of a treatment into context with its economic value in order to be able to use treatments rationally.

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* Indicates the major publication for the study

CHARACTERISTICS OF STUDIES

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

Attila 1992

Methods	Study type: individual RCT Randomisation method: not reported Blinding: double-blind Intention-to-treat analysis used: yes
Participants	**Inclusion criteria of the trial** • Seborrhoeic dermatitis of the scalp **Exclusion criteria of the trial** • Other dermatological conditions of the scalp (e.g. psoriasis or secondary infected eczema) • Use of antimicrobial agents was not allowed for 2 weeks prior to the study Number of randomised participants: 72 in the whole study. We only included participants in the hydrocortisone group (N = 23) and in the placebo group (N = 24) in this Cochrane review Number of dropouts: 8 in the whole study (not reported separately in different intervention groups) Sex: 49 male, 23 female Mean age (range): 35 (14 to 79) years Country: Finland
Interventions	**Treatment**

Attila 1992 *(Continued)*

	• Hydrocortisone 1% liniment, applied on the scalp once daily for 4 weeks **Comparator/s** • Placebo (propylene glycol 30% liniment), applied on the scalp once daily for 4 weeks • Clotrimazole 1% and hydrocortisone 1% liniment, applied on the scalp once daily for 4 weeks
Outcomes	1. Severity of scaling, erythema, itching, exudation, stinging, and papule formation (none - mild - moderate - severe) 2. Global assessment (completely healed - clearly better - no change - deteriorated) 3. Area of affected skin (completely cured - good response - somewhat better - no response) 4. Overall efficacy of the treatment evaluated by participants and investigators (excellent - good - some help - poor)
Notes	Standard deviations were not given

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "Patients were randomly allocated"
Allocation concealment (selection bias)	Unclear risk	No information was provided
Similarity of the study groups (selection bias)	Unclear risk	Quote: "There were no significant differences between the treatment groups" Differences in the severity of symptoms was not reported
Blinding of participants (performance bias)	Unclear risk	Whilst the study was reported to be double-blind, it was not clear who was blinded
Blinding of care providers (performance bias)	Unclear risk	Whilst the study was reported to be double-blind, it was not clear who was blinded
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Whilst the study was reported to be double-blind, it was not clear who was blinded
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Dropout rate was not reported separately for the intervention groups
Selective reporting (reporting bias)	Low risk	Predefined outcomes as stated in the article were reported
Other bias	Unclear risk	2 authors were affiliated to the pharmaceutical industry

Basak 2001

Methods	Study type: individual RCT Randomisation method: not reported Blinding: not reported

Basak 2001 *(Continued)*

	Intention-to-treat analysis used: not reported
Participants	**Inclusion criteria of the trial** • Not reported, but all had seborrhoeic dermatitis of the scalp clinically characterised by erythema, scaling, and itching **Exclusion criteria of the trial** • Not reported Number of randomised participants: 60 in total (betamethasone N = 30, calcipotriol N = 30) Number of dropouts: 7, all from 1 treatment arm (23%) Sex: not reported Age: not reported Country: Turkey
Interventions	**Treatment** • Calcipotriol solution 50 µg/ml, applied on the scalp twice daily for 28 days **Comparator/s** • Betamethasone 17-valerate 1 mg/ml, applied on the scalp twice daily for 28 days If there was only slight improvement at the end of 4 weeks, treatment was continued for another 4-week period After cessation of treatment, participants entered a follow-up period for 4 weeks Before the start of treatment, there was a 1-week wash-out period, during which only a mild non-medicated shampoo was used
Outcomes	1. Severity of erythema, scaling, and itching of the scalp rated on a 4-point scale (0 to 3) 2. Total clearance 3. Total score (the sum of the individual scores) 4. Adverse events 5. Routine biochemical analysis including serum total calcium levels
Notes	Results were reported mainly at 4 weeks. The dropout rate was unbalanced and considerable

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	This was not reported in detail Quote: "randomly assigned"
Allocation concealment (selection bias)	Unclear risk	This was not reported
Similarity of the study groups (selection bias)	Unclear risk	This was not reported in sufficient detail
Blinding of participants (performance bias)	High risk	There was no mention of blinding in the report

Basak 2001 *(Continued)*

Blinding of care providers (performance bias)	High risk	There was no mention of blinding in the report
Blinding of outcome assessment (detection bias) All outcomes	High risk	There was no mention of blinding in the report
Incomplete outcome data (attrition bias) All outcomes	High risk	More than 20% of participants withdrew from the calcipotriol arm
Selective reporting (reporting bias)	Unclear risk	Not all results related to predefined outcomes were reported in sufficient detail
Other bias	Unclear risk	No other bias was identified

Cicek 2009

Methods	Study type: individual RCT Randomisation method: not reported sufficiently Blinding: not reported Intention-to-treat analysis used: not fully
Participants	**Inclusion criteria of the trial** • Seborrhoeic dermatitis (facial) **Exclusion criteria of the trial** • Psoriasis, acne rosacea, acne vulgaris, and other dermatoses of the face • Topical treatments (corticosteroids, antifungals, antibiotics, zinc pyrithione, selenium, salicylates, retinoids, benzoyl peroxide, or α-hydroxy acids) during the 15 days before inclusion in the protocol • Oral treatment with lithium, antifungals, inhaled corticosteroids, or systemic corticosteroids during the 6 months prior to entry • Pregnancy or lactation • HIV-positive people were excluded Number of randomised participants: 64 in total (pimecrolimus N = 21, methylprednisolone N = 22, metronidazole N = 21) Number of dropouts: 4 (6%) Sex: 32 males, 32 females Mean age (range): pimecrolimus arm = 31.6 (19 to 56) years, methylprednisolone arm = 34.2 (17 to 65) years, metronidazole arm = 30.7 (17 to 44) years Country: Turkey
Interventions	**Treatment** • Pimecrolimus 1% cream, applied to the face twice daily for 8 weeks **Comparator/s** • Methylprednisolone aceponate 0.1% cream, applied to the face twice daily for 8 weeks

Cicek 2009 *(Continued)*

	• Metronidazole 0.75% gel, applied to the face twice daily for 8 weeks
Outcomes	1. Mean severity score (consisting of erythema and scaling scores with scales of 0 to 3) 2. Participants' self-assessed pruritus (scale 0 to 3) 3. Furthermore, erythema, scaling and pruritus scores (0 to 3) as side-effects
Notes	Erythema and pruritus were used to assess both efficacy and side-effects. It was not reported how the judgement between a lack of efficacy and a side-effect was done. Erythema, scaling, and pruritus scores were not reported separately but as part of mean clinical severity score

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "The patients were divided into three randomized groups"
Allocation concealment (selection bias)	Unclear risk	No information was provided
Similarity of the study groups (selection bias)	Low risk	Differences were not statistically significant
Blinding of participants (performance bias)	High risk	No information was provided
Blinding of care providers (performance bias)	High risk	No information was provided
Blinding of outcome assessment (detection bias) All outcomes	High risk	No information was provided
Incomplete outcome data (attrition bias) All outcomes	High risk	Dropout rate was 20% in 1 group only and reported to be due to side-effects; these participants were excluded from the study. The side-effect rate was reported for the remaining participants only
Selective reporting (reporting bias)	Low risk	No selective reporting bias was identified
Other bias	High risk	Erythema and pruritus were used both as efficacy and adverse effect elements. How the judgement between efficacy effect and adverse effect classification was conducted was not reported

Cornell 1986

Methods	Study type: RCT of body parts Randomisation method: not reported Blinding: double-blind Intention-to-treat analysis used: yes
Participants	**Inclusion criteria of the trial** • Seborrhoeic dermatitis

Cornell 1986 *(Continued)*

Exclusion criteria of the trial

- Pregnant women
- People with known allergies to any component of the test medications
- People who had used topical or systemic corticosteroid or other treatment for SeD during the month preceding the study
- People with clinical evidence of skin atrophy, those requiring topical or systemic medication that would affect the course of the dermatologic disease, or people requiring more than 90 gm (45 gm per side) of study medication applied bi-weekly

Number of randomised participants: 51 in total

Number of dropouts: 6 (12%)

Sex: 23 males, 28 females

Age (range): 19 to 82 years

Country: USA

Interventions	**Treatment** • Alclometasone 0.05% ointment, applied to the scalp, face, and trunk twice daily for 6 weeks **Comparator/s** • Hydrocortisone 1.0% ointment, applied to the scalp, face, and trunk twice daily for 6 weeks
Outcomes	1. Changes in telangiectasia 2. Overall severity of the dermatoses (scaling, erythema, and crusting, scale 0 to 3) 3. Total clearance
Notes	The location of seborrhoeic dermatitis lesions was not mentioned as inclusion criteria. However, the outcomes were evaluated on the face/neck, retroauricular areas, and scalp. The primary objective of the study was to compare atrophogenic potential of the products, but their efficacy was also evaluated. This is 1 of 2 included studies that compared 2 mild steroids with each other. The results concerning side-effects are controversial. Score data can not be used because standard deviations and P values are lacking

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "Study was a randomized"
Allocation concealment (selection bias)	Unclear risk	This was not reported
Similarity of the study groups (selection bias)	Low risk	Pretreatment symptom scores were identical between groups
Blinding of participants (performance bias)	Low risk	Double-blind: Colour-coded side-labelled tubes were used
Blinding of care providers (performance bias)	Unclear risk	Whilst the study was reported to be double-blind, it was not clear who was blinded
Blinding of outcome assessment (detection bias)	Unclear risk	Whilst the study was reported to be double-blind, it was not clear who was blinded

Cornell 1986 *(Continued)*

All outcomes		
Incomplete outcome data (attrition bias) All outcomes	Low risk	None were identified
Selective reporting (reporting bias)	Low risk	Predefined outcomes were reported
Other bias	Low risk	No other bias was identified

Cornell 1989

Methods	Study type: individual RCT Randomisation method: computer-generated randomisation Blinding: blinded Intention-to-treat analysis used: yes
Participants	**Inclusion criteria of the trial** • Seborrhoeic dermatitis of the scalp **Exclusion criteria of the trial** • Known intolerance of or hypersensitivity to topical corticosteroids • Previous non-responsiveness to topical corticosteroids • Pregnancy or lactation • Concurrent illness that would contraindicate corticosteroid therapy • A need for concomitant therapies that would confound the results Number of randomised participants: 54 in total (amcinonide N = 26, betamethasone N = 28) Number of dropouts: 0 Sex: 30 males, 24 females Mean age (range): amcinonide arm = 42 (26 to 81), betamethasone arm = 45 (23 to 73) years Country: USA
Interventions	**Treatment** • Amcinonide 0.1% lotion, applied to scalp twice daily for 3 weeks **Comparator/s** • Betamethasone valerate 0.1% lotion, applied to the scalp twice daily for 3 weeks
Outcomes	1. Erythema, excoriation, crusting/scales, and pruritus (scale 0, 0.5, 1.0, 1.5, 2.0, 2.5, and 3.0) 2. Overall therapeutic efficacy (evaluated by investigators and participants, scale 1 to 7) 3. Adverse effects
Notes	This was the only included study comparing 2 strong steroids with each other. Necessary data were calculated from other statistics

Cornell 1989 *(Continued)*

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	A computer-generated randomisation list was used
Allocation concealment (selection bias)	Unclear risk	No information was provided
Similarity of the study groups (selection bias)	Low risk	There were no statistically significant differences between groups
Blinding of participants (performance bias)	Unclear risk	Whilst the study was reported to be double-blind, it was not clear who was blinded
Blinding of care providers (performance bias)	Unclear risk	Whilst the study was reported to be double-blind, it was not clear who was blinded
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Whilst the study was reported to be double-blind, it was not clear who was blinded
Incomplete outcome data (attrition bias) All outcomes	Low risk	The dropout rate was small
Selective reporting (reporting bias)	Low risk	Predefined outcomes were reported
Other bias	Low risk	No other bias was identified

Cornell 1993

Methods	Study type: RCT of body parts Randomisation method: computerised randomisation Blinding: double-blind Intention-to-treat analysis used: yes
Participants	**Inclusion criteria of the trial** • Seborrhoeic dermatitis of the scalp **Exclusion criteria of the trial** • Pregnant and nursing women • People with known hypersensitivities to any of the products or their ingredients • People with evidence of atrophy Number of randomised participants: 30 in total Number of dropouts: 1 (3%) Sex: 14 males, 16 females

Cornell 1993 *(Continued)*

	Age (mean): 37.7 years Country: USA
Interventions	**Treatment** • Desonide 0.05% cream, applied to the scalp twice daily for 8 weeks **Comparator/s** • Hydrocortisone 1.0% cream, applied to the scalp twice daily for 8 weeks
Outcomes	1. Total number of telangiectasia
Notes	1 of 2 included studies comparing mild steroids with each other. The adverse events rate was calculated from a table

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Computerised randomisation was used
Allocation concealment (selection bias)	Unclear risk	No information was provided
Similarity of the study groups (selection bias)	Unclear risk	Bilateral disease severity was not reported separately
Blinding of participants (performance bias)	Low risk	Colour-coded side-labelled tubes were used
Blinding of care providers (performance bias)	Unclear risk	Whilst the study was reported to be double-blind, it was not clear who was blinded
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Whilst the study was reported to be double-blind, it was not clear who was blinded
Incomplete outcome data (attrition bias) All outcomes	Low risk	The number of dropouts was small
Selective reporting (reporting bias)	Low risk	No selective reporting bias was identified
Other bias	Unclear risk	The pharmaceutical industry supported the study, and the corresponding author was affiliated with the pharmaceutical industry

Dreno 2002a

Methods	Study type: individual RCT Randomisation method: not reported Blinding: double-blind

Dreno 2002a *(Continued)*

	Intention-to-treat analysis used: included all randomised participants who had at least 1 efficacy evaluation after baseline
Participants	**Inclusion criteria of the trial** • Facial seborrhoeic dermatitis **Exclusion criteria of the trial** • Cutaneous diseases requiring a specific topical treatment of the face (e.g. atopic dermatitis, psoriasis), general or local lithium therapy, facial topical or oral immediate-release corticosteroids in less than 2 weeks and slow-release corticosteroids in less than 2 months Number of randomised participants: 129 in total (lithium N = 66, placebo N = 63; however, there were follow-up data available only for 63 participants in the lithium group and 61 participants in the placebo group, and 1 participant was left out of the analyses as he did not fulfil the inclusion criteria) Number of dropouts: 22 (17%) Sex: 85 males, 44 females Mean age (range): lithium arm = 38.6 (19 to 69) years, placebo arm = 40.2 (19 to 73) years Country: France
Interventions	**Treatment** • Lithium gluconate 8% ointment, applied to the face twice daily for 8 weeks **Comparator/s** • Placebo (vehicle only) twice daily for 8 weeks
Outcomes	1. Complete remission 2. An overall remission rate (complete and partial) 3. Improvement of erythema, desquamation, burning, pruritus, stretching, and skin oiliness 4. Adverse events
Notes	For symptoms scores (erythema and desquamation), results were presented only in figures without numerical data. Results concerning burning, pruritus, and stretching, as well as skin oiliness, were mentioned very briefly in the text without numerical or visual data given. For this reason, these data could not be used in the meta-analysis in this review

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "randomly allocated"
Allocation concealment (selection bias)	Unclear risk	This was not reported
Similarity of the study groups (selection bias)	Low risk	There were no statistically significant differences between groups
Blinding of participants (performance bias)	Unclear risk	Whilst the study was reported to be double-blind, it was not clear who was blinded

Dreno 2002a *(Continued)*

Blinding of care providers (performance bias)	Unclear risk	Whilst the study was reported to be double-blind, it was not clear who was blinded
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Whilst the study was reported to be double-blind, it was not clear who was blinded
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	It is unclear whether the percentages were calculated using ITT or per-protocol analysis
Selective reporting (reporting bias)	Unclear risk	Most results were not reported in sufficient detail
Other bias	Unclear risk	The pharmaceutical industry supported the study

Dreno 2003

Methods	Study type: individual RCT Randomisation method: computer-generated Blinding: Investigators were blinded until the first follow-up visit (not reported for participant or care provider) Intention-to-treat analysis used: yes
Participants	**Inclusion criteria of the trial** • Facial seborrhoeic dermatitis **Exclusion criteria of the trial** • Scalp seborrhoeic dermatitis requiring antifungal, selenium sulphide, or corticosteroid therapy • Any other cutaneous disease of the face requiring a specific topical treatment during the previous 15 days; oral treatment with tetracyclines, lithium, antifungals, or inhaled corticosteroids during the previous month; and systemic corticosteroids and retinoids during the previous 2 months • SeD associated with Parkinson's disease; HI-virus; or ears, nose, and throat carcinoma • Severe concomitant disease • Allergy to any of the tested treatment components Number of randomised participants: 288 in total (lithium N = 152, ketoconazole N = 136) Number of dropouts: 34 withdrawn and 19 excluded from analyses because of major protocol deviation (18%) Sex: 183 males, 105 females Age (mean): lithium arm = 29.2 years, ketoconazole arm = 41.3 years Country: France
Interventions	**Treatment** • Lithium gluconate 8% ointment, applied to the face twice daily for 8 weeks **Comparator/s** • Ketoconazole 2%, applied to the face twice weekly for 4 weeks and then once weekly for 4 weeks

Dreno 2003 *(Continued)*

Outcomes	1. Complete remission without any premature withdrawal for inefficacy or safety 2. Rate of participants with complete remission 3. Rate of participants with partial remission 4. Spontaneously reported adverse events
Notes	This was the only included study comparing lithium with azole

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Randomisation was computer-generated
Allocation concealment (selection bias)	Low risk	This was probably low risk Quote: "computer-generated blocks and the randomisation code was concealed in sealed envelopes"
Similarity of the study groups (selection bias)	Low risk	There were no statistically significant differences between groups
Blinding of participants (performance bias)	High risk	Participants were not blinded
Blinding of care providers (performance bias)	Unclear risk	This was not reported in detail
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	This was not reported in detail. The investigators were blinded at the allocation period
Incomplete outcome data (attrition bias) All outcomes	Low risk	The percentage of dropouts was less than 20% and comparable between groups
Selective reporting (reporting bias)	Low risk	No selective reporting bias was identified
Other bias	Unclear risk	The pharmaceutical industry organised and sponsored the study

Elewski 2009a

Methods	Study type: individual RCT Randomisation method: not reported Blinding: investigator-blinded Intention-to-treat analysis used: yes
Participants	**Inclusion criteria of the trial** • Facial seborrhoeic dermatitis **Exclusion criteria of the trial**

Elewski 2009a *(Continued)*

- Unwilling to stop treatment for dandruff or SeD on the scalp
- Presented with severe (score = 4) SeD on the face as assessed by the investigator
- Use of any topical antiseborrhoeic dermatitis or antidandruff product in the 14 days before baseline or systemic medication 30 days before baseline
- Chronic or active liver disease, renal impairment, severe facial acne, rosacea, or any other disease that would interfere with the study or place the person under undue risk
- Known hypersensitivity to the ingredients of the products

Number of randomised participants: 77 in total (desonide N = 39, Promiseb® N = 38)

Number of dropouts: 5 (7%)

Sex: 56 males, 21 females

Mean age (range): 51.9 (21.1 to 84.5) years

Country: USA

Interventions	**Treatment** • Desonide 0.05% cream, applied to the face twice daily for 2 and 4 weeks **Comparator/s** • Non-steroidal cream (Promiseb®), applied to the face twice daily for 2 and 4 weeks
Outcomes	1. Proportion of participants with IGA (Investigator Global Assessment)-rated (score 0 to 4) success at either day 14 or day 28 2. Erythema (score 0 to 4), scaling (score 0 to 4), pruritus (score 0 to 4), and mean total IGA scores at days 14 and 28 3. Proportion of participants who were cleared at day 14 that were still clear at day 28 4. Safety score (scale 0 to 3) 5. Spontaneous reported adverse events
Notes	No standard deviations were given for symptom scores. Additional data were requested (results in numerical form with standard deviations and P values), but could not be received. This was the only included study comparing steroid with Promiseb® topical cream

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "randomized"
Allocation concealment (selection bias)	Unclear risk	No information was provided
Similarity of the study groups (selection bias)	Unclear risk	This was not reported sufficiently
Blinding of participants (performance bias)	High risk	The study was "investigator blind"
Blinding of care providers (performance bias)	Unclear risk	The study was "investigator blind". It was not clear whether the care providers were investigators
Blinding of outcome assessment (detection bias)	Low risk	The investigator was blinded

Elewski 2009a *(Continued)*

All outcomes		
Incomplete outcome data (attrition bias) All outcomes	Low risk	The number of dropouts was small
Selective reporting (reporting bias)	Low risk	No selective reporting bias was identified
Other bias	Unclear risk	The pharmaceutical industry supported the study, and the author was affiliated to the pharmaceutical industry. The pharmaceutical industry provided the comparator treatment

Faergemann 1986

Methods	Study type: individual RCT Randomisation method: not reported Blinding: double-blind Intention-to-treat analysis used: not reported
Participants	**Inclusion criteria of the trial** • Seborrhoeic dermatitis of the scalp **Exclusion criteria of the trial** • No topical or systemic treatment with antifungal agents or corticosteroids for 3 weeks prior to the start of the study Number of randomised participants: 70 participants in the whole study. In this review, we only considered the participants in the hydrocortisone (N = 24) and miconazole (N = 23) arms Number of dropouts: 3 (5%) Sex: 36 males, 34 females Mean age (range): 38 (21 to 69) years Country: Sweden
Interventions	**Treatment** • Hydrocortisone 1% solution, applied to the scalp once daily for 3 weeks **Comparator/s** • Miconazole 2% • Miconazole 2% and hydrocortisone 1% solution, applied to the scalp once daily for 3 weeks
Outcomes	1. Number of cured participants and treatment failures 2. Relapse rate 3. Efficacy of prophylaxis
Notes	The combination treatment arm of the trial was not included in this review. Adverse events were not reported

Faergemann 1986 *(Continued)*

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "randomly allocated"
Allocation concealment (selection bias)	Unclear risk	This was not reported
Similarity of the study groups (selection bias)	Unclear risk	Baseline data were not reported
Blinding of participants (performance bias)	Unclear risk	Whilst the study was reported to be double-blind, it was not clear who was blinded
Blinding of care providers (performance bias)	Unclear risk	Whilst the study was reported to be double-blind, it was not clear who was blinded
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Whilst the study was reported to be double-blind, it was not clear who was blinded
Incomplete outcome data (attrition bias) All outcomes	Low risk	The number of dropouts was small
Selective reporting (reporting bias)	Low risk	Predefined outcomes were reported
Other bias	Unclear risk	The pharmaceutical industry provided the intervention solutions

Firooz 2006

Methods	Study type: individual RCT Randomisation method: computer-generated randomisation list Blinding: investigator-blind Intention-to-treat analysis used: yes
Participants	**Inclusion criteria of the trial** • Facial seborrhoeic dermatitis **Exclusion criteria of the trial** • Malignant or active viral lesions on the face • People who had used antibiotics, immunosuppressive drugs, or phototherapy 1 month before treatment, and any topical therapy suspected to affect facial SeD during the 1 week before the beginning of the study Number of randomised participants: 40 in total (pimecrolimus N = 20, hydrocortisone N = 20) Number of dropouts: 3 (8%) Sex: 28 males, 12 females

Firooz 2006 *(Continued)*

	Age (mean): pimecrolimus arm = 28.65 years, hydrocortisone arm = 37.45 years Country: Iran
Interventions	**Treatment** • Pimecrolimus 1% cream, applied to the face twice daily for 2 weeks **Comparator/s** • Hydrocortisone 1% cream, applied to the face twice daily for 2 weeks
Outcomes	1. Complete disappearance of disease 2. Severity of pruritus, erythema, and scaling (scales 0 to 3) 3. Adverse events 4. Relapses
Notes	-

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Randomisation was computer-generated
Allocation concealment (selection bias)	Unclear risk	This was not reported
Similarity of the study groups (selection bias)	Low risk	There were no statistically significant differences between groups
Blinding of participants (performance bias)	High risk	Only investigators were blinded
Blinding of care providers (performance bias)	Unclear risk	Quote: "investigator blind" This probably refers to outcome assessment
Blinding of outcome assessment (detection bias) All outcomes	Low risk	The investigator was blinded. We assume this refers to outcome assessment
Incomplete outcome data (attrition bias) All outcomes	Low risk	The number of dropouts was acceptable
Selective reporting (reporting bias)	Low risk	Predefined outcomes were reported
Other bias	Unclear risk	The pharmaceutical industry provided - free of charge - the intervention creams

Fredriksson 1978

Methods	Study type: individual RCT

Fredriksson 1978 *(Continued)*

	Randomisation method: not reported Blinding: not clearly reported; at least the participants were blinded Intention-to-treat analysis used: no
Participants	**Inclusion criteria of the trial** • Seborrhoeic dermatitis of the scalp **Exclusion criteria of the trial** • Not reported Number of randomised participants: 64 in total (betamethasone N = 32, hydrocortisone N = 32) Number of dropouts: 2 (3%) Sex: 35 males, 27 females Age (range): 15 to 61 years Country: Sweden
Interventions	**Treatment** • Betamethasone valerate 0.1% lotion, applied to the scalp for 4 weeks **Comparator/s** • Hydrocortisone 17-butyrate 0.1% lotion, applied to the scalp for 4 weeks
Outcomes	1. Erythema, infiltration, peeling, crust, and itching scores (5-point scale) 2. Freedom of symptoms (percentage of participants)
Notes	Dosing frequency was not reported. Adverse events were not reported

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "randomly allocated"
Allocation concealment (selection bias)	Unclear risk	This was not reported in detail
Similarity of the study groups (selection bias)	Unclear risk	No information was provided
Blinding of participants (performance bias)	Low risk	Quote: "Patients...received the lotion in identical, coded bottles"
Blinding of care providers (performance bias)	Unclear risk	Quote: "Patients...received the lotion in identical, coded bottles" This was not reported in sufficient detail
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote: "Patients...received the lotion in identical, coded bottles" This was not reported in sufficient detail

Fredriksson 1978 *(Continued)*

Incomplete outcome data (attrition bias) All outcomes	Low risk	The dropout rate was acceptable
Selective reporting (reporting bias)	Low risk	There were limitations in reporting, but results were displayed for all predefined outcomes
Other bias	Low risk	No other bias was identified

General Practitioner 1982

Methods	Study type: individual RCT Randomisation method: not reported Blinding: double-blind Intention-to-treat analysis used: no
Participants	**Inclusion criteria of the trial** • Seborrhoeic dermatitis without secondary infection **Exclusion criteria of the trial** • Not reported (secondary infection) Number of randomised participants: 55 in total (hydrocortisone 17-butyrate N = 28, betamethasone N = 28) Number of dropouts: 1 (2%) Sex: 33 males, 22 females Mean age (range): 40.4 (15 to 75) years Country: United Kingdom
Interventions	**Treatment** • Hydrocortisone 17-butyrate for 3 weeks **Comparator/s** • Betamethasone valerate (probably 0.1%) for 3 weeks
Outcomes	1. Pruritus, erythema, scaling, crusting, and ulceration with a 4-point scale (0 to 3) 2. Side-effects 3. Total severity scores in participants with an occupation involving possible contact with irritants
Notes	Dosing frequency was not reported. The location of the SeD lesions was not mentioned as inclusion criteria. It was however reported that the outcomes were evaluated in the head and neck

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	This was not reported in detail

General Practitioner 1982 *(Continued)*

		Quote: "in a random manner"
Allocation concealment (selection bias)	Unclear risk	This was not reported
Similarity of the study groups (selection bias)	Unclear risk	Quote: "The two groups matched one another in relation to these various factors, except that there was a higher proportion of male patients in the Betnovate group and minor differences in relation to age, duration and treatment given during the previous two weeks...with the exception of the eyelids, which were relatively more severely involved in the Locoid group than in the Betnovate group"
Blinding of participants (performance bias)	Unclear risk	Whilst the study was reported to be double-blind, it was not clear who was blinded
Blinding of care providers (performance bias)	Unclear risk	Whilst the study was reported to be double-blind, it was not clear who was blinded
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Whilst the study was reported to be double-blind, it was not clear who was blinded
Incomplete outcome data (attrition bias) All outcomes	Low risk	The dropout rate was small
Selective reporting (reporting bias)	Low risk	Predefined outcomes were reported
Other bias	Low risk	No other bias was identified

Gip 1979

Methods	Study type: individual RCT Randomisation method: not reported Blinding: double-blind Intention-to-treat analysis used: probably yes, as there were no dropouts
Participants	**Inclusion criteria of the trial** • Seborrhoeic dermatitis of the scalp **Exclusion criteria of the trial** • Not reported Number of randomised participants: 35 in total (betamethasone N = 17, hydrocortisone 17-butyrate N = 18) Number of dropouts: 0 Sex: 17 males, 18 females Age (mean): betamethasone arm = 49.9 years, hydrocortisone arm = 46.8 years Country: Sweden

Gip 1979 *(Continued)*

Interventions	**Treatment** • Betamethasone 17-valerate 0.1% lotion, applied to the scalp twice daily for 4 weeks **Comparator/s** • Hydrocortisone 17-butyrate 0.1% lotion, applied to the scalp twice daily for 4 weeks
Outcomes	1. Itching, erythema, scaling, and crusting scores (scale 1 to 5) 2. Adverse events
Notes	-

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "randomly allocated" The randomisation method was not reported
Allocation concealment (selection bias)	Unclear risk	No information was provided
Similarity of the study groups (selection bias)	Low risk	Baseline characteristics were comparable
Blinding of participants (performance bias)	Unclear risk	Whilst the study was reported to be double-blind, it was not clear who was blinded
Blinding of care providers (performance bias)	Unclear risk	Whilst the study was reported to be double-blind, it was not clear who was blinded
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Whilst the study was reported to be double-blind, it was not clear who was blinded
Incomplete outcome data (attrition bias) All outcomes	Low risk	No dropouts were reported
Selective reporting (reporting bias)	Low risk	Predefined outcomes were reported in sufficient detail
Other bias	Low risk	No other bias was identified

Harris 1972

Methods	Study type: individual RCT Randomisation method: not reported Blinding: double-blind Intention-to-treat analysis used: no
Participants	**Inclusion criteria of the trial**

Harris 1972 *(Continued)*

	• Seborrhoeic dermatitis of the scalp **Exclusion criteria of the trial** • Not reported Number of randomised participants: 391 in total (initial assignment numbers were not reported; at 2 weeks, 140 participants were using betamethasone, and 163 participants were using placebo) Number of dropouts: 88 (23%) Sex: 171 males, 132 females Age: not reported Country: USA
Interventions	**Treatment** • Betamethasone valerate 0.1% lotion, applied twice daily for 2 weeks **Comparator/s** • Placebo (vehicle only) lotion, applied twice daily for 2 weeks
Outcomes	1. Total clearance 2. Lichenification, excoriation, inflammation, crusting, scaling, vesiculation, exudation, fissures, maceration, pruritus, burning, pain, secondary bacterial infection (score 1 to 4)
Notes	Response was regarded as excellent with clearance of 75% or more. This is less than in other included studies, and therefore we excluded the results from the meta-analysis. For scores, no standard deviations or exact P values were given. The actual number of participants randomised to each group was unknown

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "randomly assigned"
Allocation concealment (selection bias)	Unclear risk	Quote: "The test preparations were supplied...in identical packages, code labelled for blind randomized assignment to patients...Master codes for each study were maintained separately from the investigators..."
Similarity of the study groups (selection bias)	Unclear risk	No information was provided
Blinding of participants (performance bias)	Low risk	Quote: "double-blind" Quote: "Neither patient nor physician was aware of which of the two was being used"
Blinding of care providers (performance bias)	Low risk	Quote: "double-blind" Quote: "Neither patient nor physician was aware of which of the two was being used"
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "double-blind" The codes were kept separately from the investigators

Harris 1972 *(Continued)*

Incomplete outcome data (attrition bias) All outcomes	High risk	The dropout rate was 23%. The actual number of participants randomised to each group was not reported. There is considerable uncertainty in the reporting of the therapeutic response Quote: "Patients who did not return due to a successful response were included in the excellent group and patients who did not return because of treatment failure were included in the poor group"
Selective reporting (reporting bias)	Unclear risk	Predefined outcomes were reported, but not in sufficient detail. For example, the standard deviations were not given
Other bias	Unclear risk	The author was affiliated to a pharmaceutical company

Hersle 1996

Methods	Study type: individual RCT Randomisation method: not reported Blinding: double-blind Intention-to-treat analysis used: no
Participants	**Inclusion criteria of the trial** • Seborrhoeic dermatitis of the scalp **Exclusion criteria of the trial** • Known hypersensitivity to any of the components of the test medication • Need for other medication that might affect the disease (e.g. systemic corticosteroids or systemic antimycotics) • Use of topical remedies for SeD during the 7 days before enrolment or any investigated drug within 1 month before enrolment Number of randomised participants: 54 in total (the initial assignment numbers were not reported by treatment group; at 4 weeks, 27 participants were treated with mometasone, and 22 participants were treated with ketoconazole) Number of dropouts: 5 (9%) Sex: 40 males, 14 females Mean age (range): 58 (22 to 85) years Country: Sweden
Interventions	**Treatment** • Mometasone furoate 0.1% solution, applied to the scalp once daily for 4 weeks **Comparator/s** • Ketoconazole 2% shampoo, applied twice a week for 4 weeks
Outcomes	1. Erythema, scaling, and pruritus (scale 0 to 3) 2. Total clearance

Hersle 1996 *(Continued)*

Notes	Participants and investigators evaluated reduction of pruritus, scaling, and erythema scores, but numerical information of these was not reported. We approximated the numbers from figures. The actual number of participants randomised to each group was unknown

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Randomised, but not reported in sufficient detail
Allocation concealment (selection bias)	Unclear risk	No information was provided
Similarity of the study groups (selection bias)	Unclear risk	No information was provided
Blinding of participants (performance bias)	Unclear risk	Whilst the study was reported to be double-blind, it was not clear who was blinded
Blinding of care providers (performance bias)	Unclear risk	Whilst the study was reported to be double-blind, it was not clear who was blinded
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Whilst the study was reported to be double-blind, it was not clear who was blinded
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	The actual number of participants randomised to each group was unknown. The dropout rate was 10%, but the study did not report if this was balanced between groups
Selective reporting (reporting bias)	Unclear risk	The primary outcomes were not prespecified in detail, yet the outcomes reported were those that are usually used in such studies
Other bias	Unclear risk	The pharmaceutical industry supported the study

Katsambas 1989

Methods	Study type: individual RCT Randomisation method: not reported Blinding: double-blind Intention-to-treat analysis used: yes
Participants	**Inclusion criteria of the trial** • Seborrhoeic dermatitis of the scalp **Exclusion criteria of the trial** • Not reported Number of randomised participants: 50 in total (hydrocortisone N = 26, ketoconazole N = 24) Number of dropouts: 0

Katsambas 1989 *(Continued)*

	Sex: not reported Age: not reported Country: Greece
Interventions	**Treatment** • Hydrocortisone 1% cream, applied to the scalp, face, sternum, and ears twice daily for 4 weeks **Comparator/s** • Ketoconazole 2% cream, applied to the scalp, face, sternum, and ears twice daily for 4 weeks
Outcomes	1. Combined erythema, scaling, papules, and pruritus score, global evaluation (total improvement, good, fair, poor) 2. Growth of*Pityrosporum ovale*
Notes	-

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "randomized fashion"
Allocation concealment (selection bias)	Unclear risk	Quote: "randomized fashion" There was no mention of the allocation concealment
Similarity of the study groups (selection bias)	Unclear risk	This was not reported
Blinding of participants (performance bias)	Unclear risk	Whilst the study was reported to be double-blind, it was not clear who was blinded
Blinding of care providers (performance bias)	Unclear risk	Whilst the study was reported to be double-blind, it was not clear who was blinded
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Whilst the study was reported to be double-blind, it was not clear who was blinded
Incomplete outcome data (attrition bias) All outcomes	Low risk	There were no dropouts
Selective reporting (reporting bias)	Low risk	Predefined outcomes were reported
Other bias	Unclear risk	1 author was affiliated to the pharmaceutical industry

Koc 2009

Methods	Study type: individual RCT Randomisation method: participants were randomised according to a random digit table

Koc 2009 *(Continued)*

	Blinding: no (open-label) Intention-to-treat analysis used: no
Participants	**Inclusion criteria of the trial** • Seborrhoeic dermatitis **Exclusion criteria of the trial** • Coexistent other dermatoses involving the face or other affected area (e.g. psoriasis, rosacea, and acne vulgaris) • Allergy to medications • Use of any topical or systematic treatments in the previous month • Participants who had severe SeD requiring systemic treatment Number of randomised participants: 48 in total (pimecrolimus N = 23, ketoconazole N = 25) Number of dropouts: 10 (21%) Sex: 34 males, 4 females Mean age (range): pimecrolimus arm = 32.3 (21 to 50), ketoconazole arm = 29.8 (20 to 47) Country: Turkey
Interventions	**Treatment** • Pimecrolimus 1% cream, applied twice daily for 6 weeks **Comparator/s** • Ketoconazole 2% cream, applied twice daily for 6 weeks The total follow-up time was 12 weeks
Outcomes	1. Total clinical severity scores (including erythema, scaling, and infiltration with scale 0 to 3) 2. Adverse events
Notes	We received additional data from the first author The affected area or site of SeD lesions as inclusion criteria were not reported. However, coexistent dermatoses involving the face or other affected areas were mentioned as exclusion criteria, suggesting that facial SeD was an inclusion criterion

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "random digits table"
Allocation concealment (selection bias)	Unclear risk	Quote: "random digits table"
Similarity of the study groups (selection bias)	Low risk	Quote: "The treatment groups were not statistically significantly different at baseline"
Blinding of participants (performance bias)	High risk	This was an open-label study

Koc 2009 *(Continued)*

Blinding of care providers (performance bias)	High risk	This was an open-label study
Blinding of outcome assessment (detection bias) All outcomes	High risk	This was an open-label study
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	The dropout rate over was 20%; reasons were not given in detail. There was discrepancy between text and figure 1 with regard to distribution of dropouts
Selective reporting (reporting bias)	Low risk	Predefined outcomes as stated in the article were reported
Other bias	Low risk	Note: The affected area was not reported

Kousidou 1992

Methods	Study type: individual RCT Randomisation method: not reported Blinding: double-blind Intention-to-treat analysis used: not reported
Participants	**Inclusion criteria of the trial** • Seborrhoeic dermatitis **Exclusion criteria of the trial** • Not reported Number of randomised participants: 40 in total (hydrocortisone N = 20, ketoconazole N = 20) Number of dropouts: 1 (3%) Sex: 21 males, 19 females Age (mean): 33.7 years Country: Greece
Interventions	**Treatment** • Hydrocortisone 1% cream, applied to the affected areas once daily for 4 weeks **Comparator/s** • Ketoconazole 2% cream, applied to the affected areas once daily for 4 weeks
Outcomes	1. Erythema score (scale 0 to 9), scaling score (scale 0 to 10), pruritus score (scale 0 to 6), decrease in the number of *Pityrosporum ovale* colonies, and global evaluation (total improvement, good, fair, poor) 2. Adverse events
Notes	No standard deviations nor exact P values were given in the report. We have approximated the actual numbers from figures

Kousidou 1992 *(Continued)*

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "They were randomized"
Allocation concealment (selection bias)	Unclear risk	This was not reported
Similarity of the study groups (selection bias)	Low risk	Quote: "At the start of treatment, erythema, scaling, and pruritus were present in all patients of both groups without any statistically significant difference in the mean scores"
Blinding of participants (performance bias)	Unclear risk	Whilst the study was reported to be double-blind, it was not clear who was blinded
Blinding of care providers (performance bias)	Unclear risk	Whilst the study was reported to be double-blind, it was not clear who was blinded
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Whilst the study was reported to be double-blind, it was not clear who was blinded
Incomplete outcome data (attrition bias) All outcomes	Low risk	The dropout rate was small
Selective reporting (reporting bias)	Low risk	Predefined outcomes were reported
Other bias	Unclear risk	2 authors were affiliated to the pharmaceutical industry

Langtry 1997

Methods	Study type: RCT of body parts Randomisation method: not reported Blinding: double-blind Intention-to-treat analysis used: not used
Participants	**Inclusion criteria of the trial** • Advanced AIDS and facial seborrhoeic dermatitis **Exclusion criteria of the trial** • Not reported Number of randomised participants: 12 in total Number of dropouts: 6 participants (50%) by 2 weeks; 7 participants by end of study at 8 weeks Sex: only male participants Age: not reported

Langtry 1997 *(Continued)*

	Country: UK
Interventions	**Treatment** • Lithium succinate 8% ointment, applied to the face twice daily for 8 weeks **Comparator/s** • Placebo (ointment base), applied to the face twice daily for 8 weeks
Outcomes	1. Redness, greasiness, scaling, and overall severity scores (100 mm analogue line)
Notes	50% of participants had dropped out by 2 weeks, and only 5 participants out of 12 completed the study. However, the last visit occurred at 47 +/- 15 days (standard deviation) giving a wide variation there. We decided to use the results obtained at 2 weeks. It was not reported whether the paired t-test was used, and the available data did not allow recalculations. Therefore, the results have been presented qualitatively. The trial included only men with HIV as participants

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "Each was randomly assigned to be applied"
Allocation concealment (selection bias)	Unclear risk	No information was provided
Similarity of the study groups (selection bias)	Unclear risk	Bilateral disease severity was not reported in detail
Blinding of participants (performance bias)	Low risk	Quote: "Both doctor and patient were blinded"
Blinding of care providers (performance bias)	Low risk	Quote: "Both doctor and patient were blinded"
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "Both doctor and patient were blinded"
Incomplete outcome data (attrition bias) All outcomes	High risk	The dropout rate was 50% by 2 weeks and 58% by the end of the study at 8 weeks
Selective reporting (reporting bias)	Low risk	Predefined outcomes were reported
Other bias	Unclear risk	The pharmaceutical industry supported the study. 2 authors were affiliated to the pharmaceutical industry

Ludvigsen 1983

Methods	Study type: individual RCT Randomisation method: computer-based randomisation

Ludvigsen 1983 *(Continued)*

	Blinding: double-blind Intention-to-treat analysis used: not used
Participants	**Inclusion criteria of the trial** • Seborrhoeic dermatitis of the scalp **Exclusion criteria of the trial** • Not reported Number of randomised participants: 30 in total (betamethasone N = 15, hydrocortisone N = 15, but 1 of the participants in the latter group proved to be too young to be included, and the results were not used) Number of dropouts: 1 participant was excluded after randomisation because of their young age (not considered a dropout); 1 participant was lost to follow up (considered a dropout, 3%) Sex: 17 males, 12 females Mean age (range): 49.9 (19 to 82) years Country: Denmark
Interventions	**Treatment** • Betamethasone 0.05% lotion, applied to the scalp twice daily for 3 weeks **Comparator/s** • Hydrocortisone 0.1%, applied to the scalp twice daily for 3 weeks
Outcomes	1. Erythema, scaling, follicular papule formation, crusting, itching, and burning/local irritation scores (scale 0 to 3) 2. Total clearance evaluated by participants and clinician 3. Adverse events
Notes	Participants used drugs for 3 weeks or until complete healing. Outcomes were assessed at 3 weeks. Scores were calculated only for those who had the symptom

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "A computer programme was used to give the randomization code, which was stratified into blocks of 10 with a restriction against more than three successive patients receiving the same therapy"
Allocation concealment (selection bias)	Unclear risk	Quote: "randomization code, which was stratified into blocks of 10 with a restriction against more than three successive patients receiving the same therapy"
Similarity of the study groups (selection bias)	Low risk	Quote: "No statistically significant difference in patient classification of mean age, sex distribution and initial symptom score distribution was found between the two treatment groups but there was a numerically lower mean age in the HCB-treated group" 44 years versus 56 years

Ludvigsen 1983 *(Continued)*

Blinding of participants (performance bias)	Unclear risk	The study was "double-blind"; this was not reported in detail. The participants were given Locoid® or Diproderm®, and it was not reported if the packages were blinded
Blinding of care providers (performance bias)	Unclear risk	Whilst the study was reported to be double-blind, it was not clear who was blinded
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Whilst the study was reported to be double-blind, it was not clear who was blinded
Incomplete outcome data (attrition bias) All outcomes	Low risk	The dropout rate was small
Selective reporting (reporting bias)	Unclear risk	Predefined outcomes were reported, but they were assessed as scores only for those who had the symptom
Other bias	Low risk	No other bias was identified

Lynfield 1988

Methods	Study type: individual RCT Randomisation method: computer-based randomisation Blinding: double-blind Intention-to-treat analysis used: not used
Participants	**Inclusion criteria of the trial** • Seborrhoeic dermatitis of the scalp and other hairy areas **Exclusion criteria of the trial** • Allergies to tested products • Pregnant or lactating women • Acute systemic illness (including convalescence) • Active cutaneous infections • Participants who required concomitant systemic medications and therapies with potential for healing or relief during the course of the trial (e.g. antihistamines, topical or systemic corticosteroids, antimetabolites, psoralen with ultraviolet A), or other specific treatment for a dermatologic condition Number of randomised participants: 168 in total (amcinonide N = 86, placebo N = 82) Number of dropouts: 10 (6%) Sex: 121 males, 47 females Mean age (range): amcinonide arm = 51.2 (20 to 88) years, placebo arm = 50.9 (18 to 87) years Country: USA
Interventions	**Treatment** • Amcinonide 0.1% lotion, applied to the scalp or other selected lesions twice daily for 3 weeks **Comparator/s**

Lynfield 1988 *(Continued)*

	• Placebo, applied twice daily for 3 weeks
Outcomes	1. Erythema, crusting/scales, excoriation and pruritus scores (scale 0.0 - 0.5 - 1.0 - 1.5 - 2.0 - 2.5 - 3.0) 2. Overall therapeutic efficacy (scale 1 to 7)
Notes	Final evaluations were performed as soon as the participant had cleared completely if this occurred before week 3

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "a computer-generated randomization list designed to produce approximately equal numbers of patients in each study arm"
Allocation concealment (selection bias)	Unclear risk	This was not reported in detail
Similarity of the study groups (selection bias)	Low risk	Quote: "There were no statistically significant differences between the two treatment groups for any of the demographic variables...for severity of the objective signs of erythema and scaling and the subjective symptom of pruritus"
Blinding of participants (performance bias)	Unclear risk	Whilst the study was reported to be double-blind, it was not clear who was blinded
Blinding of care providers (performance bias)	Unclear risk	Whilst the study was reported to be double-blind, it was not clear who was blinded
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Whilst the study was reported to be double-blind, it was not clear who was blinded
Incomplete outcome data (attrition bias) All outcomes	Low risk	The dropout rate was acceptable
Selective reporting (reporting bias)	Low risk	Predefined outcomes were reported
Other bias	Low risk	No other bias was identified

Medansky 1992

Methods	Study type: individual RCT Randomisation method: not reported Blinding: "third-party-blind"; it is not specified who was blinded Intention-to-treat analysis used: not reported, but probably was; no dropouts during the treatment phase
Participants	**Inclusion criteria of the trial** • Not reported. All participants were 13 to 70 years of age and had a clear diagnosis of seborrhoeic dermatitis with facial involvement present for 7 to 8 years

Medansky 1992 *(Continued)*

	Exclusion criteria of the trial • Not reported Number of randomised participants: 117 in total (mometasone N = 59, hydrocortisone N = 58) Number of dropouts: no dropouts during the treatment phase Sex: 68 males, 49 females Mean age (range): mometasone arm = 45 (15 to 70) years, hydrocortisone arm = 43 (13 to 70) years Country: not reported, probably USA
Interventions	**Treatment** • Mometasone furoate cream 0.1%, applied once daily on the face for 6 weeks **Comparator/s** • Hydrocortisone cream 1%, applied twice daily on face for 6 weeks All antiseborrhoeic agents were prohibited for at least 2 weeks prior to the initiation of treatment, and systemic corticosteroids were prohibited for at least 4 weeks
Outcomes	1. Global clearance evaluation, individual and total disease sign/symptom severity scores (sum of individual scores for erythema, scaling, and pruritus/burning, scale 0 to 3 in each) in target area lesions 2. Participants' own evaluation of the response to treatment (excellent, good, fair, poor) 3. Side-effects
Notes	Any medications that might have affected the course of the disease were not allowed during the course of the study. The last evaluation was made at 2 weeks post-treatment. 1 area on the face of each participant was selected for evaluation of treatment effectiveness

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	This was not reported in detail Quote: "randomly assigned"
Allocation concealment (selection bias)	Unclear risk	This was not reported
Similarity of the study groups (selection bias)	Low risk	Quote: "The two treatment groups were comparable for all comparisons"
Blinding of participants (performance bias)	High risk	Quote: "Third-party-blind" - obviously not referring to the participant
Blinding of care providers (performance bias)	High risk	Quote: "Third-party-blind" - obviously not referring to the care-giver
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote: "Third-party-blind" - possibly referring to the outcome assessor
Incomplete outcome data (attrition bias) All outcomes	Low risk	There were no dropouts

Medansky 1992 *(Continued)*

Selective reporting (reporting bias)	Low risk	Results concerning predefined outcomes were reported, with the exception of participants' own assessment where the results were not given in a numerical form
Other bias	Unclear risk	At least 4 out of 8 authors were affiliated to the pharmaceutical industry

Ortonne 1992

Methods	Study type: individual RCT Randomisation method: not reported Blinding: "a single blind" Intention-to-treat analysis used: not used
Participants	**Inclusion criteria of the trial** • Seborrhoeic dermatitis (scalp associated with other locations) **Exclusion criteria of the trial** • Pregnant or nursing women • HIV-positive people • People with pityriasis capitis • People with psoriasis vulgaris Number of randomised participants: 62 in total (betamethasone N = 31, ketoconazole N = 31) Number of dropouts: 9 (15%) Sex: 39 males, 23 females Mean age (range): betamethasone arm = 41 (23 to 68) years, ketoconazole arm = 35 (18 to 65) years Country: France
Interventions	**Treatment** • Betamethasone dipropionate 0.05% lotion, applied to affected areas Phase 1: once daily for the first week, every other day in the second week, twice weekly until the end of the first month of treatment Phase 2: once weekly for 3 months **Comparator/s** • Ketoconazole 2% foaming gel, applied to affected areas Phase 1: twice weekly for 1 month Phase 2: once weekly for 3 months Phase 3: This was a wash-out phase for both treatment arms (1 month)
Outcomes	1. Severity of erythema, scaling, and itching of the scalp (scale 0 to 3) 2. Mycological evaluation (scale 0 to 3) 3. Global evaluation of improvement by investigator and participant (excellent, good, moderate, poor) 4. Participants' evaluation of the treatment's efficacy

Ortonne 1992 *(Continued)*

	5. Relapse rate
Notes	Total clearance is not evaluated in the report

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	This was not reported in detail Quote: "randomized fashion"
Allocation concealment (selection bias)	Unclear risk	This was not reported
Similarity of the study groups (selection bias)	Low risk	Quote: "The treatment groups were comparable for all the patient characteristics, as well as for all symptoms and localizations"
Blinding of participants (performance bias)	High risk	This was a single-blind study; it did not specify which party was blinded
Blinding of care providers (performance bias)	High risk	This was a single-blind study; it did not specify who was blinded
Blinding of outcome assessment (detection bias) All outcomes	High risk	This was a single-blind study; it did not specify who was blinded
Incomplete outcome data (attrition bias) All outcomes	Low risk	The dropout rate was acceptable
Selective reporting (reporting bias)	Low risk	Predefined outcomes were reported
Other bias	Low risk	No other bias was identified

Ortonne 2011

Methods	Study type: individual RCT Randomisation method: "central computed randomization list, block-size of 4" Blinding: "blinded investigators" Intention-to-treat analysis used: yes
Participants	**Inclusion criteria of the trial** • Adults (18 years or more) with moderate or severe scalp seborrhoeic dermatitis **Exclusion criteria of the trial** • Pregnancy or lactating state • Women planning pregnancy • HIV positivity

Ortonne 2011 *(Continued)*

	Number of randomised participants: 326 in the whole study; we used only the results of the clobetasol group (N = 82) and the ketoconazole group (N = 80) Number of dropouts: 12 (7%) at "end of study" Sex: 88 males, 74 females Age (mean): clobetasol arm = 44.9 years, ketoconazole arm = 44.7 years Country: Belgium, France, Germany, Mexico, South Korea
Interventions	**Treatment** • Treatment phase: clobetasol propionate shampoo 0.05%, applied for 15 minutes on dry scalp twice weekly for 28 days **Comparator/s** • Treatment phase: ketoconazole shampoo 2%, applied for 5 minutes on wet scalp twice weekly for 28 days. (In both arms followed by maintenance phase: ketoconazole once weekly; and follow-up phase: no active treatment, only mild non-medicated shampoo). (The study had 2 other arms: clobetasol and ketoconazole alternating or clobetasol four times weekly alternating with ketoconazole)
Outcomes	1. Total severity score (mean change from baseline) 2. Erythema, scaling, and pruritus severity scores (0 to 3 each, expressed as change from baseline and not in exact numbers) 3. Extent index (extent of scalp involved (0 = less than 10% to 4 = more than 70%)
Notes	Only the results for the clobetasol propionate only, and the ketoconazole only, and for the treatment phase are used in the analyses The results for the outcomes were expressed in a way not relevant for the review; therefore, we could use only information for adverse events

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "randomized in a 1:1:1:1 ratio by a designated statistician (using a central computed randomization list that generated treatment numbers in a block-size of 4)"
Allocation concealment (selection bias)	Unclear risk	This was not reported clearly
Similarity of the study groups (selection bias)	Low risk	Quote: "The demographic and baseline disease characteristics were similar among the four groups"
Blinding of participants (performance bias)	High risk	The participants were not blinded
Blinding of care providers (performance bias)	High risk	The care providers were not blinded
Blinding of outcome assessment (detection bias) All outcomes	Low risk	The investigator was blinded
Incomplete outcome data (attrition bias)	Low risk	The dropout rate was acceptable

Ortonne 2011 *(Continued)*

All outcomes		
Selective reporting (reporting bias)	Low risk	Predefined outcomes were reported
Other bias	Unclear risk	4 out of 8 authors were affiliated to the pharmaceutical industry

Papp 2012

Methods	Study type: individual RCT Randomisation method: not reported Blinding: "The primary investigator was blinded to treatment" Intention-to-treat analysis used: Only those who completed at least 4 weeks of treatment were included in the efficacy analyses on an intent-to-treat basis
Participants	**Inclusion criteria of the trial** • Age 18 years or older, with seborrhoeic dermatitis on the face, an erythema score of 1 or greater, and an area index of 5% or greater **Exclusion criteria of the trial** • Clinically significant medical conditions that were not well controlled • Any condition interfering with the ability to evaluate facial seborrhoeic dermatitis • Any known or suspected hypersensitivity to any constituent of study medication • Untreated or uncontrolled infection involving the face • Untreated cutaneous malignancies on the face at the baseline visit • Women who was pregnant, breastfeeding, or planning on becoming pregnant during the course of the study period Number of randomised participants: 30 in total (tacrolimus N = 16, hydrocortisone N = 14) Number of dropouts: 1 (3%) Sex: 24 males, 6 females Mean age (range): tacrolimus arm = 52.8 (25 to 70) years, hydrocortisone arm = 52.9 (20 to 80) years Country: Canada
Interventions	**Treatment** • Tacrolimus ointment 0.1%, applied on the face twice daily for 84 days **Comparator/s** • Hydrocortisone ointment 1%, applied on the face twice daily for 84 days
Outcomes	1. Seborrhea Area and Severity Index-Face (SASI-F) 2. Physician Static Global Assessment-Face 3. Participants' self-assessment of seborrhoea (11-point scale) 4. Safety and tolerability
Notes	The only outcomes relevant for this review were adverse effects

Papp 2012 *(Continued)*

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "randomly assigned" This was not reported in sufficient detail
Allocation concealment (selection bias)	Unclear risk	This was not reported
Similarity of the study groups (selection bias)	Low risk	Quote: "The two treatment groups were well balanced for baseline demographics"
Blinding of participants (performance bias)	High risk	For participants, the study was open-label
Blinding of care providers (performance bias)	High risk	Only the primary investigator was blinded to treatment
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	The primary investigator was blinded to treatment, but the participant was not. Therefore, outcomes evaluated and reported by the participant or a care provider other than the primary investigator were subject to detection bias
Incomplete outcome data (attrition bias) All outcomes	Low risk	The dropout rate was acceptable
Selective reporting (reporting bias)	Low risk	Predefined outcomes were reported
Other bias	Unclear risk	Quote: "This study was an investigator-initiated research project funded by Astellas Pharma Canada Inc" 1 author was financially supported by Astellas Pharma Canada Inc. The primary investigator reported receiving grants and honoraria from Astellas Pharma Canada Inc

Pari 1998

Methods	Study type: individual RCT Randomisation method: "stratified blocked random method" Blinding: double-blind Intention-to-treat analysis used: at least partly
Participants	**Inclusion criteria of the trial** • Seborrhoeic dermatitis of the face and trunk **Exclusion criteria of the trial** • People on chlorpromazine, cimetidine, alpha-methyldopa, INAH (isonicotinic acid hydrazide), or steroids • Infants • People with Parkinsonism or AIDS

Pari 1998 *(Continued)*

	Number of randomised participants: 36 in total (clobetasol N = 19, ketoconazole N = 17) Number of dropouts: 5 (14%) Sex: not reported Age: not reported Country: India
Interventions	**Treatment** • Clobetasol 17-butyrate 0.05% cream, applied to the affected areas (except scalp) twice daily for 4 weeks **Comparator/s** • Ketoconazole 2% cream, applied to the affected areas (except scalp) twice daily for 4 weeks
Outcomes	1. Severity score (severity combined with erythema, scaling, and papules) 2. Itching (scale not reported) 3. Remission rate 4. Relapse rate (at the end of 3 months) 5. Side-effect profile
Notes	Results were not reported separately for face and trunk. Adverse events were not reported

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "A stratified blocked random method was used to allocate the recruited patients into two groups according to severity"
Allocation concealment (selection bias)	Unclear risk	This was not reported in detail
Similarity of the study groups (selection bias)	Unclear risk	This was not reported in detail
Blinding of participants (performance bias)	Low risk	Quote: "Neither the doctor nor the patient knew"
Blinding of care providers (performance bias)	Low risk	Quote: "Neither the doctor nor the patient knew"
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	The study did not report whether the outcome was assessed by a third party
Incomplete outcome data (attrition bias) All outcomes	Low risk	The dropout rate was acceptable
Selective reporting (reporting bias)	High risk	The predefined outcomes included side-effects, but they were not reported
Other bias	Low risk	No other bias was identified

Piepponen 1992

Methods	Study type: individual RCT Randomisation method: not reported Blinding: double-blind Intention-to-treat analysis used: yes
Participants	**Inclusion criteria of the trial** • Seborrhoeic dermatitis with desquamation or dandruff **Exclusion criteria of the trial** • SeD without desquamation • Pregnant women • Unco-operative or used concomitantly other antidandruff agents Number of randomised participants: 101 in total (hydrocortisone N = 50, ketoconazole N = 51) Number of dropouts: 4 (4%) Sex: 38 males, 63 females Age (mean): 52.9 years Country: Finland
Interventions	**Treatment** • Hydrocortisone 1% liniment, applied to the scalp once daily for 4 weeks **Comparator/s** • Ketoconazole 2% shampoo, applied twice weekly for 4 weeks
Outcomes	1. Erythema, desquamation, and pruritus scores (scale 0 to 3) 2. Global assessment evaluated by participant and investigator (scale: normalised - markedly improved - slightly improved - unchanged - deteriorated) 3. Safety assessment
Notes	The participants were diagnosed with either SeD or dandruff. The proportion of participants with dandruff was 37%. Location of SeD lesions was not mentioned as inclusion criteria, but the interventions were used on the skin of the scalp. Necessary data were calculated from other statistics

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "This randomized...study" This was not reported in sufficient detail
Allocation concealment (selection bias)	Unclear risk	This was not reported
Similarity of the study groups (selection bias)	Low risk	Quote: "There were no significant differences between the treatment groups"

Piepponen 1992 *(Continued)*

Blinding of participants (performance bias)	Unclear risk	Whilst the study was reported to be double-blind, it was not clear who was blinded
Blinding of care providers (performance bias)	Unclear risk	Whilst the study was reported to be double-blind, it was not clear who was blinded
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Whilst the study was reported to be double-blind, it was not clear who was blinded
Incomplete outcome data (attrition bias) All outcomes	Low risk	The dropout rate was acceptable
Selective reporting (reporting bias)	Low risk	Predefined outcomes were reported
Other bias	Unclear risk	The first author was affiliated to the pharmaceutical industry, and the pharmaceutical industry provided medication

Ramirez 1993

Methods	Study type: individual RCT Randomisation method: not reported Blinding: double-blind Intention-to-treat analysis used: not reported
Participants	**Inclusion criteria of the trial** • Established diagnosis of seborrhoeic dermatitis of the scalp with lesions suitable for evaluation of the response to the test agent • Age of at least 12 years **Exclusion criteria of the trial** • Pregnant or nursing women • Hypersensitivity to any of the components of the test material • Under systemic corticosteroid medication within the previous month or topical corticosteroid therapy within the previous week • If the scalp showed signs of atrophy Number of randomised participants: 100 in total (fluocinolone N = 50, vehicle N = 50) Number of dropouts: 2 (2%) Sex: 75 males, 25 females Age (range): 16 to 83 years Country: USA
Interventions	**Treatment** • Fluocinolone acetonide shampoo 0.01%, applied on the scalp once a day for 5 minutes for 14 days **Comparator/s**

Ramirez 1993 *(Continued)*

	• Vehicle alone, applied on the scalp once a day for 5 minutes for 14 days After 2 weeks, the participants were asked to discontinue use of the test product and were re-evaluated 7 days post-treatment
Outcomes	1. Target areas on the scalp were designated and recorded on a dermograph 2. Global assessments (erythema, scaling, and pruritus), using an 8-point scale (0 to 3.5) 3. Improvement 4. Adverse effects
Notes	Non-medicated shampoo to be used when necessary

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	This was not reported in detail Quote: "The patients...were each assigned a number and randomly allocated...according to a schedule known only to the sponsor"
Allocation concealment (selection bias)	Unclear risk	This was not reported
Similarity of the study groups (selection bias)	Unclear risk	This was not reported. According to information in Table 1 of the report, there were no significant differences between the groups in erythema, scaling, and pruritus scores
Blinding of participants (performance bias)	Unclear risk	Whilst the study was reported to be double-blind, it was not clear who was blinded
Blinding of care providers (performance bias)	Unclear risk	Whilst the study was reported to be double-blind, it was not clear who was blinded
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Whilst the study was reported to be double-blind, it was not clear who was blinded
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	The dropout rate was acceptable
Selective reporting (reporting bias)	Low risk	Predefined outcomes were reported
Other bias	Unclear risk	The first author was affiliated to industry, and the sponsor provided non-medicated shampoos

Reygagne 2007

Methods	Study type: individual RCT Randomisation method: computer-based randomisation Blinding: investigator-blinded

Reygagne 2007 *(Continued)*

	Intention-to-treat analysis used: yes
Participants	**Inclusion criteria of the trial** • Seborrhoeic dermatitis of the scalp **Exclusion criteria of the trial** • Total severity score less than 2 Number of randomised participants: 55 in total (11 participants in each group) Number of dropouts: 4 (7%) Sex: 30 males, 25 females Mean age (range): 36.9 (18 to 64) years Country: France
Interventions	**Treatment** • Clobetasol 0.05%, applied to the scalp twice weekly for 4 weeks (applied for 2.5, 5, or 10 minutes) **Comparator/s** • Ketoconazole 2% foaming gel, applied to the scalp twice weekly for 4 weeks (for 5 minutes) • Placebo (vehicle), applied to the scalp twice weekly for 4 weeks (for 10 minutes)
Outcomes	1. Erythema and desquamation (7-point scale from 0 to 3), itching (100 mm analogue scale), and global improvement assessed by the investigator (7-point scale: -1 = worse than baseline to +5 = clear) 2. Safety evaluations (burning, 7-point scale from 0 to 3) and adverse events
Notes	The design of this trial was different from any other included study. The treatments were applied for different times: clobetasol propionate shampoo 0.05% for 2.5, 5, or 10 minutes; clobetasol propionate vehicle for 10 minutes; or ketoconazole foaming gel 2% for 5 minutes. After that, they were to be rinsed off. These kind of application methods were not used in any other included studies; therefore, we did not use the results in the meta-analysis. Results were not obtainable for all groups from the printed article. The actual symptom scores relevant for this review were not given in the text. Itching scores were given in a figure, but the figure displays only the results for the placebo (vehicle) and the azole group, which was irrelevant for this review. Only the results for complete clearance were given in the text

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "were randomized according to a computerized randomization schedule"
Allocation concealment (selection bias)	Unclear risk	This was not reported
Similarity of the study groups (selection bias)	Low risk	According to the report, there were no significant differences between the treatment groups for any of the symptoms, race, age, and gender distribution
Blinding of participants (performance bias)	High risk	Quote: "investigator blinded"
Blinding of care providers (performance bias)	High risk	Quote: "investigator blinded"

Reygagne 2007 *(Continued)*

Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "investigator-blinded"
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	The overall dropout rate was acceptable, but varied between 0%, 9%, and 18% in different treatment arms
Selective reporting (reporting bias)	Low risk	All predefined outcomes were reported
Other bias	Unclear risk	Some authors were affiliated to a pharmaceutical company

Rigopoulos 2004

Methods	Study type: individual RCT Randomisation method: computer-based randomisation Blinding: no (open-label) Intention-to-treat analysis used: yes
Participants	**Inclusion criteria of the trial** • Seborrhoeic dermatitis **Exclusion criteria of the trial** • Other dermatoses of face • Topical treatments during the 6 months prior to entry in the study • Pregnancy or lactation Number of randomised participants: 20 in total (pimecrolimus N = 11, betamethasone N = 9) Number of dropouts: 0 Sex: 16 males, 4 females Mean age (range): pimecrolimus arm = 36.4 (24 to 45) years, betamethasone arm = 37.2 (24 to 47) years Country: Greece
Interventions	**Treatment** • Pimecrolimus 1% cream, applied to the face twice daily until symptoms were absent **Comparator/s** • Betamethasone 0.1% cream, applied to the face twice daily until symptoms were absent
Outcomes	1. Erythema, pruritus, and scaling scores (scale 0 to 3) 2. Clearance and relapse rate
Notes	The participants were instructed to discontinue use of the medicine as soon as symptoms were absent. All participants stopped treatment by day 9 because symptoms had disappeared We could not use erythema, pruritus, and scaling scores in the meta-analysis because standard deviations or exact P values were not given in the report

Rigopoulos 2004 *(Continued)*

	The location of SeD lesions were not mentioned as inclusion criteria, but other dermatoses of the face were reported as exclusion criteria suggesting that the skin of the face was a site of interest in the trial

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "Patients were randomly assigned to treatment...using a program that allocated every consecutive group of two patients to one patient in each group. The random numbers were generated by a computer and were assigned to the patients by the investigator's assistant"
Allocation concealment (selection bias)	Unclear risk	The randomisation and allocation program allocated every consecutive group of 2 participants to 1 participant in each group, so the assistant would have known the latter participant's group in advance. However, the same assistant enrolled and assigned the treatment of the participants, whereas the investigator was masked
Similarity of the study groups (selection bias)	Low risk	Quote: "The mean baseline score for erythema, pruritus and scaling did not differ significantly between the two treatment groups"
Blinding of participants (performance bias)	High risk	The study was not blinded
Blinding of care providers (performance bias)	Unclear risk	This was not reported
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote: "in an attempt to make the assessments investigator masked"
Incomplete outcome data (attrition bias) All outcomes	Low risk	None were identified
Selective reporting (reporting bias)	Low risk	Predefined outcomes were reported
Other bias	Low risk	No other bias was identified

Rudner 1970

Methods	Study type: individual RCT Randomisation method: a standard randomisation sheet was used Blinding: double-blind Intention-to-treat analysis used: no
Participants	**Inclusion criteria of the trial** • Not reported. Each had seborrhoeic dermatitis occurring primarily in the nasolabial folds **Exclusion criteria of the trial** • Not reported

Rudner 1970 *(Continued)*

	Number of randomised participants: 50 in total (the initial group assignment numbers have not been reported. By the end of the study, there were 24 participants in the fluocinolone group and 19 participants in the vehicle group) Number of dropouts: 7 (14%) Sex of those who completed (baseline was not reported): 21 males and 22 females Age: not reported as mean, median, or range (reported as number of participants in 6 different age groups) Country: USA
Interventions	**Treatment** • Fluocinolone acetonide solution 0.01%, applied on the face twice a day for 84 days (12 weeks) **Comparator/s** • Propylene glycol solution, applied on the face twice daily for 84 days (12 weeks) Each participant was instructed to shampoo the scalp once weekly with Drytergent®
Outcomes	1. Clinical severity scores (erythema and scaling, scale 1+ to 3+) excluding scalp, clinical photographs
Notes	Only inpatients were included

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	This was not reported in detail Quote: "standard randomization sheet"
Allocation concealment (selection bias)	Unclear risk	This was not reported
Similarity of the study groups (selection bias)	Unclear risk	This was not reported
Blinding of participants (performance bias)	Low risk	The study was double-blind, but it was not reported specifically which parties were blinded. Nevertheless, the participants received the intervention and the comparison in identical containers
Blinding of care providers (performance bias)	Unclear risk	Whilst the study was reported to be double-blind, it was not clear who was blinded
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Whilst the study was reported to be double-blind, it was not clear who was blinded
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	The dropout rate was 24% in the control group. The initial group assignment numbers were not reported
Selective reporting (reporting bias)	Unclear risk	Prespecified outcomes were reported
Other bias	Low risk	No other bias was identified

Shin 2009

Methods	Study type: individual RCT Randomisation method: not reported Blinding: no (open-label) Intention-to-treat analysis used: no
Participants	**Inclusion criteria of the trial** • Seborrhoeic dermatitis of the scalp **Exclusion criteria of the trial** • Allergic to the tested products • Other dermatosis of the scalp • Phototherapy during the month before enrolment • Use of other topical therapeutic drugs or shampoos during the 2 months before • Immunosuppressive treatment including systemic steroids during the 3 months before enrolment • Significant renal disease or liver disease • Chronic diseases like asthma, diabetes, and hypertension • Pregnancy or lactation Number of randomised participants: 83 in total (tacrolimus N = 27, betamethasone N = 27, zinc pyrithione N = 29) Number of dropouts: altogether, 27 at 8 weeks (33%). At week 4, the dropout rate was 23% in the treatment arm that received treatment for 4 weeks only. The dropout rate at 4 weeks was not reported for the group that continued the treatment for 8 weeks. The dropout rate for this group was 38% at week 8 Sex: not reported Age (mean): tacrolimus arm = 38.0 years, betamethasone arm = 39.0 years, zinc pyrithione arm = 34.7 years Country: Korea
Interventions	**Treatment** • Tacrolimus 0.1% ointment, applied to the scalp twice daily for 4 weeks **Comparator/s** • Betamethasone lotion, applied to the scalp twice daily for 4 weeks • Zinc pyrithione 1% shampoo, applied to the scalp 3 times a week for 4 weeks
Outcomes	1. Clinical severity scores (dandruff and lesional extent, scale 0 to 3) evaluated by investigator
Notes	"At week 4, 53 patients continued the same treatment for an additional 4 weeks, but the other 30 patients stopped the treatments and were followed up at week 8." We only used the results from week 4 in this review because the only efficacy outcome that we could use was dandruff score, and the results for dandruff score were given at 4 weeks only. The dropout rate for those that used the interventions for 8 weeks was 38%. We requested and received additional data from the contact author

Risk of bias

Bias	Authors' judgement	Support for judgement

Shin 2009 *(Continued)*

Random sequence generation (selection bias)	Unclear risk	Quote: "randomly allocated"
Allocation concealment (selection bias)	Unclear risk	Quote: "randomly allocated"
Similarity of the study groups (selection bias)	Unclear risk	The differences in baseline clinical severity scores and dandruff scores were evaluated only for those who completed the 8-week follow-up-study. We used the results at 4 weeks
Blinding of participants (performance bias)	High risk	This was an open-label study
Blinding of care providers (performance bias)	High risk	This was an open-label study
Blinding of outcome assessment (detection bias) All outcomes	High risk	This was an open-label study
Incomplete outcome data (attrition bias) All outcomes	High risk	The dropout rate was 23% in the treatment arm that received treatment for 4 weeks only, but there was considerable variation between the groups (dropout rate was 50% in the betamethasone group, 0% in the tacrolimus group, and 20% in the zinc pyrithione group). The dropout rate at 4 weeks was not reported for the group that continued the treatment for 8 weeks. At 8 weeks, the dropout rates varied between 16% in the zinc pyrithione group, 24% in the betamethasone group, and 76% in the tacrolimus group. There were no intention-to-treat analyses
Selective reporting (reporting bias)	Low risk	No selective reporting bias was identified
Other bias	Low risk	No other bias was identified

Stratigos 1988

Methods	Study type: individual RCT Randomisation method: not reported Blinding: double-blind Intention-to-treat analysis used: no
Participants	**Inclusion criteria of the trial** • Seborrhoeic dermatitis **Exclusion criteria of the trial** • Not reported Number of randomised participants: 78 in total (6 participants were excluded because of a lack of treatment data. Finally, there were 36 participants in both groups.). The initial assignment numbers in each group were not reported Number of dropouts: 6 (8%)

Stratigos 1988 *(Continued)*

	Sex: not reported Mean age (range): hydrocortisone arm = 32.0 (18 to 73) years, ketoconazole arm = 34 (18 to 78 years) Country: Greece
Interventions	**Treatment** • Hydrocortisone 1% cream, applied to the affected areas once daily for 4 weeks **Comparator/s** • Ketoconazole 2% cream, applied once daily for 4 weeks
Outcomes	1. Global evaluation (total clearing - good - fair - poor - not evaluable) 2. Erythema, scaling, papules, and itching scores (scale 0 to 3)
Notes	Most of the results were not given in numerical form. We have approximated the numbers from figures, where applicable. The location of SeD lesions was not mentioned as inclusion criteria, but the sites of interest were reported to include the scalp, retroauricular area, eyebrows, hairline, nasolabial folds, sternum, external ear canal, and bridge of the nose

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	This was not reported in detail
Allocation concealment (selection bias)	Unclear risk	This was not reported
Similarity of the study groups (selection bias)	Low risk	Quote: "Both groups were comparable for age, weight, height, sex distribution, and duration of the infection"
Blinding of participants (performance bias)	Unclear risk	Whilst the study was reported to be double-blind, it was not clear who was blinded
Blinding of care providers (performance bias)	Unclear risk	Whilst the study was reported to be double-blind, it was not clear who was blinded
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Whilst the study was reported to be double-blind, it was not clear who was blinded
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	The dropout rate was acceptable. The initial number of participants in each group was not reported
Selective reporting (reporting bias)	Low risk	Predefined outcomes were reported
Other bias	Unclear risk	Some of the authors were affiliated to the pharmaceutical industry

Van't Veen 1998

Methods	Study type: individual RCT

Van't Veen 1998 *(Continued)*

	Randomisation method: not mentioned Blinding: no (open-label trial) Intention-to-treat analysis used: yes
Participants	**Inclusion criteria of the trial** • Mild or moderate seborrhoeic dermatitis of the scalp **Exclusion criteria of the trial** • People with plaques or severe crusts on the scalp or with signs suggestive of psoriasis • Any underlying condition or concomitant treatment that might interfere with or account for SeD • Use of systemic steroid during the 4 weeks preceding the study • Pregnant and breastfeeding women Number of randomised participants: 69 in total (betamethasone N = 34, ketoconazole N = 35) Number of dropouts: 0 Sex: 33 males, 36 females Mean age (range): betamethasone arm = 45.6 (20 to 75) years, ketoconazole arm = 40.1 (18 to 73) years Country: the Netherlands
Interventions	**Treatment** • Betamethasone 17-valerate 0.1% lotion, applied to the scalp twice daily for the first week, once daily in the second week, and twice weekly in the third and fourth weeks **Comparator/s** • Ketoconazole 20 mg/g hydrogel, applied to the scalp twice weekly for 4 weeks
Outcomes	1. Itching, scaling, and greasiness scores (scale 0 to 4) 2. Overall improvement evaluated by participants and investigators (cured - markedly improved - improved - unchanged - worsened) 3. Adverse events
Notes	"72 patients gave written informed consent and entered the wash-out period, but 2 had spontaneous remission and 1 withdrew for a non-study-related reason leaving 69 patients randomized". The results were given in figures and not in exact numbers. We approximated the numbers from figures, where feasible

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	This was not reported in detail Quote: "randomly allocated"
Allocation concealment (selection bias)	Unclear risk	This was not reported in detail Quote: "randomly allocated"
Similarity of the study groups (selection bias)	Low risk	Quote: "The groups were very well matched for demography and clinical characteristics"

Van't Veen 1998 *(Continued)*

Blinding of participants (performance bias)	High risk	This was an open-label study
Blinding of care providers (performance bias)	High risk	This was an open-label study
Blinding of outcome assessment (detection bias) All outcomes	High risk	This was an open-label study
Incomplete outcome data (attrition bias) All outcomes	Low risk	The dropout rate was acceptable
Selective reporting (reporting bias)	Low risk	All prespecified outcomes were reported, albeit not sufficiently enough for use in the meta-analysis
Other bias	Unclear risk	1 author was affiliated to Glaxo-Wellcome (The Netherlands) BV, and Glaxo-Wellcome provided all products Quote: "Financial support for the study was generously provided by Glaxo-Wellcome (The Netherlands) BV"

Warshaw 2007

Methods	Study type: individual RCT Randomisation method: computer-generated blocks of 4 Blinding: double-blind Intention-to-treat analysis used: Both ITT and PP analyses were used
Participants	**Inclusion criteria of the trial** • Facial seborrhoeic dermatitis **Exclusion criteria of the trial** • Pregnancy or nursing • Allergies to products • Acne vulgaris or rosacea • People with poorly controlled chronic conditions • Those with cancer, neurologic conditions, or HIV infection (or other immunosuppression) Number of randomised participants: 96 in total (pimecrolimus N = 47, vehicle N = 49) Number of dropouts: 2 (2%) Sex: 85 males, 11 females Mean age (range): pimecrolimus arm = 59.5 (27 to 84) years, placebo arm = 59.6 (20 to 88) years Country: USA
Interventions	**Treatment** • Pimecrolimus 1% cream, applied to the face twice daily for 4 weeks

Warshaw 2007 *(Continued)*

	Comparator/s • Placebo (vehicle), applied to the face twice daily for 4 weeks
Outcomes	1. Erythema and scaling score (scale 0 to 3) 2. Total target area score (sum of erythema and scaling score) 3. IGA score (Investigator's Global Assessment score, scale 0 to 4) 4. Adverse events
Notes	-

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "The computer-generated randomization assignment (blocks of 4) was only accessible to the research pharmacist during the study"
Allocation concealment (selection bias)	Low risk	Quote: "The computer-generated randomization assignment (blocks of 4) was only accessible to the research pharmacist during the study"
Similarity of the study groups (selection bias)	Unclear risk	Quote: "At baseline, both groups had similar demographics...with the exception that a higher percentage of participants in the pimecrolimus group (38%) had previously used medication to treat their seborrhoeic dermatitis, compared with participants in the vehicle group (29%). In addition, participants in the vehicle group had milder disease at baseline compared with those in the pimecrolimus group with regard to mean scale target area score...and with regard to mean facial IGA"
Blinding of participants (performance bias)	Low risk	The study was double-blind Quote: "The two creams were packaged in identical tubes"
Blinding of care providers (performance bias)	Low risk	Quote: "double-blind" Blinded parties were not specified. Nevertheless, the research pharmacist was the only person that knew the participants' assignments
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "double-blind" Blinded parties were not specified. Nevertheless, the research pharmacist was the only person that knew the participants' assignments
Incomplete outcome data (attrition bias) All outcomes	Low risk	The dropout rate was acceptable
Selective reporting (reporting bias)	Low risk	Prespecified outcomes were reported
Other bias	Unclear risk	Quote: "This investigator-initiated study was supported by Novartis Pharmaceuticals Corporation" Novartis Pharmaceuticals Corporation employed at least 2 of the authors

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

Study	Reason for exclusion
Aertgeerts 1985	Only 1 of 161 participants had SeD
Albrecht 1986	Only 9 of 383 participants had SeD
Alebiosu 2003	Only 2 of the participants had dandruff; there was no mention about the proportion of SeD participants
Alexander 1967	The intervention was not anti-inflammatory (tar)
Amos 1994	The interventions were not anti-inflammatory (tar and ketoconazole)
Anonymous 1994a	This study was not a RCT, and the interventions were not anti-inflammatory
Anonymous 1994b	This was a review
Arenas 1999	The intervention was not anti-inflammatory (ichthyol/octopirox/salicylic acid)
Attarzadeh 2013	Allocation of treatment (emu oil or either clotrimazole or hyrocortisone) was not randomised as treatment 1 was always used on the right side, and treatment 2 was used on the left side of the face
Banerjee 1975	The interventions were a combinations of drugs (a combination of nitrofurazone and hydrocortisone acetate compared with a combination of framycetin sulfate and dexamethasone acetate and a combination of neomycin, bacitracin, polymyxin B sulfate, and hydrocortisone)
Barbanoj 2005	The intervention was not anti-inflammatory (eberconazole), and participants were healthy volunteers
Basak 1999	This was a poster. The efficacy and safety results were not given in numerical form, and it was not possible to ensure that efficacy was assessed in ways relevant for the review
Bertamino 1975	Less than 75% of participants had seborrhoeic dermatitis; randomisation was not explained clearly
Binder 1972	Less than 75% of participants had seborrhoeic dermatitis; the affected area was not reported
Boyle 1986	The intervention was a combination of lithium succinate and zinc
Camarasa 1975	Only 1 participant out of 37 had SeD
Carboni 1982	The comparison was between 2 formulas of clobetasol
Christodoulou 1983	The intervention was in peroral form
Cuelenaere 1992	The interventions was a combination of lithium succinate and zinc sulphate
Curley 1990	The diagnosis of the participants was mainly psoriasis or eczema; only a few had SeD
Davies 1999	The intervention was tar or ciclopirox olamine, which are not relevant for this review
de la Brassine 1984	Randomisation, site, and age were unclear
Dobrev 2003	1 intervention is a combination of drugs (salicylic acid, plant tar, and green microalgae), and others were not anti-inflammatory (selenium sulphide, zinc pyrithione, and a combination of ketoconazole, metronidazole, and sulphur)
Elewski 2009b	This was a review

Study	Reason for exclusion
Elie 1983	Only 17 out of 40 participants had SeD
Eun 2009	This was a poster, which did not contain enough data
Franz 2000	Participants had psoriasis not SeD
Fredriksson 1975a	The study was not randomised
Fredriksson 1985	The intervention was not anti-inflammatory (tar)
Freeman 2002	Less than 75% of participants had seborrhoic dermatitis in the desonide group
Fritz 1995	The intervention was a combination of lithium and zinc sulphate
Futterer 1981	The comparison was irrelevant (piroctone olamine and zinc pyrithione)
Gayko 2006	The intervention was a combination of ichthyol and ketoconazole
Gentry 1973	Age and affected area are unknown
Goffin 1996	The interventions were not anti-inflammatory (econazole nitrate, piroctone olamine, senium sulphide, and zinc pyrithione)
Gould 1988	The reference was a summary of a paper. The used efficacy measures were not reported in detail. The results were not reported in numerical form
Grossman 1997	The interventions were not anti-inflammatory (zinc pyrithione and ketoconazole)
High 2006	The study was not randomised or controlled
Hochman 1988	The interventions were combinations of non-anti-inflammatory agents (sulphur + salicylic acid)
Humke 2002	The nature of the intervention was unclear: a new shampoo free of ketoconazole versus a ketoconazole-containing shampoo
Jacksonville 1969	The age of the participants was unknown; randomisation was unclear; and the time-in-between was not reported
Jafferany 2008	This was a review
Jaramillo 1992	The intervention was not anti-inflammatory (zinc pyrithione)
Jensen 2009	This was a poster. The age of the participants was not reported. The outcomes used were not in the interest of this review
Jensen 2010	This was a poster. There was no information on the age of the participants or the affected/investigated site. The used outcomes were not reported, and the results of interest in this review were not reported in numerical form
Kaminester 2002	The intervention was not anti-inflammatory (sulphacetamide)
Karsono 2010	The intervention was not anti-inflammatory (zinc pyrithione)
Kim 2012	This was a poster. The results of interest for this review were not reported in detail or in numerical form. No useful data could be added to the analyses

Study	Reason for exclusion
Kim 2013	This study included an induction phase with an active treatment only (not controlled) and thereafter a controlled maintenance phase
Kircik 2009	Participants were healthy volunteers, and the intervention was not anti-inflammatory
Levy 1974	There was only 1 participant with SeD
Li 2000	The interventions were irrelevant for the review (Triatop®, which is a ketoconazole-containing compound, and tar)
Lin 2010	This was a review
Luo 1993	The intervention was antifungal (bifonazole)
López Padilla 1996	The interventions were not anti-inflammatory (ketoconazole and climbazole)
Marks 1974	The outcomes used in the study were not relevant for the review. There were no useful data to be added to the analyses
Mensing 2008	Only 10 out of 27 participants had SeD, and there was no control treatment
Nolting 1983	Less than 75% of participants had SeD, and results were not reported separately for SeD participants
Nolting 1985	Only 1 out of 80 participants had the diagnosis of SeD
Pierard-Franchimont 1995	The interventions were not anti-inflammatory (econazole, ketoconazole, piroctone olamine, and selenium sulphide)
Pierard-Franchimont 1999	The intervention was not anti-inflammatory (tar). This was a poster
Pierard-Franchimont 2000	The intervention was not anti-inflammatory (tar)
Pierard-Franchimont 2002a	The interventions were a combination of non-anti-inflammatory agents (ketoconazole, piroctone olamine, and zinc pyrithione formulations)
Pierard-Franchimont 2002b	The intervention was a combination of antifungal and anti-inflammatory drugs (ketoconazole and desonide combination)
Pierard-Franchimont 2002c	The interventions were not anti-inflammatory (ketoconazole and zinc pyrithione)
Reiffenstuhl 1973	Only 3 out of 54 participants had SeD, and there was no control intervention
Reinhard 1974	Only 5 out of 122 participants had SeD
Sohn 1978	This was a non-randomised study
Tomoka 1973	Only 2 out of 84 participants had SeD
Turnbull 1982	Less than 75% of participants had seborrhoeic dermatitis
Veien 1980	The intervention was a combination of 2 non-anti-inflammatory agents (coal tar and zinc pyrithione)
Wacker 1989	Randomisation and proportion of SeD participants was unclear

Study	Reason for exclusion
Weiss 2011	The intervention was not anti-inflammatory (ketoconazole)
Wollina 2006	This was a review
Wollina 2007	This was a review
Yawalkar 1983	Less than 75% of participants had SeD

Characteristics of studies awaiting assessment *[ordered by study ID]*

Fredriksson 1975b

Methods	Randomised, controlled, double-blind study Duration: 44 days with 3 phases (control, treatment, and follow-up period)
Participants	• 20 adult men with severe seborrheic dermatitis of the scalp
Interventions	• Dexamethasone 0.012% in an aerosol alcohol-isopropyl myristate formula • Fluocinolone acetonide 0.01%
Outcomes	Scored degree of seborrheic involvement (summary scores)
Notes	The participants were not blinded. Only the evaluating physician was blinded (single-blind). Side-effects were not reported

Snyder 1969

Methods	Randomised, controlled, double-blind study Duration: not reported
Participants	• 67 participants aged 15 to 60 years with seborrheic dermatitis of the face
Interventions	• Fluocinolone acetonide solution (0.01%) in a propylene glycol base • Propylene glycol
Outcomes	Clinical effectiveness defined as test drug preferred and identified; improvement (either partial or complete decrease of redness, scaling and itching), side effects
Notes	-

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

EudraCT 2005-006208-21

Trial name or title	Clinical efficacy of pimecrolimus cream in seborrheic dermatitis. Efficacy of pimecrolimus in normalizing clinical symptoms, explorative study of barrier function, hydration, lipid content and differentiation in seborrheic dermatitis: a randomized, double-blind study in adults with seborrheic dermatitis treated with 1% pimecrolimus cream versus 2% ketoconazole cream as control

EudraCT 2005-006208-21 *(Continued)*

Methods	This is a randomised, controlled, double-blind study Duration: 4 weeks
Participants	• 18 years or older with mild to severe seborrhoeic dermatitis
Interventions	• Pimecrolimus cream 1% • Ketoconazole cream 2%
Outcomes	**Primary outcome/s of the trial** • Change of IGA scores in 1 week **Secondary outcome/s of the trial** • Change in IGA scoring in relation to the face • Pruritus, erythema, and scaling scores • Cosmetic acceptability assessment • Epidermal effects • Changes in *Malassezia* counting at 4 weeks
Starting date	Entered into database: August 2006
Contact information	Department of Dermatology, University of Kiel, Germany
Notes	Ongoing. Database accessed on 17 December 2012

EudraCT 2006-003984-30

Trial name or title	A multicenter, randomized, double-blind, two-arm, vehicle-controlled, parallel-group, two stage study to evaluate and demonstrate the efficacy and to evaluate the safety of pimecrolimus 1% cream in the treatment of seborrhoeic dermatitis in patients 12 years of age and older
Methods	This is a randomised, double-blind, parallel group, 2-stage study Initial estimate of the duration of the trial: 9 months
Participants	• People with seborrhoeic dermatitis aged 18 years or older
Interventions	• Pimecrolimus 1% cream (Elidel®) • Placebo cream
Outcomes	**Primary outcome/s of the trial** • Overall clearance (IGA of 0) assessed at 1, 2, or 3 weeks. 1 of these assessment time points will be selected for the final analysis of the primary end point **Secondary outcome/s of the trial** • Facial clearance • Time to overall clearance • Time to facial clearance • Change in pruritus • Severity of lesional erythema and scaling • Time to relapse • Safety

EudraCT 2006-003984-30 *(Continued)*

	• Health-related quality of life • Amount of study drug/participant/episode
Starting date	Entered into database: October 2006
Contact information	Novartis Pharma Services AG, Switzerland
Notes	Completed, but no publications provided in searched databases. In the title, the age of the participants is limited to 12 or older whereas in the inclusion criteria, the age limit is 18 or older. The trial has 2 stages, but these are not defined clearly. Database accessed on 17 December 2012

EudraCT 2007-007088-25

Trial name or title	Efficacy and tolerance of V0071 GM 01A in inflammatory seborrhoeic dermatitis of the scalp
Methods	This is a randomised, open-label (investigator-masked in initiation therapy), parallel group study (phase II) Initial estimate of the duration of the trial: 11 months
Participants	• People aged 18 to 65 years with inflammatory seborrhoeic dermatitis of the scalp or with dandruff
Interventions	• V0071 GM 01A (betamethasone dipropionate 0.05%) shampoo • Ketoconazole 2% foaming gel
Outcomes	**Primary outcome/s of the trial** • Erythema and scaling sum scores on each half head at 2 weeks **Secondary outcome/s of the trial** • Efficacy of intervention on inflammatory seborrhoeic dermatitis • Local and global tolerance of the interventions
Starting date	Entered into database: January 2008
Contact information	Pierre Fabre Dermatologie, France
Notes	Ongoing study. Database accessed on 17 December 2012

EudraCT 2009-013120-23

Trial name or title	Efficacité et tolérance du LBC 45 dans la dermite séborrhéique du cuir chevelu
Methods	This is a randomised, controlled, double-blind, parallel group, phase II study Initial estimate of the duration of the trial: 70 days
Participants	• 18 years or older with seborrhoeic dermatitis of the scalp of moderate to severe intensity • Disease for at least 2 months
Interventions	• Lithium gluconate gel 8/100 g/g • Placebo gel

EudraCT 2009-013120-23 *(Continued)*

Outcomes	**Primary outcome/s of the trial** • The sum of erythema and scaling scores at day 56 **Secondary outcome/s of the trial** • None mentioned
Starting date	Entered into database: August 2009
Contact information	LABCATAL, France
Notes	Ongoing study. Database accessed on 17 December 2012

EudraCT 2010-022861-93

Trial name or title	Confirmation de l'efficacité et de la tolérance du LBC 45 dans la dermite séborrhéique du cuir chevelu
Methods	This is a randomised, controlled, single-blind, parallel group, phase II study Initial estimate of the duration of the trial: 70 days
Participants	• 18 years or older • Moderate to severe seborrhoeic dermatitis of the scalp for at least 2 months
Interventions	• Lithium gluconate gel 8% • Ciclopirox olamine shampoo 1.5% and placebo gel
Outcomes	**Primary outcome/s of the trial** • The efficacy of lithium gluconate compared with placebo after 8 weeks of treatment and assessed with sum scores (erythema and scaling) **Secondary outcome/s of the trial** • The efficacy of lithium gluconate in moderate to severe seborrhoeic dermatitis of the scalp compared with ciclopirox olamine after 4 and 8 weeks of treatment • The efficacy of lithium gluconate compared with placebo after 4 weeks • The local and general tolerance to lithium gluconate after 4 and 8 weeks • Participants' preferences between lithium gluconate and ciclopirox olamine at 8 weeks • To compare the efficacy of different modes of application of lithium gluconate at 4 and 8 weeks
Starting date	Entered into database: October 2010
Contact information	Laboratoire LABCATAL, France
Notes	Ongoing study. Database accessed on 17 December 2012

NCT00403559

Trial name or title	A 4 week randomized double-blind parallel group active comparator controlled study of Elidel for the treatment of seborrheic dermatitis

NCT00403559 *(Continued)*

Methods	This is a randomised, double-blind, parallel group study
Participants	• 18 years or older with seborrhoeic dermatitis
Interventions	• Pimecrolimus cream 1% • Ketoconazole cream 2%
Outcomes	**Primary outcome/s of the trial** • The change of IGA from baseline to week 1 **Secondary outcome/s of the trial** • Per cent of participants with facial clearance
Starting date	January 2007
Contact information	Joseph F Fowler Jr, Dermatology Specialists Research
Notes	Completed in January 2009, but no publications provided. Database accessed on 17 December 2012

NCT01011621

Trial name or title	Comparative evaluation of the efficacy and tolerability of prednisolone acetate 0.5% cream versus betamethasone valerate 0.1% cream in the treatment of pediatric and adult dermatosis
Methods	This is a randomised, open-label, parallel group phase III study
Participants	• 12 to 60 year-old people with mild to moderate corticosensitive dermatosis (atopic dermatitis, contact dermatitis, seborrhoeic dermatitis, or psoriasis)
Interventions	• 0.5% prednisolone acetate cream • 0.1% betamethasone valerate cream
Outcomes	**Primary outcome/s of the trial** • "Evaluate efficacy and safety" at 2 weeks **Secondary outcome/s of the trial** • "Evaluate physicians' and patients' perception of the efficacy and tolerability of treatment" at 2 weeks
Starting date	February 2010
Contact information	Cláudia Domingues cdomingues@mantecorp.com
Notes	The study is not yet open for participant recruitment. At this point, it is impossible to know if this study will be relevant for this review. Database accessed on 17 December 2012

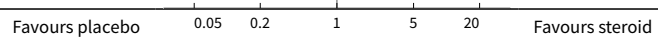
DATA AND ANALYSES

Comparison 1. Steroid vs placebo

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Total clearance (at 4 weeks or less)	3	313	Risk Ratio (M-H, Random, 95% CI)	3.76 [1.22, 11.56]
1.1 Mild steroids	1	47	Risk Ratio (M-H, Random, 95% CI)	1.57 [0.29, 8.53]
1.2 Strong steroids	2	266	Risk Ratio (M-H, Random, 95% CI)	5.92 [0.99, 35.52]
2 Total clearance (over 4 weeks)	1		Risk Ratio (M-H, Fixed, 95% CI)	Totals not selected
2.1 Strong steroids	1		Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
3 Mean change in erythema score (at 4 weeks or less)	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
3.1 Strong steroids	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
4 Erythema score (at 4 weeks or less)	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
4.1 Strong steroids	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
5 Mean change in scaling score (at 4 weeks or less)	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
5.1 Strong steroids	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
6 Scaling scores (at 4 weeks or less)	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
6.1 Strong steroids	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
7 Mean change in pruritus score (at 4 weeks or less)	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
7.1 Strong steroids	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
8 Pruritus scores (at 4 weeks or less)	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
8.1 Strong steroids	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
9 Any adverse effect (at 4 weeks or less)	3	508	Risk Ratio (M-H, Fixed, 95% CI)	0.89 [0.29, 2.72]
9.1 Mild steroids	1	47	Risk Ratio (M-H, Fixed, 95% CI)	0.35 [0.01, 8.11]
9.2 Strong steroids	2	461	Risk Ratio (M-H, Fixed, 95% CI)	1.05 [0.31, 3.58]

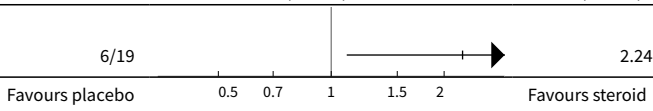
Analysis 1.1. Comparison 1 Steroid vs placebo, Outcome 1 Total clearance (at 4 weeks or less).

Study or subgroup	Steroid n/N	Placebo n/N	Risk Ratio M-H, Random, 95% CI	Weight	Risk Ratio M-H, Random, 95% CI
1.1.1 Mild steroids					
Attila 1992	3/23	2/24		25.98%	1.57[0.29,8.53]
Subtotal (95% CI)	**23**	**24**		**25.98%**	**1.57[0.29,8.53]**
Total events: 3 (Steroid), 2 (Placebo)					
Heterogeneity: Not applicable					
Test for overall effect: Z=0.52(P=0.6)					
1.1.2 Strong steroids					
Lynfield 1988	32/86	10/82		52.55%	3.05[1.61,5.8]
Ramirez 1993	18/49	1/49		21.47%	18[2.5,129.64]
Subtotal (95% CI)	**135**	**131**		**74.02%**	**5.92[0.99,35.52]**
Total events: 50 (Steroid), 11 (Placebo)					
Heterogeneity: Tau^2=1.23; Chi^2=3.19, df=1(P=0.07); I^2=68.62%					
Test for overall effect: Z=1.94(P=0.05)					
Total (95% CI)	**158**	**155**		**100%**	**3.76[1.22,11.56]**
Total events: 53 (Steroid), 13 (Placebo)					
Heterogeneity: Tau^2=0.52; Chi^2=4.05, df=2(P=0.13); I^2=50.59%					
Test for overall effect: Z=2.31(P=0.02)					
Test for subgroup differences: Chi^2=1.12, df=1 (P=0.29), I^2=10.39%					



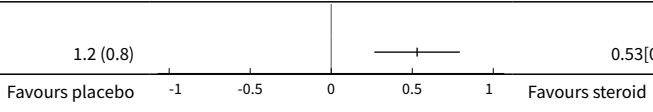
Analysis 1.2. Comparison 1 Steroid vs placebo, Outcome 2 Total clearance (over 4 weeks).

Study or subgroup	Steroid n/N	Placebo n/N	Risk Ratio M-H, Fixed, 95% CI	Risk Ratio M-H, Fixed, 95% CI
1.2.1 Strong steroids				
Rudner 1970	17/24	6/19		2.24[1.1,4.56]



Analysis 1.3. Comparison 1 Steroid vs placebo, Outcome 3 Mean change in erythema score (at 4 weeks or less).

Study or subgroup	Steroid N	Steroid Mean(SD)	Placebo N	Placebo Mean(SD)	Mean Difference Fixed, 95% CI	Mean Difference Fixed, 95% CI
1.3.1 Strong steroids						
Lynfield 1988	72	1.7 (0.8)	62	1.2 (0.8)		0.53[0.27,0.79]

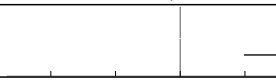


Analysis 1.4. Comparison 1 Steroid vs placebo, Outcome 4 Erythema score (at 4 weeks or less).

Study or subgroup	Steroid N	Steroid Mean(SD)	Placebo N	Placebo Mean(SD)	Mean Difference Fixed, 95% CI	Mean Difference Fixed, 95% CI
1.4.1 Strong steroids						
Ramirez 1993	49	0.5 (0.6)	49	1.2 (0.8)		-0.79[-1.07,-0.51]

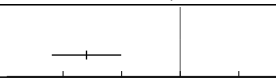
Analysis 1.5. Comparison 1 Steroid vs placebo, Outcome 5 Mean change in scaling score (at 4 weeks or less).

Study or subgroup	Steroid N	Steroid Mean(SD)	Placebo N	Placebo Mean(SD)	Mean Difference Fixed, 95% CI	Mean Difference Fixed, 95% CI
1.5.1 Strong steroids						
Lynfield 1988	74	2.1 (0.9)	62	1.3 (0.8)		0.77[0.49,1.05]



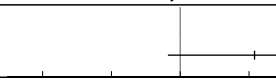
Analysis 1.6. Comparison 1 Steroid vs placebo, Outcome 6 Scaling scores (at 4 weeks or less).

Study or subgroup	Steroid N	Steroid Mean(SD)	Placebo N	Placebo Mean(SD)	Mean Difference Fixed, 95% CI	Mean Difference Fixed, 95% CI
1.6.1 Strong steroids						
Ramirez 1993	49	0.6 (0.7)	49	1.4 (0.8)		-0.8[-1.1,-0.5]



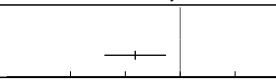
Analysis 1.7. Comparison 1 Steroid vs placebo, Outcome 7 Mean change in pruritus score (at 4 weeks or less).

Study or subgroup	Steroid N	Steroid Mean(SD)	Placebo N	Placebo Mean(SD)	Mean Difference Fixed, 95% CI	Mean Difference Fixed, 95% CI
1.7.1 Strong steroids						
Lynfield 1988	63	1.4 (0.8)	53	1.1 (0.9)		0.27[-0.04,0.58]

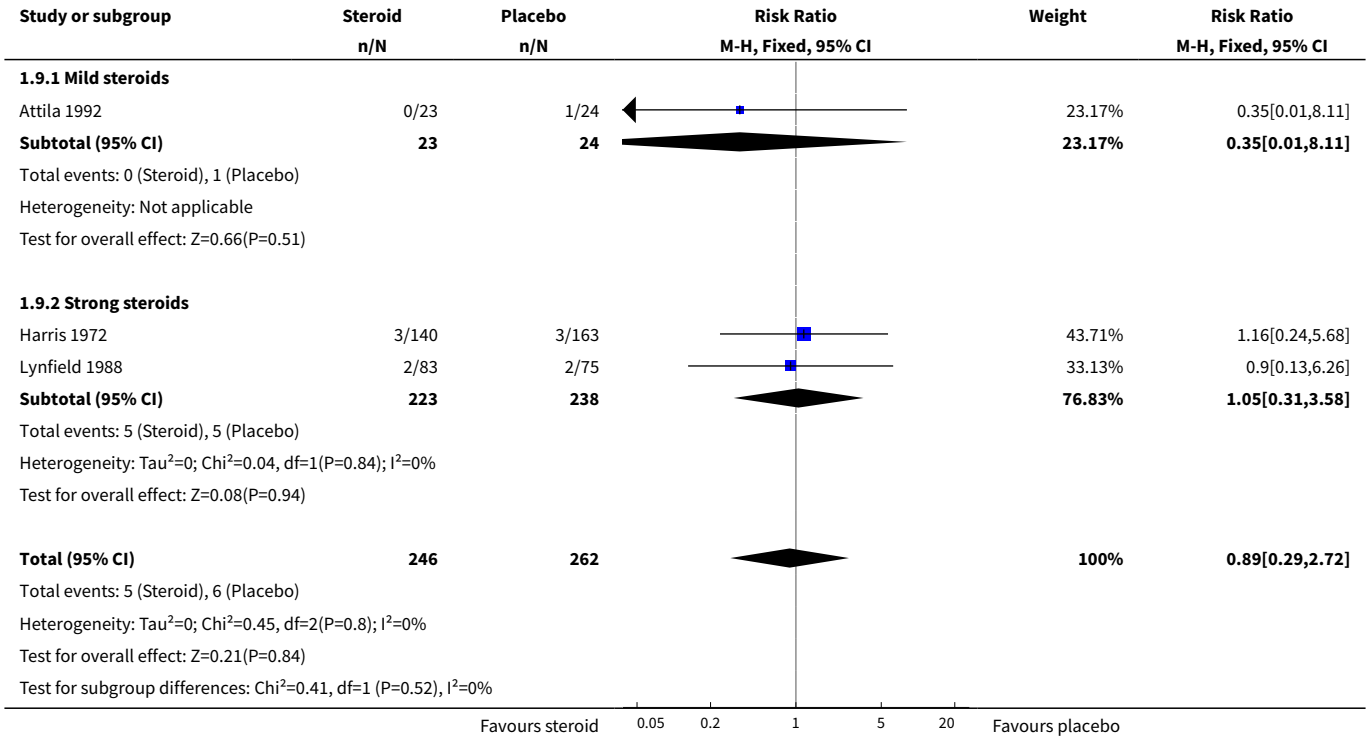


Analysis 1.8. Comparison 1 Steroid vs placebo, Outcome 8 Pruritus scores (at 4 weeks or less).

Study or subgroup	Steroid N	Steroid Mean(SD)	Placebo N	Placebo Mean(SD)	Mean Difference Fixed, 95% CI	Mean Difference Fixed, 95% CI
1.8.1 Strong steroids						
Ramirez 1993	49	0.3 (0.5)	49	0.7 (0.9)		-0.41[-0.69,-0.13]



Analysis 1.9. Comparison 1 Steroid vs placebo, Outcome 9 Any adverse effect (at 4 weeks or less).



Comparison 2. Steroid vs calcineurin inhibitor

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Total clearance (at 4 weeks or less)	2	60	Risk Ratio (M-H, Fixed, 95% CI)	1.08 [0.88, 1.32]
1.1 Mild steroids	1	40	Risk Ratio (M-H, Fixed, 95% CI)	1.13 [0.83, 1.55]
1.2 Strong steroids	1	20	Risk Ratio (M-H, Fixed, 95% CI)	1.0 [0.83, 1.20]
2 Erythema score (at 4 weeks or less)	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
2.1 Mild steroids	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
3 Scaling score (at 4 weeks or less)	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
3.1 Mild steroids	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
4 Mean change in dandruff score (at 4 weeks or less)	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
4.1 Strong steroids	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]

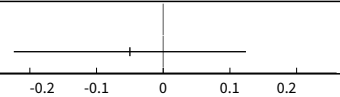
Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
5 Any adverse effects at 4 weeks or less	2	60	Risk Ratio (M-H, Fixed, 95% CI)	0.22 [0.05, 0.89]
5.1 Mild steroids	1	40	Risk Ratio (M-H, Fixed, 95% CI)	0.14 [0.02, 1.06]
5.2 Strong steroids	1	20	Risk Ratio (M-H, Fixed, 95% CI)	0.41 [0.05, 3.28]
6 Any adverse effects (at 4 weeks or more)	2	72	Risk Ratio (M-H, Fixed, 95% CI)	0.62 [0.26, 1.47]
6.1 Mild steroids	2	72	Risk Ratio (M-H, Fixed, 95% CI)	0.62 [0.26, 1.47]

Analysis 2.1. Comparison 2 Steroid vs calcineurin inhibitor, Outcome 1 Total clearance (at 4 weeks or less).

Study or subgroup	Steroid n/N	Calcineurin inhibitor n/N	Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
2.1.1 Mild steroids					
Firooz 2006	17/20	15/20		58.93%	1.13[0.83,1.55]
Subtotal (95% CI)	**20**	**20**		**58.93%**	**1.13[0.83,1.55]**
Total events: 17 (Steroid), 15 (Calcineurin inhibitor)					
Heterogeneity: Not applicable					
Test for overall effect: Z=0.78(P=0.43)					
2.1.2 Strong steroids					
Rigopoulos 2004	9/9	11/11		41.07%	1[0.83,1.2]
Subtotal (95% CI)	**9**	**11**		**41.07%**	**1[0.83,1.2]**
Total events: 9 (Steroid), 11 (Calcineurin inhibitor)					
Heterogeneity: Not applicable					
Test for overall effect: Not applicable					
Total (95% CI)	**29**	**31**		**100%**	**1.08[0.88,1.32]**
Total events: 26 (Steroid), 26 (Calcineurin inhibitor)					
Heterogeneity: Tau^2=0; Chi^2=0.74, df=1(P=0.39); I^2=0%					
Test for overall effect: Z=0.73(P=0.46)					
Test for subgroup differences: Chi^2=0.46, df=1 (P=0.5), I^2=0%					

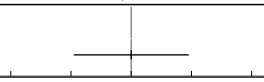
Analysis 2.2. Comparison 2 Steroid vs calcineurin inhibitor, Outcome 2 Erythema score (at 4 weeks or less).

Study or subgroup	Steroid N	Steroid Mean(SD)	Calcineurin inhibitor N	Calcineurin inhibitor Mean(SD)	Mean Difference Fixed, 95% CI	Mean Difference Fixed, 95% CI
2.2.1 Mild steroids						
Firooz 2006	19	0.1 (0.2)	18	0.1 (0.3)		-0.05[-0.22,0.12]



Analysis 2.3. Comparison 2 Steroid vs calcineurin inhibitor, Outcome 3 Scaling score (at 4 weeks or less).

Study or subgroup	Steroid N	Steroid Mean(SD)	Calcineurin inhibitor N	Calcineurin inhibitor Mean(SD)	Mean Difference Fixed, 95% CI	Mean Difference Fixed, 95% CI
2.3.1 Mild steroids						
Firooz 2006	19	0.2 (0.4)	18	0.2 (0.4)		0[-0.24,0.24]



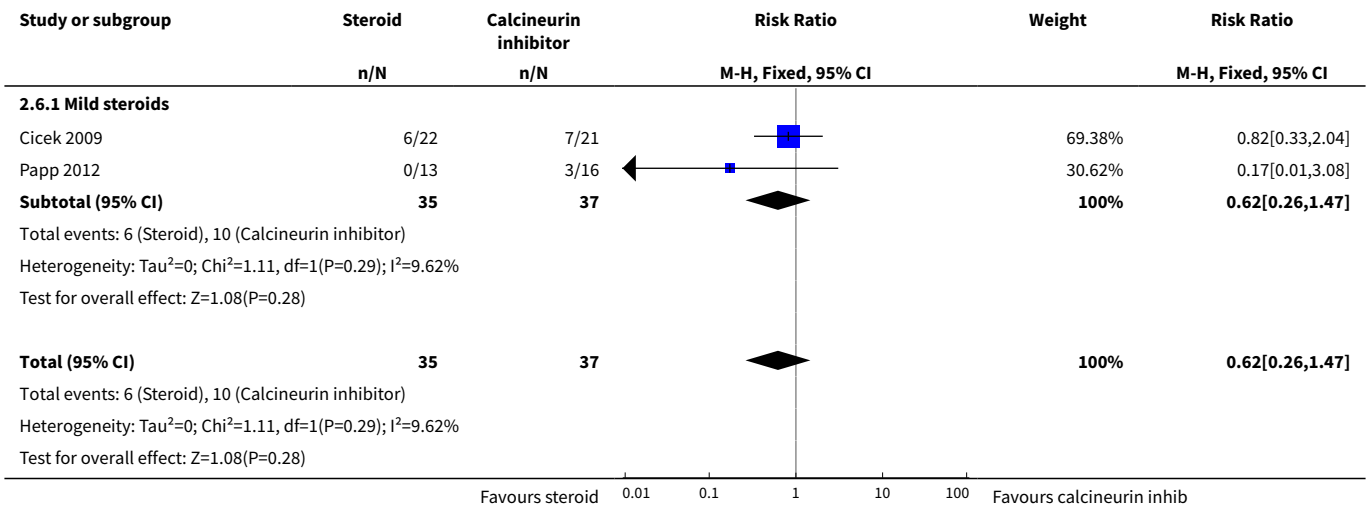
Analysis 2.4. Comparison 2 Steroid vs calcineurin inhibitor, Outcome 4 Mean change in dandruff score (at 4 weeks or less).

Study or subgroup	Steroid N	Steroid Mean(SD)	Calcineurin inhibitor N	Calcineurin inhibitor Mean(SD)	Mean Difference Fixed, 95% CI	Mean Difference Fixed, 95% CI
2.4.1 Strong steroids						
Shin 2009	18	-0.6 (1)	14	-0.4 (0.5)		-0.2[-0.73,0.33]

Analysis 2.5. Comparison 2 Steroid vs calcineurin inhibitor, Outcome 5 Any adverse effects at 4 weeks or less.

Study or subgroup	Steroid n/N	Calcineurin inhibitor n/N	Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
2.5.1 Mild steroids					
Firooz 2006	1/20	7/20		72.16%	0.14[0.02,1.06]
Subtotal (95% CI)	**20**	**20**		**72.16%**	**0.14[0.02,1.06]**
Total events: 1 (Steroid), 7 (Calcineurin inhibitor)					
Heterogeneity: Not applicable					
Test for overall effect: Z=1.91(P=0.06)					
2.5.2 Strong steroids					
Rigopoulos 2004	1/9	3/11		27.84%	0.41[0.05,3.28]
Subtotal (95% CI)	**9**	**11**		**27.84%**	**0.41[0.05,3.28]**
Total events: 1 (Steroid), 3 (Calcineurin inhibitor)					
Heterogeneity: Tau^2=0; Chi^2=0, df=0(P<0.0001); I^2=100%					
Test for overall effect: Z=0.84(P=0.4)					
Total (95% CI)	**29**	**31**		**100%**	**0.22[0.05,0.89]**
Total events: 2 (Steroid), 10 (Calcineurin inhibitor)					
Heterogeneity: Tau^2=0; Chi^2=0.52, df=1(P=0.47); I^2=0%					
Test for overall effect: Z=2.12(P=0.03)					
Test for subgroup differences: Chi^2=0.51, df=1 (P=0.48), I^2=0%					

Analysis 2.6. Comparison 2 Steroid vs calcineurin inhibitor, Outcome 6 Any adverse effects (at 4 weeks or more).



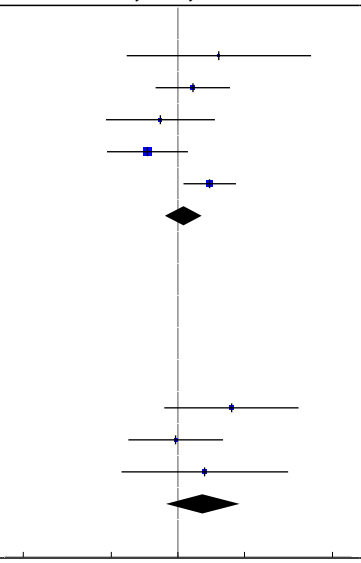
Comparison 3. Steroid vs azole

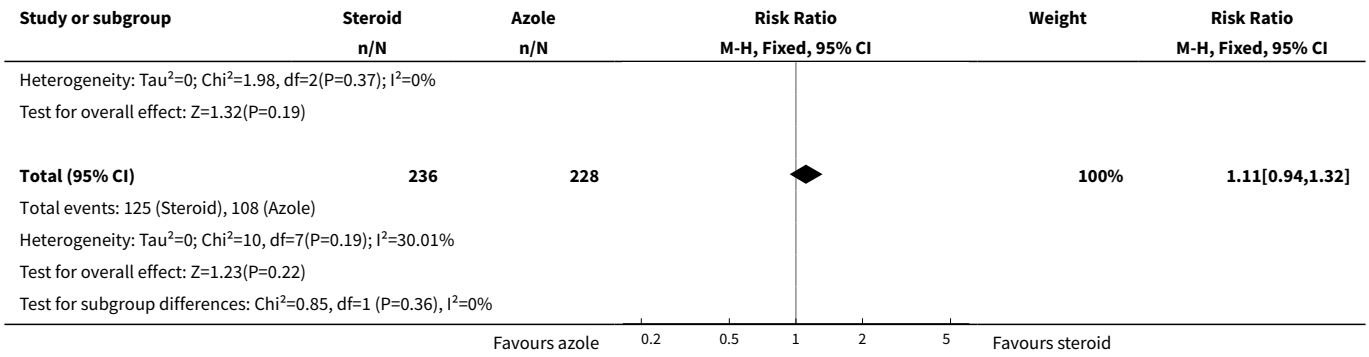
Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Total clearance (at 4 weeks or less)	8	464	Risk Ratio (M-H, Fixed, 95% CI)	1.11 [0.94, 1.32]
1.1 Mild steroids	5	310	Risk Ratio (M-H, Fixed, 95% CI)	1.06 [0.87, 1.28]
1.2 Strong steroids	3	154	Risk Ratio (M-H, Fixed, 95% CI)	1.29 [0.88, 1.90]
2 Total clearance (at 4 weeks or less, evaluated by participant)	2		Risk Ratio (M-H, Random, 95% CI)	Totals not selected
2.1 Mild steroids	1		Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
2.2 Strong steroids	1		Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
3 Erythema score (at 4 weeks or less)	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
3.1 Strong steroids	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
4 Mean change in erythema score at 4 weeks or less	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
4.1 Mild steroids	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
5 Scaling score (at 4 weeks or less)	2		Std. Mean Difference (IV, Fixed, 95% CI)	Subtotals only
5.1 Strong steroids	2	118	Std. Mean Difference (IV, Fixed, 95% CI)	-2.72 [-3.24, -2.21]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
6 Mean change in scaling score at 4 weeks or less	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
6.1 Mild steroids	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
7 Pruritus score (at 4 weeks or less)	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
7.1 Mild steroids	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
8 Mean change in pruritus score at 4 weeks or less	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
8.1 Mild steroids	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
9 Any adverse effects at 4 weeks or less	6	381	Risk Ratio (M-H, Fixed, 95% CI)	1.45 [0.74, 2.85]
9.1 Mild steroids	4	263	Risk Ratio (M-H, Fixed, 95% CI)	1.00 [0.44, 2.26]
9.2 Strong steroids	2	118	Risk Ratio (M-H, Fixed, 95% CI)	3.25 [0.86, 12.36]
10 Any adverse effects at 4 weeks or more	2		Risk Ratio (M-H, Fixed, 95% CI)	Totals not selected
10.1 Mild steroids	1		Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
10.2 Strong steroids	1		Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]

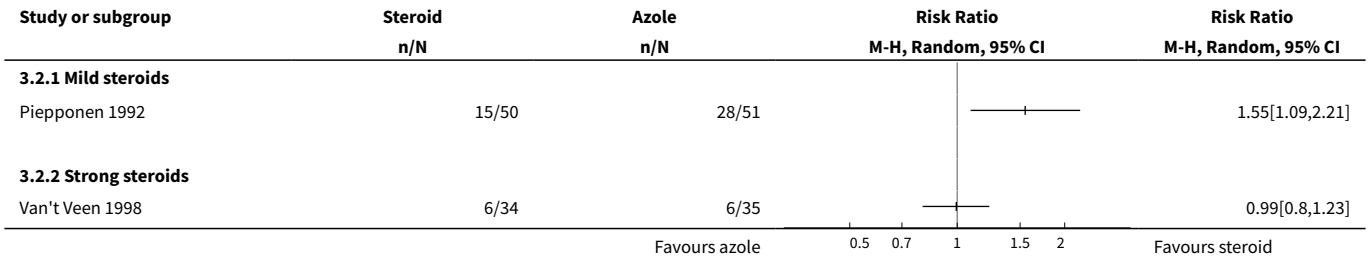
Analysis 3.1. Comparison 3 Steroid vs azole, Outcome 1 Total clearance (at 4 weeks or less).

Study or subgroup	Steroid n/N	Azole n/N	Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
3.1.1 Mild steroids					
Faergemann 1986	8/24	5/23		4.66%	1.53[0.59,4]
Katsambas 1989	19/26	15/24		14.23%	1.17[0.79,1.72]
Kousidou 1992	10/20	12/20		10.94%	0.83[0.47,1.47]
Piepponen 1992	20/50	28/51		25.28%	0.73[0.48,1.11]
Stratigos 1988	32/36	23/36		20.98%	1.39[1.06,1.83]
Subtotal (95% CI)	**156**	**154**		**76.08%**	**1.06[0.87,1.28]**
Total events: 89 (Steroid), 83 (Azole)					
Heterogeneity: Tau^2=0; Chi^2=8.44, df=4(P=0.08); I^2=52.62%					
Test for overall effect: Z=0.58(P=0.56)					
3.1.2 Strong steroids					
Hersle 1996	15/27	7/22		7.04%	1.75[0.87,3.51]
Pari 1998	12/19	11/17		10.59%	0.98[0.6,1.6]
Van't Veen 1998	9/34	7/35		6.29%	1.32[0.56,3.15]
Subtotal (95% CI)	**80**	**74**		**23.92%**	**1.29[0.88,1.9]**
Total events: 36 (Steroid), 25 (Azole)					

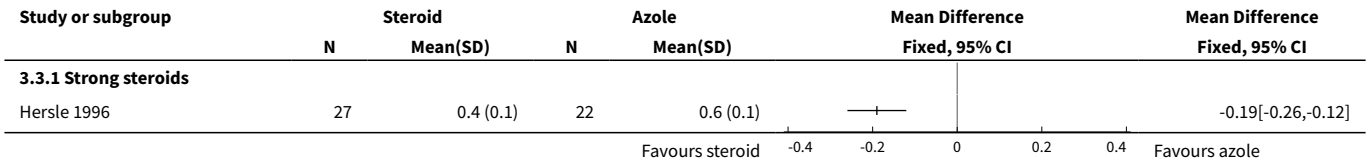




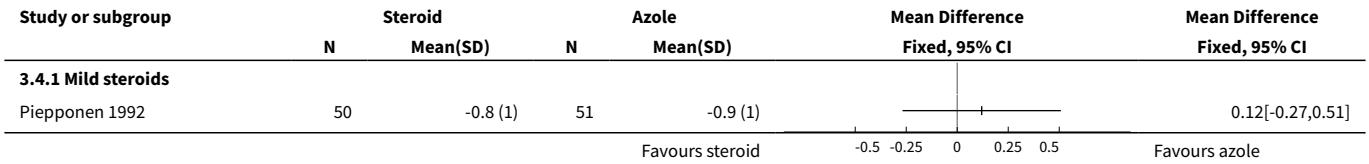
Analysis 3.2. Comparison 3 Steroid vs azole, Outcome 2 Total clearance (at 4 weeks or less, evaluated by participant).



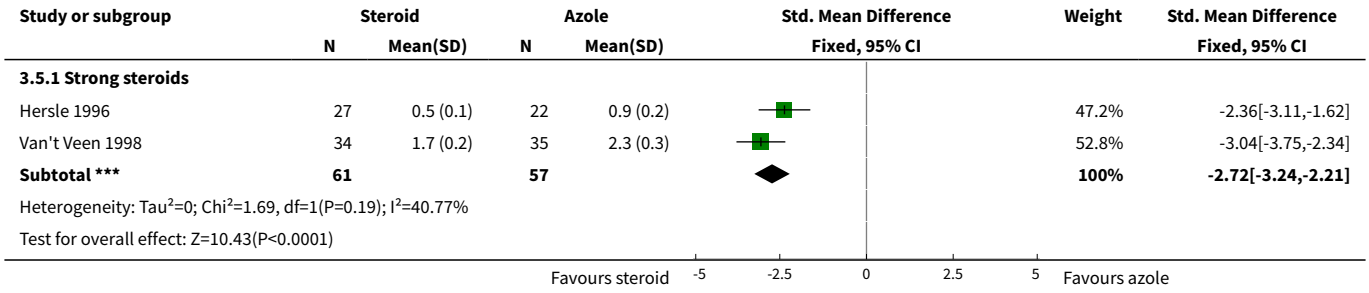
Analysis 3.3. Comparison 3 Steroid vs azole, Outcome 3 Erythema score (at 4 weeks or less).



Analysis 3.4. Comparison 3 Steroid vs azole, Outcome 4 Mean change in erythema score at 4 weeks or less.

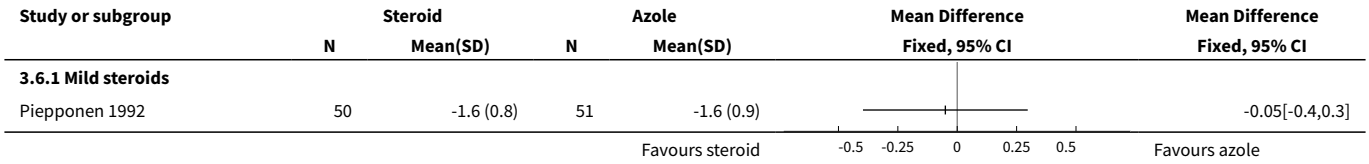


Analysis 3.5. Comparison 3 Steroid vs azole, Outcome 5 Scaling score (at 4 weeks or less).



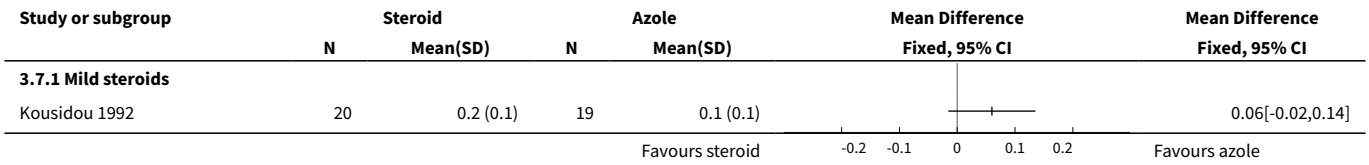
Study or subgroup	Steroid N	Steroid Mean(SD)	Azole N	Azole Mean(SD)	Std. Mean Difference Fixed, 95% CI	Weight	Std. Mean Difference Fixed, 95% CI
3.5.1 Strong steroids							
Hersle 1996	27	0.5 (0.1)	22	0.9 (0.2)		47.2%	-2.36[-3.11,-1.62]
Van't Veen 1998	34	1.7 (0.2)	35	2.3 (0.3)		52.8%	-3.04[-3.75,-2.34]
Subtotal ***	**61**		**57**			**100%**	**-2.72[-3.24,-2.21]**
Heterogeneity: Tau^2=0; Chi^2=1.69, df=1(P=0.19); I^2=40.77%							
Test for overall effect: Z=10.43(P<0.0001)							

Analysis 3.6. Comparison 3 Steroid vs azole, Outcome 6 Mean change in scaling score at 4 weeks or less.



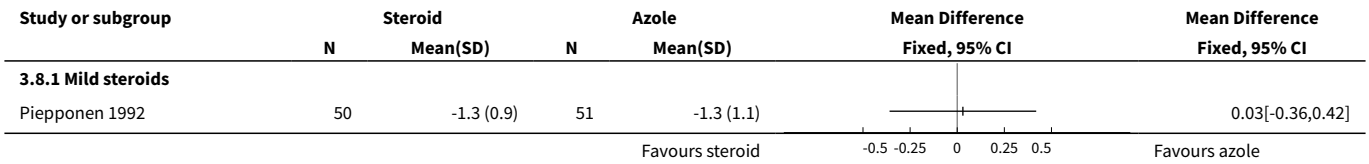
Study or subgroup	Steroid N	Steroid Mean(SD)	Azole N	Azole Mean(SD)	Mean Difference Fixed, 95% CI	Mean Difference Fixed, 95% CI
3.6.1 Mild steroids						
Piepponen 1992	50	-1.6 (0.8)	51	-1.6 (0.9)		-0.05[-0.4,0.3]

Analysis 3.7. Comparison 3 Steroid vs azole, Outcome 7 Pruritus score (at 4 weeks or less).



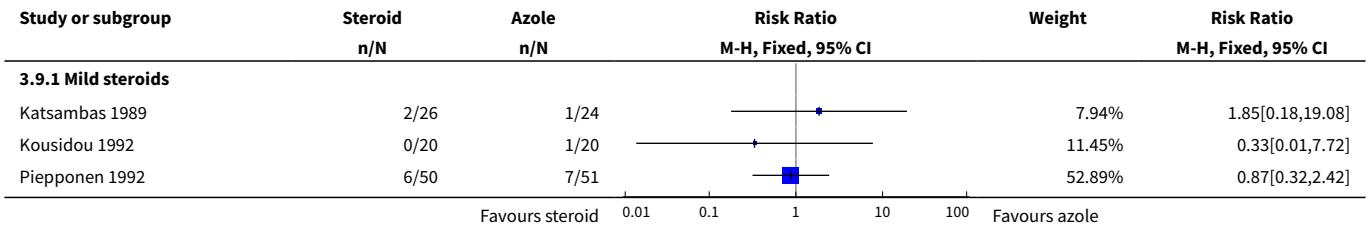
Study or subgroup	Steroid N	Steroid Mean(SD)	Azole N	Azole Mean(SD)	Mean Difference Fixed, 95% CI	Mean Difference Fixed, 95% CI
3.7.1 Mild steroids						
Kousidou 1992	20	0.2 (0.1)	19	0.1 (0.1)		0.06[-0.02,0.14]

Analysis 3.8. Comparison 3 Steroid vs azole, Outcome 8 Mean change in pruritus score at 4 weeks or less.

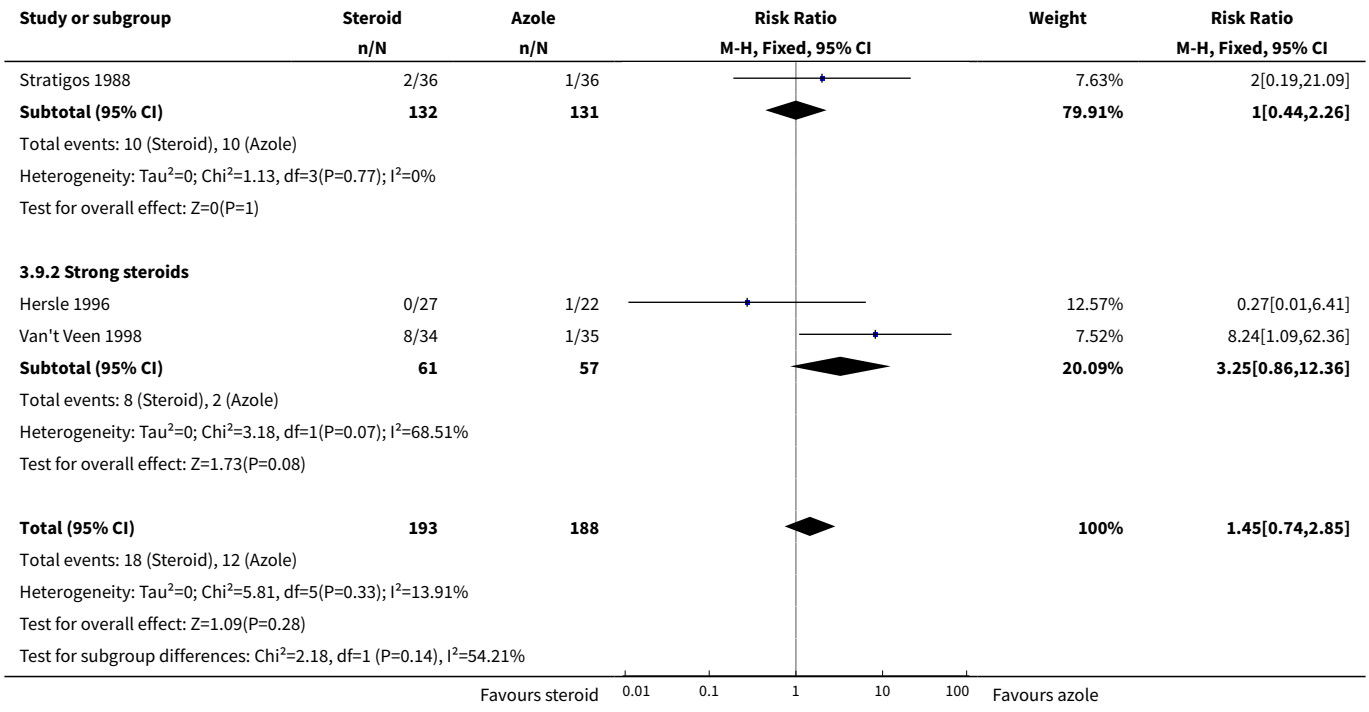


Study or subgroup	Steroid N	Steroid Mean(SD)	Azole N	Azole Mean(SD)	Mean Difference Fixed, 95% CI	Mean Difference Fixed, 95% CI
3.8.1 Mild steroids						
Piepponen 1992	50	-1.3 (0.9)	51	-1.3 (1.1)		0.03[-0.36,0.42]

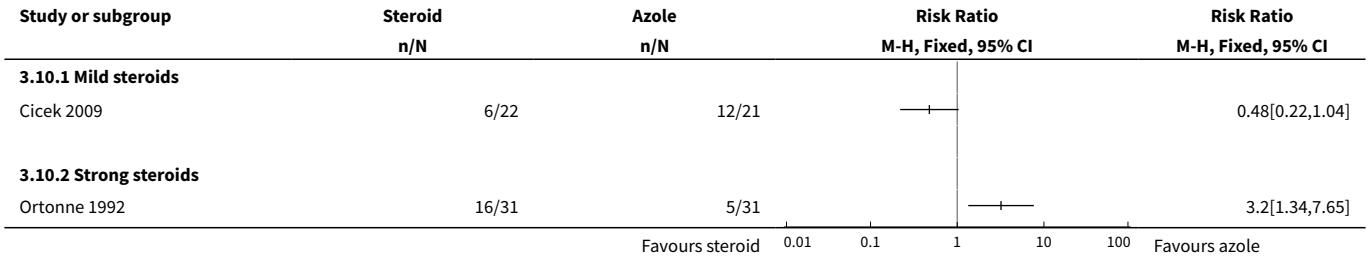
Analysis 3.9. Comparison 3 Steroid vs azole, Outcome 9 Any adverse effects at 4 weeks or less.



Study or subgroup	Steroid n/N	Azole n/N	Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
3.9.1 Mild steroids					
Katsambas 1989	2/26	1/24		7.94%	1.85[0.18,19.08]
Kousidou 1992	0/20	1/20		11.45%	0.33[0.01,7.72]
Piepponen 1992	6/50	7/51		52.89%	0.87[0.32,2.42]



Analysis 3.10. Comparison 3 Steroid vs azole, Outcome 10 Any adverse effects at 4 weeks or more.



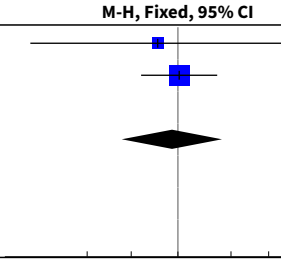
Comparison 4. Mild steroid vs strong steroid

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Total clearance (at 4 weeks or less)	2	93	Risk Ratio (M-H, Fixed, 95% CI)	0.96 [0.65, 1.40]
2 Total clearance (at 4 weeks or less, evaluated by participant)	1		Risk Ratio (M-H, Fixed, 95% CI)	Totals not selected
3 Total clearance at 4 weeks or more	1		Risk Ratio (M-H, Fixed, 95% CI)	Totals not selected
4 Erythema score (at 4 weeks or less)	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
5 Scaling score (at 4 weeks or less)	2	63	Std. Mean Difference (IV, Fixed, 95% CI)	-0.05 [-0.55, 0.45]
6 Pruritus score (at 4 weeks or less)	3	114	Std. Mean Difference (IV, Fixed, 95% CI)	0.13 [-0.24, 0.50]
7 Any adverse effects (at 4 weeks or less)	3	118	Risk Ratio (M-H, Fixed, 95% CI)	1.37 [0.32, 5.93]
8 Any adverse effects (at 4 weeks or more)	1		Risk Ratio (M-H, Fixed, 95% CI)	Totals not selected

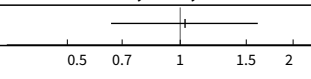
Analysis 4.1. Comparison 4 Mild steroid vs strong steroid, Outcome 1 Total clearance (at 4 weeks or less).

Study or subgroup	Strong steroid n/N	Mild steroid n/N	Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
Fredriksson 1978	6/32	7/32		36.06%	0.86[0.32,2.27]
Ludvigsen 1983	13/15	12/14		63.94%	1.01[0.76,1.35]
Total (95% CI)	**47**	**46**		**100%**	**0.96[0.65,1.4]**
Total events: 19 (Strong steroid), 19 (Mild steroid)					
Heterogeneity: Tau^2=0; Chi^2=0.19, df=1(P=0.66); I^2=0%					
Test for overall effect: Z=0.23(P=0.82)					



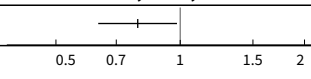
Analysis 4.2. Comparison 4 Mild steroid vs strong steroid, Outcome 2 Total clearance (at 4 weeks or less, evaluated by participant).

Study or subgroup	Strong steroid n/N	Mild steroid n/N	Risk Ratio M-H, Fixed, 95% CI	Risk Ratio M-H, Fixed, 95% CI
Ludvigsen 1983	11/15	10/14		1.03[0.65,1.61]



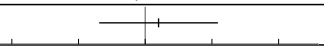
Analysis 4.3. Comparison 4 Mild steroid vs strong steroid, Outcome 3 Total clearance at 4 weeks or more.

Study or subgroup	Strong steroid n/N	Mild steroid n/N	Risk Ratio M-H, Fixed, 95% CI	Risk Ratio M-H, Fixed, 95% CI
Medansky 1992	38/58	49/59		0.79[0.63,0.98]



Analysis 4.4. Comparison 4 Mild steroid vs strong steroid, Outcome 4 Erythema score (at 4 weeks or less).

Study or subgroup	Strong steroid N	Strong steroid Mean(SD)	Mild steroid N	Mild steroid Mean(SD)	Mean Difference Fixed, 95% CI	Mean Difference Fixed, 95% CI
Gip 1979	17	1.3 (0.8)	18	1.2 (0.5)		0.1[-0.34,0.54]



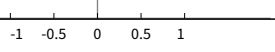
Favours strong steroid — Favours mild steroid

Analysis 4.5. Comparison 4 Mild steroid vs strong steroid, Outcome 5 Scaling score (at 4 weeks or less).

Study or subgroup	Strong steroid N	Strong steroid Mean(SD)	Mild steroid N	Mild steroid Mean(SD)	Std. Mean Difference Fixed, 95% CI	Weight	Std. Mean Difference Fixed, 95% CI
Gip 1979	17	1.4 (1)	18	1.2 (0.5)		55.97%	0.25[-0.42,0.92]
Ludvigsen 1983	14	0.1 (0.4)	14	0.3 (0.5)		44.03%	-0.43[-1.18,0.32]
Total ***	**31**		**32**			**100%**	**-0.05[-0.55,0.45]**

Heterogeneity: $Tau^2=0$; $Chi^2=1.76$, df=1(P=0.19); $I^2=43.05\%$

Test for overall effect: Z=0.19(P=0.85)



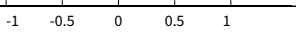
Favours strong steroid — Favours mild steroid

Analysis 4.6. Comparison 4 Mild steroid vs strong steroid, Outcome 6 Pruritus score (at 4 weeks or less).

Study or subgroup	Strong steroid N	Strong steroid Mean(SD)	Mild steroid N	Mild steroid Mean(SD)	Std. Mean Difference Fixed, 95% CI	Weight	Std. Mean Difference Fixed, 95% CI
General Practitioner 1982	26	0.6 (0.8)	28	0.5 (0.6)		47.44%	0.11[-0.42,0.65]
Gip 1979	17	1.4 (0.9)	18	1.2 (0.7)		30.56%	0.24[-0.42,0.91]
Ludvigsen 1983	13	0.2 (0.6)	12	0.2 (0.6)		22%	0[-0.78,0.78]
Total ***	**56**		**58**			**100%**	**0.13[-0.24,0.5]**

Heterogeneity: $Tau^2=0$; $Chi^2=0.22$, df=2(P=0.9); $I^2=0\%$

Test for overall effect: Z=0.68(P=0.5)



Favours strong steroid — Favours mild steroid

Analysis 4.7. Comparison 4 Mild steroid vs strong steroid, Outcome 7 Any adverse effects (at 4 weeks or less).

Study or subgroup	Strong steroid n/N	Mild steroid n/N	Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
General Practitioner 1982	1/26	0/28		16.39%	3.22[0.14,75.75]
Gip 1979	1/17	2/18		66.06%	0.53[0.05,5.32]
Ludvigsen 1983	1/15	0/14		17.55%	2.81[0.12,63.83]
Total (95% CI)	**58**	**60**		**100%**	**1.37[0.32,5.93]**

Total events: 3 (Strong steroid), 2 (Mild steroid)

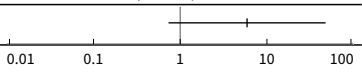
Heterogeneity: $Tau^2=0$; $Chi^2=1.14$, df=2(P=0.57); $I^2=0\%$

Test for overall effect: Z=0.42(P=0.67)

Favours strong steroid — Favours mild steroid

Analysis 4.8. Comparison 4 Mild steroid vs strong steroid, Outcome 8 Any adverse effects (at 4 weeks or more).

Study or subgroup	Strong steroid n/N	Mild steroid n/N	Risk Ratio M-H, Fixed, 95% CI	Risk Ratio M-H, Fixed, 95% CI
Medansky 1992	6/59	1/58		5.9[0.73,47.49]

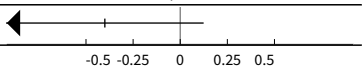


Comparison 5. Steroid vs zinc pyrithione

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Scaling score (< 4 weeks)	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected

Analysis 5.1. Comparison 5 Steroid vs zinc pyrithione, Outcome 1 Scaling score (< 4 weeks).

Study or subgroup	Betametasone N	Betametasone Mean(SD)	Zinc pyrithione N	Zinc pyrithione Mean(SD)	Mean Difference Fixed, 95% CI	Mean Difference Fixed, 95% CI
Shin 2009	27	0.6 (1)	29	1 (1)		-0.4[-0.92,0.12]

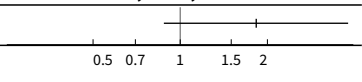


Comparison 6. Desonide (mild steroid) vs Promiseb®

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Total clearance (at 4 weeks or less)	1		Risk Ratio (M-H, Fixed, 95% CI)	Totals not selected

Analysis 6.1. Comparison 6 Desonide (mild steroid) vs Promiseb®, Outcome 1 Total clearance (at 4 weeks or less).

Study or subgroup	Desonide n/N	Promiseb® n/N	Risk Ratio M-H, Fixed, 95% CI	Risk Ratio M-H, Fixed, 95% CI
Elewski 2009a	15/39	8/38		1.83[0.88,3.8]



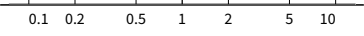
Comparison 7. Steroid vs calcipotriol

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Total clearance (at 4 weeks or less)	1		Risk Ratio (M-H, Fixed, 95% CI)	Totals not selected

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
2 Any adverse effects (at 4 weeks or less)	1		Risk Ratio (M-H, Fixed, 95% CI)	Totals not selected

Analysis 7.1. Comparison 7 Steroid vs calcipotriol, Outcome 1 Total clearance (at 4 weeks or less).

Study or subgroup	Steroid n/N	Calcipotriol n/N	Risk Ratio M-H, Fixed, 95% CI	Risk Ratio M-H, Fixed, 95% CI
Basak 2001	20/30	7/30		2.86[1.42,5.73]



Favours calcipotriol — Favours steroid

Analysis 7.2. Comparison 7 Steroid vs calcipotriol, Outcome 2 Any adverse effects (at 4 weeks or less).

Study or subgroup	Steroid n/N	Calcipotriol n/N	Risk Ratio M-H, Fixed, 95% CI	Risk Ratio M-H, Fixed, 95% CI
Basak 2001	2/30	17/30		0.12[0.03,0.47]

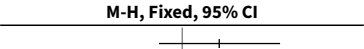
Favours steroid — Favours calcipotriol

Comparison 8. Calcineurin inhibitor vs placebo

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Total clearance (at 4 weeks or less)	1		Risk Ratio (M-H, Fixed, 95% CI)	Totals not selected
2 Mean change in erythema score at 4 weeks or less	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
3 Mean change in scaling score at 4 weeks or less	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
4 Outcome: any adverse effects	1		Risk Ratio (M-H, Fixed, 95% CI)	Totals not selected

Analysis 8.1. Comparison 8 Calcineurin inhibitor vs placebo, Outcome 1 Total clearance (at 4 weeks or less).

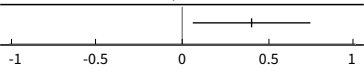
Study or subgroup	Calcineurin inhibitor n/N	Placebo n/N	Risk Ratio M-H, Fixed, 95% CI	Risk Ratio M-H, Fixed, 95% CI
Warshaw 2007	19/47	14/49		1.41[0.81,2.48]



Favours placebo — Favours calcineurin inhib

Analysis 8.2. Comparison 8 Calcineurin inhibitor vs placebo, Outcome 2 Mean change in erythema score at 4 weeks or less.

Study or subgroup	Calcineurin inhibitor N	Calcineurin inhibitor Mean(SD)	Placebo N	Placebo Mean(SD)	Mean Difference Fixed, 95% CI	Mean Difference Fixed, 95% CI
Warshaw 2007	41	1.9 (0.7)	45	1.5 (0.9)		0.4[0.06,0.74]

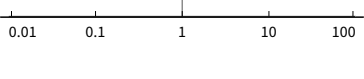


Analysis 8.3. Comparison 8 Calcineurin inhibitor vs placebo, Outcome 3 Mean change in scaling score at 4 weeks or less.

Study or subgroup	Calcineurin inhibitor N	Calcineurin inhibitor Mean(SD)	Placebo N	Placebo Mean(SD)	Mean Difference Fixed, 95% CI	Mean Difference Fixed, 95% CI
Warshaw 2007	41	2 (0.7)	45	1.7 (0.7)		0.3[0,0.6]

Analysis 8.4. Comparison 8 Calcineurin inhibitor vs placebo, Outcome 4 Outcome: any adverse effects.

Study or subgroup	Calcineurin inhibitor n/N	Placebo n/N	Risk Ratio M-H, Fixed, 95% CI	Risk Ratio M-H, Fixed, 95% CI
Warshaw 2007	22/47	16/49		1.43[0.87,2.37]

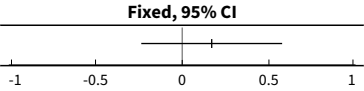


Comparison 9. Calcineurin inhibitor vs azole

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Erythema score (over 4 weeks)	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
2 Scaling score (over 4 weeks)	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
3 Any adverse effects (over 4 weeks)	2		Risk Ratio (M-H, Random, 95% CI)	Totals not selected

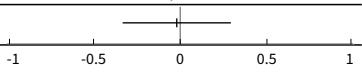
Analysis 9.1. Comparison 9 Calcineurin inhibitor vs azole, Outcome 1 Erythema score (over 4 weeks).

Study or subgroup	Calcineurin inhibitor N	Calcineurin inhibitor Mean(SD)	Azole N	Azole Mean(SD)	Mean Difference Fixed, 95% CI	Mean Difference Fixed, 95% CI
Koc 2009	18	0.7 (0.7)	20	0.6 (0.6)		0.17[-0.24,0.58]



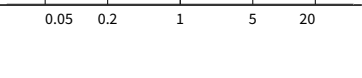
Analysis 9.2. Comparison 9 Calcineurin inhibitor vs azole, Outcome 2 Scaling score (over 4 weeks).

Study or subgroup	Calcineurin inhibitor N	Calcineurin inhibitor Mean(SD)	Azole N	Azole Mean(SD)	Mean Difference Fixed, 95% CI	Mean Difference Fixed, 95% CI
Koc 2009	18	0.3 (0.5)	20	0.4 (0.5)		-0.02[-0.33,0.29]



Analysis 9.3. Comparison 9 Calcineurin inhibitor vs azole, Outcome 3 Any adverse effects (over 4 weeks).

Study or subgroup	Calcineurin inhibitor n/N	Azole n/N	Risk Ratio M-H, Random, 95% CI	Risk Ratio M-H, Random, 95% CI
Cicek 2009	7/21	12/21		0.58[0.29,1.19]
Koc 2009	12/23	4/25		3.26[1.22,8.69]

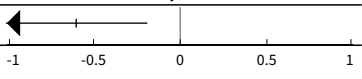


Comparison 10. Calcineurin inhibitor vs zinc pyrithione

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Dandruff score (< 4 weeks)	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected

Analysis 10.1. Comparison 10 Calcineurin inhibitor vs zinc pyrithione, Outcome 1 Dandruff score (< 4 weeks).

Study or subgroup	Tacrolimus N	Tacrolimus Mean(SD)	Zinc pyrithione N	Zinc pyrithione Mean(SD)	Mean Difference Fixed, 95% CI	Mean Difference Fixed, 95% CI
Shin 2009	27	0.4 (0.5)	29	1 (1)		-0.6[-1.01,-0.19]



Comparison 11. Lithium vs placebo

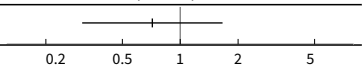
Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Total clearance (over 4 weeks)	1		Risk Ratio (M-H, Fixed, 95% CI)	Totals not selected
2 Any adverse effects at 4 weeks or more	1		Risk Ratio (M-H, Fixed, 95% CI)	Totals not selected

Analysis 11.1. Comparison 11 Lithium vs placebo, Outcome 1 Total clearance (over 4 weeks).

Study or subgroup	Lithium gluconate n/N	Placebo n/N	Risk Ratio M-H, Fixed, 95% CI	Risk Ratio M-H, Fixed, 95% CI
Dreno 2002a	18/66	2/63		8.59[2.08,35.52]

Analysis 11.2. Comparison 11 Lithium vs placebo, Outcome 2 Any adverse effects at 4 weeks or more.

Study or subgroup	Lithium n/N	Placebo n/N	Risk Ratio M-H, Fixed, 95% CI	Risk Ratio M-H, Fixed, 95% CI
Dreno 2002a	8/62	11/61		0.72[0.31,1.66]

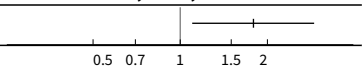


Comparison 12. Lithium vs azole

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Total clearance (< 4 weeks)	1		Risk Ratio (M-H, Fixed, 95% CI)	Totals not selected
2 Total clearance (at 4 weeks or more)	1		Risk Ratio (M-H, Fixed, 95% CI)	Totals not selected

Analysis 12.1. Comparison 12 Lithium vs azole, Outcome 1 Total clearance (< 4 weeks).

Study or subgroup	Lithium gluconate n/N	Ketoconazole n/N	Risk Ratio M-H, Fixed, 95% CI	Risk Ratio M-H, Fixed, 95% CI
Dreno 2003	40/152	20/136		1.79[1.1,2.9]



Analysis 12.2. Comparison 12 Lithium vs azole, Outcome 2 Total clearance (at 4 weeks or more).

Study or subgroup	Lithium gluconate n/N	Ketoconazole n/N	Risk Ratio M-H, Fixed, 95% CI	Risk Ratio M-H, Fixed, 95% CI
Dreno 2003	78/152	39/136		1.79[1.32,2.43]

ADDITIONAL TABLES

Table 1. Reygagne 2007

The study investigated clobetasol propionate shampoo (0.05%) with three different application times (2.5 minutes, 5 minutes, and 10 minutes) and the comparisons included ketoconazole and vehicle. Each group included 11 participants. Some of the results are unobtainable from the figures in the report, and only results stated in the text could be used. The study lasted 4 weeks. The study has not been included in the meta-analyses as the mode of application was different from all other studies.

	Steroid	Vehicle	Azole
Total clearance	18.2% to 45.5% (in different application groups)	9.1%	9.1%
Erythema scores[1]	0.1 in clobetasol 5-minute group; otherwise, not reported (P value = 0.024 for comparison with vehicle)	0.7	0.1
Scaling scores (loose desquamation)[2]	0.3 in clobetasol 10-minute group, and 0.4 in clobetasol 5-minute group; otherwise, not reported (P value = 0.027 for comparison between clobetasol 10-minute group and vehicle group)	1.0	Not reported
Pruritus score	- 4.8 mm in clobetasol 5-minute group; otherwise, not reported (P value = 0.007 for comparison with vehicle)	- 34 mm	- not reported in text (8.9 mm approximated from figure)
Any adverse effects	1 participant (9%) in all groups experienced burning. 1 participant in clobetasol 10-minute group reported dry skin. 1 participant in clobetasol 5-minute group reported folliculitis	1 participant (9%) experienced burning. Eczema was reported in 1 person	1 participant (9%) experienced burning

[1]Outcome "erythema scores" refers to erythema scores at end of study. A lower score relates to a better treatment effect.
[2]Outcome "scaling scores" refers to scaling scores at end of study. A lower score relates to a better treatment effect.

APPENDICES

Appendix 1. CENTRAL (Cochrane Library) search strategy

#1 MeSH descriptor: [Malassezia] this term only
#2 ("scalp dermatoses" or "scalp dermatosis" or "scalp dermatitis" or "scalp eczema"):ti,ab,kw
#3 ("seborrheic dermatitis" or "seborrhoeic dermatitis" or malassezia or "cradle cap" or dandruff or "seborrheic eczema" or "seborrhoeic eczema"):ti,ab,kw
#4 MeSH descriptor: [Dermatitis, Seborrheic] this term only
#5 MeSH descriptor: [Scalp Dermatoses] this term only
#6 #1 or #2 or #3 or #4 or #5

Appendix 2. MEDLINE (OVID) search strategy

1. exp Dermatitis, Seborrheic/
2. seborrh$ dermatitis.mp.
3. scalp dermatos$.mp.
4. exp Scalp Dermatoses/
5. scalp dermatitis.mp.
6. scalp eczema.mp.
7. dandruff.mp.
8. Malassezia.mp. or exp Malassezia/
9. cradle cap.mp.
10. seborrh$ eczema.mp.
11. or/1-10
12. randomized controlled trial.pt.
13. controlled clinical trial.pt.
14. randomized.ab.

15. placebo.ab.
16. clinical trials as topic.sh.
17. randomly.ab.
18. trial.ti.
19. 12 or 13 or 14 or 15 or 16 or 17 or 18
20. exp animals/ not humans.sh.
21. 19 not 20
22. 11 and 21

Appendix 3. Embase (OVID) search strategy

1. random$.mp.
2. factorial$.mp.
3. (crossover$ or cross-over$).mp.
4. placebo$.mp. or PLACEBO/
5. (doubl$ adj blind$).mp.
6. (singl$ adj blind$).mp.
7. (assign$ or allocat$).mp.
8. volunteer$.mp. or VOLUNTEER/
9. Crossover Procedure/
10. Double Blind Procedure/
11. Randomized Controlled Trial/
12. Single Blind Procedure/
13. 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12
14. Seborrh$ dermatitis.ti,ab.
15. scalp dermatitis.ti,ab.
16. scalp eczema.ti,ab.
17. cradle cap.ti,ab.
18. exp *dandruff/
19. exp *Malassezia/
20. dandruff.ti,ab.
21. malassezia.ti,ab.
22. exp *seborrheic dermatitis/
23. scalp dermatos$.ti,ab.
24. seborrh$ eczema.ti,ab.
25. or/14-24
26. 13 and 25

Appendix 4. LILACS search strategy

((Pt RANDOMIZED CONTROLLED TRIAL OR Pt CONTROLLED CLINICAL TRIAL OR Mh RANDOMIZED CONTROLLED TRIALS OR Mh RANDOM ALLOCATION OR Mh DOUBLE-BLIND METHOD OR Mh SINGLE-BLIND METHOD OR Pt MULTICENTER STUDY) OR ((tw ensaio or tw ensayo or tw trial) and (tw azar or tw acaso or tw placebo or tw control$ or tw aleat$ or tw random$ or (tw duplo and tw cego) or (tw doble and tw ciego) or (tw double and tw blind)) and tw clinic$)) AND NOT ((CT ANIMALS OR MH ANIMALS OR CT RABBITS OR CT MICE OR MH RATS OR MH PRIMATES OR MH DOGS OR MH RABBITS OR MH SWINE) AND NOT (CT HUMAN AND CT ANIMALS)) [Words] and “seborrh$ dermatitis” or seborreico or dandruff or caspa or “cradle cap” or “costra lactea” or malassezia or “scalp dermatos$” or “eczema seborreico” or “dermatitis seborreica” [Words]

WHAT'S NEW

Date	Event	Description
22 August 2017	Amended	Typos corrected (two instances of vitamin C should be vitamin D)

HISTORY

Protocol first published: Issue 11, 2011
Review first published: Issue 5, 2014

Date	Event	Description
9 July 2015	Amended	A search of MEDLINE and Embase in June 2015 found studies that were, in the main, looking at single interventions, which are unlikely to alter the overall conclusion. There are a few small studies on sertaconazole, but not quite enough to merit an update, so an update has not been considered necessary at this time. Our Trials Search Co-ordinator will run a new search in summer 2016 to re-assess whether an update is needed.

CONTRIBUTIONS OF AUTHORS

HK was the contact person with the editorial base.
HK co-ordinated the contributions from the co-authors.
HK, TOk, PP, TOr, and JJ screened papers against eligibility criteria.
HK and TOk obtained data on ongoing and unpublished studies.
HK and TOk appraised the quality of papers.
HK, TOk, and JJ extracted data for the review and sought additional information about papers.
TOk and HK entered data into RevMan.
HK and VK analysed and interpreted data.
VK, HK, and TOk worked on the methods sections.
HK, EO, and TOk drafted the clinical sections of the background and responded to the clinical comments of the referees.
KA commented on the drafts (protocol and review).
JV was the consumer co-author and checked the review for readability and clarity, as well as ensuring outcomes are relevant to consumers.
JV is the guarantor of the review.

Disclaimer

The views and opinions expressed therein are those of the authors and do not necessarily reflect those of the NIHR, NHS or the Department of Health, UK, or the Finnish Medicines Agency Fimea.

DECLARATIONS OF INTEREST

PP has received a research grant from AstraZeneca and consultancy fees from ESiOR Ltd (a health economy consultancy that provides research and consulting services to the pharmaceutical industry). These projects have not been related to treatment for seborrhoeic dermatitis.

None of the other authors involved in this review have declared any interests.

SOURCES OF SUPPORT

Internal sources

- Finnish Medicines Agency (FIMEA), Finland.
- The Finnish Institute of Occupational Health, Finland.
- The Cochrane Occupational Safety and Health Review Group, Finland.
- The Nigerian Branch of the South African Cochrane Centre, Nigeria.

External sources

- The National Institute for Health Research (NIHR), UK.

  The NIHR, UK, is the largest single funder of the Cochrane Skin Group.

DIFFERENCES BETWEEN PROTOCOL AND REVIEW

In the protocol under Types of participants, we stated that we would include studies of adults or adolescents (> 16 years) with SeD. When assessing the eligibility of the trials, we used the percentage of 75 or more as a measure to judge whether the trial fulfilled this inclusion criterion. We made the decision that at least 75% of the study participants had to be over 10 years of age to fulfil the age criterion.

We did not explore heterogeneity other than regarding the strength of steroid treatment where feasible. This is reasoned by the small number of studies in each comparison. In the protocol, we planned to possibly explore age, gender, and dose (frequency) distributions as a cause for heterogeneity.

Two additional authors (JJ and TOr) were added to the people undertaking the data collection and analysis. An additional resource was added to electronic searches (GREAT).

NOTES

A search of MEDLINE and Embase in June 2015 found studies that were, in the main, looking at single interventions, which are unlikely to alter the overall conclusion. There are a few small studies on sertaconazole, but not quite enough to merit an update, so an update has not been considered necessary at this time. Our Trials Search Co-ordinator will run a new search in summer 2016 to re-assess whether an update is needed.

INDEX TERMS

Medical Subject Headings (MeSH)

Anti-Inflammatory Agents [*therapeutic use]; Antifungal Agents [therapeutic use]; Calcineurin Inhibitors; Dermatitis, Seborrheic [*drug therapy]; Dermatologic Agents [*therapeutic use]; Facial Dermatoses [*drug therapy]; Lithium Compounds [therapeutic use]; Randomized Controlled Trials as Topic; Scalp Dermatoses [*drug therapy]; Steroids [therapeutic use]

MeSH check words

Humans