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Indoor salt water baths followed by artificial ultraviolet B light for chronic plaque psoriasis (Review)

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[Intervention Review]

Indoor salt water baths followed by artificial ultraviolet B light for chronic plaque psoriasis

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ABSTRACT

Background

Chronic plaque psoriasis is an immune-mediated, chronic, inflammatory skin disease, which can impair quality of life and social interaction. Disease severity can be classified by the psoriasis area and severity index (PASI) score ranging from 0 to 72 points. Indoor artificial salt bath with or without artificial ultraviolet B (UVB) light is used to treat psoriasis, simulating sea bathing and sunlight exposure; however, the evidence base needs clear evaluation.

Objectives

To assess the effects of indoor (artificial) salt water baths followed by exposure to artificial UVB for treating chronic plaque psoriasis in adults.

Search methods

We searched the following databases up to June 2019: the Cochrane Skin Group Specialised Register, CENTRAL, MEDLINE, Embase, and LILACS. We also searched five trial registers, and checked the reference lists of included studies, recent reviews, and relevant papers for further references to relevant trials.

Selection criteria

Randomised controlled trials (RCTs) of salt bath indoors followed by exposure to artificial UVB in adults who have been diagnosed with chronic plaque type psoriasis. We included studies reporting between-participant data and within-participant data. We evaluated two different comparisons: 1) salt bath + UVB versus other treatment without UVB; eligible comparators were exposure to psoralen bath, psoralen bath + artificial ultraviolet A UVA) light, topical treatment, systemic treatment, or placebo, and 2) salt bath + UVB versus other treatment + UVB or UVB only; eligible comparators were exposure to bath containing other compositions or concentrations + UVB or UVB only.

Data collection and analysis

We used standard methodological procedures expected by Cochrane. We used GRADE to assess the certainty of the evidence.

The primary efficacy outcome was PASI-75, to detect people with a 75% or more reduction in PASI score from baseline. The primary adverse outcome was treatment-related adverse events requiring withdrawal. For the dichotomous variables PASI-75 and treatment-related adverse events requiring withdrawal, we estimated the proportion of events among the assessed participants.

The secondary outcomes were health-related quality of life using the Dermatology Life Quality Index, (DLQI) pruritus severity measured using a visual analogue scale, time to relapse, and secondary malignancies.

Main results

We included eight RCTs: six reported between-participant data (2035 participants; 1908 analysed), and two reported within-participant data (70 participants, 68 analysed; 140 limbs; 136 analysed). One study reported data for the comparison salt bath with UVB versus other treatment without UVB; and eight studies reported data for salt bath with UVB versus other treatment with UVB or UVB only. Of these eight studies, only five reported any of our pre-specified outcomes and assessed the comparison of salt bath with UVB versus UVB only. The one included trial that assessed salt bath plus UVB versus other treatment without UVB (psoralen bath + UVA) did not report any of our primary outcomes. The mean age of the participants ranged from 41 to 50 years of age in 75% of the studies. None of the included studies reported on the predefined secondary outcomes of this review. We judged seven of the eight studies as at high risk of bias in at least one domain, most commonly performance bias. Total trial duration ranged between at least two months and up to 13 months.

In five studies, the median participant PASI score at baseline ranged from 15 to 18 and was balanced between treatment arms. Three studies did not report PASI score. Most studies were conducted in Germany; all were set in Europe. Half of the studies were multi-centred (set in spa centres or outpatient clinics); half were set in a single centre in either an unspecified settings, a psoriasis daycare centre, or a spa centre. Commercial spa or salt companies sponsored three of eight studies, health insurance companies funded another, the association of dermatologists funded another, and three did not report on funding.

When comparing salt bath plus UVB versus UVB only, two between-participant studies found that salt bath plus UVB may improve psoriasis when measured using PASI 75 (achieving a 75% or more reduction in PASI score from baseline) (risk ratio (RR) 1.71, 95% confidence interval (CI) 1.24 to 2.35; 278 participants; low-certainty evidence). Assessment was conducted at the end of treatment, which was equivalent to six to eight weeks after start of treatment. The two trials which contributed data for the primary efficacy outcome were conducted by the same group, and did not blind outcome assessors. The German Spas Association funded one of the trials and the funding source was not stated for the other trial.

Two other between-participant studies found salt bath plus UVB may make little to no difference to outcome treatment-related adverse events requiring withdrawal compared with UVB only (RR 0.96, 95% CI 0.35 to 2.64; 404 participants; low-certainty evidence). One of the studies reported adverse events, but did not specify the type of events; the other study reported skin irritation. One within-participant study found similar results, with one participant reporting severe itch immediately after Dead Sea salt soak in the salt bath and UVB group and two instances of inadequate response to phototherapy and conversion to psoralen bath + UVA reported in the UVB only group (low-certainty evidence).

Authors' conclusions

Salt bath with artificial ultraviolet B (UVB) light may improve psoriasis in people with chronic plaque psoriasis compared with UVB light treatment alone, and there may be no difference in the occurrence of treatment-related adverse events requiring withdrawal. Both results are based on data from a limited number of studies, which provided low-certainty evidence, so we cannot draw any clear conclusions.

The reporting of our pre-specified outcomes was either non-existent or limited, with a maximum of two studies reporting a given outcome.

The same group conducted the two trials which contributed data for the primary efficacy outcome, and the German Spas Association funded one of these trials. We recommend further RCTs that assess PASI-75, with detailed reporting of the outcome and time point, as well as treatment-related adverse events. Risk of bias was an issue; future studies should ensure blinding of outcome assessors and full reporting.

PLAIN LANGUAGE SUMMARY

Indoor bathing in salt water followed by exposure to artificial ultraviolet B light for chronic plaque psoriasis

Review question

We reviewed the evidence about the effect of indoor bathing in salt water for adults with chronic plaque psoriasis followed by artificial ultraviolet B (UVB) light treatment. We evaluated two different comparisons: 1) Salt bath with UVB versus other treatment without UVB; eligible comparators were exposure to psoralen bath, psoralen bath + artificial ultraviolet A (UVA) light, topical treatment, systemic treatment (oral or injected medicines that work throughout the entire body), or placebo (an inactive substance). 2) Salt bath with UVB versus other treatment with UVB or UVB only; eligible comparators were exposure to bath containing other compositions or concentrations + UVB or UVB only. The degree of severity of psoriasis can be measured by the psoriasis area and severity index (PASI). Improvement can be indicated by a reduction of PASI. We requested at least a 75% reduction in PASI-75 score to evaluate a potential beneficial effect. To evaluate a potential harmful effect, we chose treatment-related side effects severe enough to stop treatment.

Background

Chronic plaque psoriasis is a skin disease characterised by red-coloured lesions with silvery scales. Bathing in the Dead Sea and exposure to the sun may improve the lesions but may not be practical for most patients. Artificial salt bath and exposure to UVB could simulate the natural exposure.

Study characteristics

The evidence is current to June 2019. We included eight trials (1976 analysed participants). One included trial assessed salt bath plus UVB versus other treatment without UVB (psoralen bath + UVA), but it did not report our primary outcomes for this comparison. Eight trials assessed our second comparison of interest: salt bath with UVB versus other treatment with UVB or UVB only, and those that reported any outcomes of interest (only five studies) specifically compared salt bath with UVB versus UVB only.

No study reported our secondary outcomes. The duration of trials in total ranged between at least two months and up to 13 months. Outcomes were assessed at the end of treatment.

We analysed trials in which different treatments were applied to different participants, and we separately analysed trials in which different treatments were applied to the same participant, but to different body parts. Participants were male or female, and their ages mostly ranged from 41 to 50 years. In five studies, the median PASI score at baseline ranged from 15 to 18 and was balanced between treatment arms. Three studies did not report PASI score. Three studies were sponsored by commercial spa or salt companies, one by health insurance companies, one by an association of dermatologists, and three did not report on funding. Half of the studies were conducted in multiple centres; the remainder were conducted in single centres. Most of the studies were conducted in Germany; all were based in Europe.

Key results

No study reported primary outcome data for the comparison salt bath with UVB versus other treatment without UVB; five studies reported primary outcome data for salt bath with UVB versus UVB only. With respect to achieving PASI-75, the pooled data of two studies indicated that salt bath + UVB may reduce psoriasis severity compared to UVB only (low-certainty evidence); however, these two studies were conducted by the same group, and the German Spas Association funded one of the trials (the other trial did not report any funding source). Neither of the studies hid the treatment allocation from the outcome assessors.

When assessing treatment-related adverse events requiring withdrawal, data from three other studies showed there may be little to no difference between salt bath plus UVB and the comparator UVB only (low-certainty evidence). The adverse events included skin irritation and severe itch immediately after Dead Sea salt soaks (salt bath + UVB group), and inadequate response to phototherapy and conversion to psoralen bath + UVA (UVB only group).

Certainty of the evidence

We judged the evidence for 'PASI-75' and 'treatment-related adverse events requiring withdrawal' as low certainty. Our confidence was affected by limitations, such as risk of bias (examples being inadequate blinding and high probability of publication bias). The reporting of our outcomes was non-existent or limited.

SUMMARY OF FINDINGS

Summary of findings 1. Salt bath + UVB compared with UVB alone for chronic plaque psoriasis

Salt bath + UVB compared with UVB alone for chronic plaque psoriasis

Patient or population: patients with chronic plaque psoriasis
Setting: indoor clinic or spa
Intervention: salt bath + UVB
Comparison: UVB alone

Outcomes	Illustrative comparative risks (95% CI)*		Relative effect (95% CI)	Number of participants (studies)	Certainty of evidence (GRADE)	Comments
	Assumed risk[c]	Corresponding risk				
PASI-75 (number of participants with event) 6 to 8 weeks after start of treatment	Study population 285 per 1000	487 per 1000 (353 to 669)	RR 1.71 (1.24 to 2.35)	278 (2 studies)	⊕⊕⊖⊖ LOW[a]	The event was defined as achieving a 75% or more reduction in PASI score from baseline.
Treatment-related adverse events requiring withdrawal (number of participants withdrawing) 3 to 8 weeks after the start of treatment[d]	Study population 35 per 1000	34 per 1000 (12 to 92)	RR 0.96 (0.35 to 2.64)	404 (2 studies)	⊕⊕⊖⊖ LOW[b]	The event was defined as dropping out of the study because of treatment-related complications.

*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; **PASI:** Psoriasis Area and Severity Index.

GRADE Working Group grades of evidence
High certainty: we are very confident that the true effect lies close to that of the estimate of the effect.
Moderate certainty: we are moderately confident in the effect estimate; the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
Low certainty: our confidence in the effect estimate is limited; the true effect may be substantially different from the estimate of the effect.
Very low certainty: we have very little confidence in the effect estimate; the true effect is likely to be substantially different from the estimate of effect.

[a] We downgraded the certainty of evidence by two levels for this outcome. We downgraded one level because of study limitations (risk of bias). Due to lack of blinding, we judged a high bias of performance bias. We downgraded one level because of high probability of publication bias. The only two between-participant studies that did contribute data on salt bath + UVB versus UVB alone (Brockow 2007a; Brockow 2007b) to this outcome were conducted by the same sponsor.

[b] We downgraded the certainty of evidence by two levels for this outcome. We downgraded one level because of study limitations (risk of bias). Due to lack of blinding, we judged a high risk of performance bias. We downgraded one level because of high probability of publication bias. There were only two between-participant studies (Klein 2011; Leaute-Labreze 2001) that contributed data on salt bath + UVB versus UVB alone to this outcome.

[c] The assumed risk is based on the mean number of events across the control groups. Calculation regarding PASI-75 response: Number of events: 22 + 14 = 36, total number of participants: 66 + 60 = 126, risk per 1000: 36 / 126 * 1000 = 285.

[d] Two between-participant studies (Klein 2011, Leaute-Labreze 2001) reported seven events with salt bath + UVB and seven events with UVB only. One additional within-participant study (Dawe 2005) reported one event with salt bath + UVB and two events with UVB only.

BACKGROUND

Description of the condition

Prevalence

Psoriasis is a multifactorial, immune-mediated chronic inflammatory skin disease (Nestle 2009), affecting roughly 2% of the world population (Christophers 2001). In population-based surveys, the prevalence of psoriasis is 2.2% in the continental USA (Stern 2004), and it is 1.5% in the UK (Gelfand 2005). In adults, prevalence ranges from 0.9% to 8.5% and incidence ranges from 78.9 to 230 per 100,000 person-years on a global scale (Parisi 2013). The occurrence of psoriasis increases with age and with distance of geographic regions from the equator; there is no clear difference in the prevalence between men and women (Parisi 2013).

Clinical signs and course

Clinically, chronic plaque psoriasis, which is also known as psoriasis vulgaris, is the most common type of psoriasis, affecting 80% to 90% of people with psoriasis (Griffiths 2007; Lebwohl 2003). It is characterised by easily defined red-coloured lesions (Nestle 2009). The plaques are a result of an inflammatory and hyperproliferative (growing faster than usual) epidermis (Nestle 2009). They are typically found on the outer sides of the elbow and knee joints as well as on the scalp and back. A genetic predisposition may be the most important basis for an onset of psoriasis (Nestle 2009). A dysregulated immune system may explain the pathogenesis of inflammation and keratinocyte activation and proliferation (Nestle 2009). The disease severity can change with time, sometimes with long periods of calm and sometimes with severe exacerbation (Parisi 2013), with or without recognised trigger factors, such as infection and other environmental factors as referred to in section 'Risk factors' in Description of the condition. The extent of the affected body surface area may be used to classify the severity as mild (less than 5%), moderate (5% to 10%), or severe (greater than 10%) (Menter 2007). Henseler suggested two forms of nonpustular psoriasis: the early onset form was associated with familial inheritance, and the late onset form occurred predominantly sporadically (Henseler 1985).

Symptoms

The main symptoms are itching and pain associated with uncomfortable scaling as a result of loss of cells from the epidermal layer of the skin (Martin 2015).

Diagnosis

A medical doctor can suspect the diagnosis on the appearance of the skin and a dermatologist may confirm the diagnosis. Scaly and erythematous plaques that may be painful and itching are typical skin characteristics (Nestle 2009). A skin biopsy may be helpful to clarify the clinical diagnosis.

Prognosis

The majority of patients experience mild skin lesions (Nestle 2009). Severe lesions may impair quality of life and social interaction.

Severity indices

Physician-reported severity indices

Fredriksson 1978 developed the Psoriasis Area and Severity Index (PASI). It is a measure of average redness, thickness, and scaliness of skin lesions weighted by the area of involvement. Table 1 displays characteristics of the PASI. Response to therapy may be assessed by the percentage of people who have achieved a 75% or more reduction in their PASI score from baseline, which is referred to as PASI-75. Itching is a substantial symptom of psoriasis, which may be assessed by a visual analogue scale (VAS) from 0 ('no itching') to 100 ('severe itching') as proposed by Zhu 2014.

Patient-reported severity indices

Finlay 1994 developed the Dermatology Life Quality Index (DLQI). The following website provides further information and interpretation: www.dermatology.org.uk. The aim of this questionnaire is to measure how much the skin problem of a person has affected his or her life over the previous week (see Table 2).

Risk factors

The process by which psoriasis arises is not fully understood. Population, family, and twin studies have shown a genetic contribution to psoriasis (Griffiths 2007; Lønnberg 2013; Rahman 2005), which includes the association of psoriasis with certain human leukocyte antigen (HLA) alleles (Gupta 2014). An allele may be described of either the part of a gene that was inherited from the father, or the other part of a gene that was inherited from the mother. HLA genes encode for certain proteins on the surface of cells that help control the immune system. Currently, it is estimated that genetic data explain only 30% of psoriasis (Barker 2014). Prieto-Perez 2013 stated that "the many genes associated with psoriasis and the immune response include tumour necrosis factor alpha, interleukin 23, and interleukin 12."

Prieto-Perez 2013 also referred to the development of new drugs (e.g. etanercept, adalimumab, infliximab, ustekinumab, secukinumab) that target cytokines (e.g. tumour necrosis factor alpha, p40 subunit of interleukin 23 and interleukin 12) and, as a result, suppress the unwanted dysregulated and more than usual immune response. Bachelez 2013 also addressed the involvement of the immune system in the pathogenesis of psoriasis and stated, for example, that interleukin 36 is strongly elevated in the keratinocytes of psoriatic tissue.

Huerta 2007 conducted a prospective cohort study with nested case-control analysis, in which a group of people were followed over a period of time. A random sample of controls was matched to people who developed psoriasis by age, sex, and calendar year. Odds ratios were adjusted for age and other risk factors. The study found an association between previous skin disorders, infectious disorders, obesity, and smoking with the onset of psoriasis. The authors did not find an association with other potential risk factors, such as stress, diabetes (high blood sugar), hypertension (high blood pressure), hyperlipidaemia (high blood fat), cardiovascular disease, or rheumatoid arthritis.

Comorbidity

Psoriasis may be associated with other diseases, such as arthritis, depression, inflammatory bowel disease, and cardiovascular diseases (Oliveira 2015). As inflammation is involved in some of the associated diseases, it can be speculated whether these diseases may be connected with psoriasis on the ground of common genetic and immune-related factors.

Health-related quality of life

Psoriasis causes considerable psychological disability and has a major impact on a person's quality of life (Rapp 1999). Thus, perception of psychosocial disability and quality of life may be paramount when assessing the importance of the condition to an individual and the subsequent treatment of the disease (Menter 2007). A patient-reported index of disease severity is described above (DLQI). Wahl interviewed 22 hospitalised patients with psoriasis and found that bodily suffering was a core variable with regard to the patients' experience of living with psoriasis (Wahl 2002). For people with psoriasis, itching is a measure of the effect the disease has on quality of life (Zhu 2014).

Cost

The financial burden on people with this disease and on healthcare providers is considerable and was about 35.2 billion dollars in the USA in 2013 (Vanderpuye-Orgle 2015). It was estimated that incremental medical costs contributed 34.7%; reduced health-related quality of life, 33.5%; and productivity losses, 31.8% (Vanderpuye-Orgle 2015).

Description of the intervention

Salt bath followed by artificial ultraviolet B light was developed to simulate exposure to salt and sunlight delivered during climatotherapy (relocation to a region with a climate more favourable to the outcome) at the Dead Sea (Huang 2018). For example, the whole body is soaked in salt water for 15 to 30 minutes, which may have various concentrations ranging from 1 g to 250 g sodium chloride dissolved in one litre water. The soaking is repeated several times a week for a maximum of 20 to 30 applications within a time period of eight weeks. After bathing, various doses of ultraviolet B (UVB) light are applied to the whole body (Gambichler 2000a). The combination of bathing in salt water with UVB bathing thereafter may be called balneophototherapy (Halverstam 2008). Patients with psoriasis could improve with balneophototherapy (Harari 2007).

Treatments for people with chronic plaque psoriasis include a variety of alternatives such as:

- topical therapy including steroidal and non-steroidal agents;
- systemic medications (Sbidian 2017) including various biological drugs (Nunez 2019), and additional investigational agents being studied (Ellis 2019);
- phototherapy including UVB irradiation alone without bathing in salt water, and
- photochemotherapy including ultraviolet A (UVA) irradiation plus psoralen, a compound that aids the absorption of UVA irradiation by making the skin more susceptible to the effects of light rays.

Ultraviolet radiation and its wavelength is defined by the International Commission on Illumination CIE 2011: "radiation for which the wavelengths are shorter than those for visible radiation; the range between 100 nm and 400 nm is commonly subdivided into: UVA: 315 nm to 400 nm; UVB: 280 nm to 315 nm; and UVC: 100 nm to 280 nm". UVB may be subdivided by some authors in broad band (280 nm to 315 nm), narrow band (311), or selective band (300 nm to 315 nm).

The choice of an appropriate therapy is associated with the grade of severity and may be used as comparators with salt baths.

- Topical therapy including steroidal and non-steroidal agents may be mainly used for mild or localised disease (Lebwohl 2005; Menter 2007).
- Systemic medications are mainly used for severe or refractory disease (Lebwohl 2005; Menter 2007), which include various oral agents as well as injectable biological agents.
- Phototherapy including UVB irradiation alone without bathing in salt water may be used predominantly for moderate or more extensive disease (Lebwohl 2005; Menter 2007).
- Phototherapy and photochemotherapy may be also used for those not responding sufficiently to topical treatment (Singh 2016; van de Kerkhof 2004); psoralen plus UVA (PUVA) light photochemotherapy may be used for moderate or severe disease (Lebwohl 2005; Menter 2007). For people with widespread chronic plaque psoriasis, phototherapy may be regarded as the first-choice treatment because it may have fewer adverse events than systemic or biological agents (Nguyen 2009). Psoralen is a photosensitising compound that aids the absorption of UVA light and increases the skin's sensitivity to light, but subsequently may have carcinogenic properties (Archier 2012). It is administered either orally, in bath water, as a cream, or as a gel. Thus, PUVA is divided into oral PUVA, bath PUVA, and topical (cream) PUVA (Chen 2013). Momtaz 1998 reported that PUVA photochemotherapy has been used in psoriasis and 23 other skin disorders. The risk of development of squamous cell carcinomas may be high if the patients have received ionising radiation or inorganic arsenic, or if patients require continuous treatment for many years. Melanomas may also develop in a few patients. Stern 1998 warned that the use of PUVA should be weighed against the persistent, dose-related increase in the risk of squamous cell cancer.

How the intervention might work

Salt bath, with or without phototherapy, is being widely used to treat moderate-to-severe psoriasis. The mechanism of action of UVB is not completely clear (Weatherhead 2013). UVB phototherapy for treating psoriasis may result in the induction of apoptosis (programmed cell death) of keratinocytes, which are the main cell types in the skin, as well as epidermal and dermal T lymphocytes (cells within the skin that are involved in inflammation) (Weatherhead 2011; Wong 2013). The minimum amount of UVB that produces redness 24 hours after exposure is used as the starting dose for UVB light treatments; this 'minimal erythema dose' decreases after salt water bathing (Gambichler 1998).

There may be increased UV transmission to the skin after soaking in salt water (Gambichler 2011), which may lead to stronger inflammation (e.g. UV-induced erythema) and also to increased apoptosis of keratinocytes and T lymphocytes, and thus improved clearance of psoriasis (Gambichler 2011; Wong 2013). The mechanism of action of low concentrations of sodium chloride in water used in indoor salt water baths followed by artificial UVB light is unknown. Speculative mechanisms have been proposed, for example, salt solutions might wash out unfavourable substances from the skin lesions, salt water bathing might increase skin sensitivity to UVB light and thereby increasing its action on the lesion, single salt components could act favourably on the cells

of the skin lesions, the intervention might inhibit cell proliferation (Schempp 2000).

Why it is important to do this review

Studies suggest that indoor salt water baths with (Brockow 2007), or without exposure to artificial UVB (Schiener 2007), may benefit patients with psoriasis. However, the evidence underlying clinical efficacy, such as longer remission from disease and higher dermatology-related quality of life, has not yet been clearly evaluated. It should be pointed out that the use of high concentrations of salt is cumbersome due to the large amounts of salt needed. Although indoor salt water baths are widely used in practice to treat chronic plaque psoriasis, no systematic review has been conducted to assess its effectiveness for reducing skin lesions and improving quality of life. Therefore, the aim of this review is to evaluate the efficacy and any severe adverse events of indoor salt water baths by focusing on patient-centred outcomes. The methods planned for this review were published as a protocol: *Indoor salt water baths followed by artificial UVB light for chronic plaque psoriasis* (Peinemann 2015).

OBJECTIVES

To assess the effects of indoor salt water baths followed by exposure to artificial ultraviolet B (UVB) light for treating chronic plaque psoriasis in adults.

METHODS

Criteria for considering studies for this review

Types of studies

Randomised controlled trials (RCTs) that randomised people or limbs to either the test intervention or a control intervention.

We did not find a reason to exclude right-left comparative studies. Nevertheless, pretreatment of the skin of a body part investigated in a cross-over design may influence the results as opposed to no pretreatment. To prevent the concerning additional bias, we excluded cross-over designs. We suggested that simultaneous application of the intervention of interest on multiple body parts of each participant may distract the scoring of the Psoriasis Area and Severity Index (PASI) response and other subjective assessments. We are positive that right-left comparative study should not include comparing different body parts. Different body parts may be affected differently and the assessment may introduce bias. We did not find a reason to exclude cluster-randomised trials. Throughout the review, we used the term 'people or limbs' to accommodate people who were randomised, as well as randomised legs, arms, and elbows.

We planned to include the following designs.

- Simple parallel group design according to the *Cochrane Handbook for Systematic Reviews of Interventions*, section 9.3.1, quote: "participants are individually randomised to one of two intervention groups, and a single measurement for each outcome from each participant is collected and analyzed" (Higgins 2011).
- Multiple observations for the same outcome, specifically repeated measurements. If the data were to be included in a meta-analysis, we planned to select a single time point and to analyse only data at this time point for studies in which it was presented.
- Multiple observations for the same outcome, specifically, multiple body parts receive different interventions according to the Handbook section 9.3.8, quote: "These trials have similarities to cross-over trials: whereas in cross-over trials individuals receive multiple treatments at different times, in these trials they receive multiple treatments at different sites." (Higgins 2011). In the present review, we considered paired comparisons within participants, such as comparisons of right versus left arm, leg, elbow, or knee. We planned to separately analyse the within-participant data and the between-participant data.
- Cluster-randomised trials according to the Cochrane Handbook section 9.3.2, quote: "groups of participants, such as schools or families are randomized to different interventions. [...] Participants within any cluster often tend to respond in a similar manner, and thus their data can no longer be assumed to be independent of one another" (Higgins 2011).

We did not include the following study designs.

- Cross-over design according to the Handbook section 9.3.3, quote: "all participants receive all interventions in sequence: they are randomized to an ordering of interventions, and participants act as their own control.". We expected a high risk of carryover according to the Handbook section 16.4.2, quote: "Carryover is the situation in which the effects of an intervention given in one period persist into a subsequent period, thus interfering with the effects of different subsequent intervention" (Higgins 2011).
- Multiple observations for the same outcome, specifically, multiple body parts receive the same intervention according to the Handbook section 9.3.7, quote: "people are randomized, but multiple parts (or sites) of the body receive the same intervention, a separate outcome judgement being made for each body part, and the number of body parts is used as the denominator in the analysis. [...] This is similar to the situation in cluster-randomized trials, except that participants are the 'clusters" (Higgins 2011).
- Comparison of different body parts within participants, such as comparing arm versus leg.

Types of participants

Adults (i.e. 18 years of age or older) of any ethnic background or gender who have been diagnosed with chronic plaque type psoriasis by a dermatologist. We excluded people with pustular psoriasis, guttate psoriasis, or inverse psoriasis.

Types of interventions

The aim of this review was to assess the efficacy of salt bath added to ultraviolet B (UVB) light. We did not seek to assess efficacy of salt bath only.

Comparison 1: salt bath + UVB versus other treatment without UVB

Test intervention

Exposure to indoor salt water bath followed by artificial UVB light for chronic plaque psoriasis. We included studies where bathing in salt water was performed indoors during or prior to exposure

to UVB. We excluded studies where bathing in salt water was performed outdoors and for leisure purposes, such as bathing in geothermal sea water, bathing in a thermal lagoon, or bathing in a salty lake.

Control intervention

Exposure to psoralen bath, psoralen bath + artificial ultraviolet A (UVA) light, topical treatment, systemic treatment, or placebo.

Comparison 2: salt bath+ UVB versus other treatment + UVB or UVB only

Test intervention

Exposure to indoor salt water bath followed by artificial UVB for chronic plaque psoriasis. We included studies where bathing in salt water is performed indoors during or prior to exposure to UVB. We excluded studies where bathing in salt water is performed outdoors and for leisure purposes, such as bathing in geothermal sea water, bathing in a thermal lagoon, or bathing in a salty lake.

Control intervention

Exposure to bath containing other compositions or concentrations + UVB or UVB only.

Types of outcome measures

We did not use the outcomes listed here as criteria for including studies; they are the outcomes of interest within studies identified for inclusion.

Primary outcomes

Between-participant data as well as within-participant data:

1. physician-assessed outcome: psoriasis area and severity index (PASI)-75;
2. physician-assessed outcome: treatment-related adverse events requiring withdrawal.

Secondary outcomes

Between-participant as well as within-participant data:

1. participant-reported outcome: dermatology life quality index (DLQI);
2. participant-reported outcome: pruritus severity using a visual analogue scale (VAS) from 0 ('no itching') to 100 ('severe itching');
3. physician-reported outcome: time to relapse;
4. physician-assessed outcome: secondary malignancies.

We did not consider using the Physician Global Assessment (PGA), because we favoured PASI, which is reportedly validated and preferred for use in clinical trials (Robinson 2012).

Search methods for identification of studies

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

Electronic searches

The Cochrane Skin Information Specialist searched the following databases up to 4 June 2019:

- the Cochrane Skin Group Specialised Register using the search strategy in Appendix 1;
- the Cochrane Central Register of Controlled Trials (CENTRAL) 2019, Issue 6 in the Cochrane Library using the strategy in Appendix 2;
- MEDLINE via Ovid (from 1946) using the strategy in Appendix 3;
- Embase via Ovid (from 1974) using the strategy in Appendix 4; and
- LILACS (Latin American and Caribbean Health Science Information database, from 1982) using the strategy in Appendix 5.

Online trials registers

We (FP, SP) searched the following online trials registers up to 6 June 2019 using the term 'psoriasis' in the field 'condition' and 'phototherapy' in the field 'intervention':

- the ISRCTN registry (www.isrctn.com) (called 'The metaRegister of Controlled Trials' in the protocol);
- ClinicalTrials.gov (www.clinicaltrials.gov) (called 'The US National Institutes of Health Ongoing Trials Register' in the protocol);
- the Australian New Zealand Clinical Trials Registry (www.anzctr.org.au);
- the World Health Organization International Clinical Trials Registry Platform (ICTRP) (apps.who.int/trialsearch/); and
- the EU Clinical Trials Register (www.clinicaltrialsregister.eu).

Searching other resources

References from bibliographies

We checked the bibliographies of included studies, relevant articles, and review articles for further references to relevant trials.

Adverse effects

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

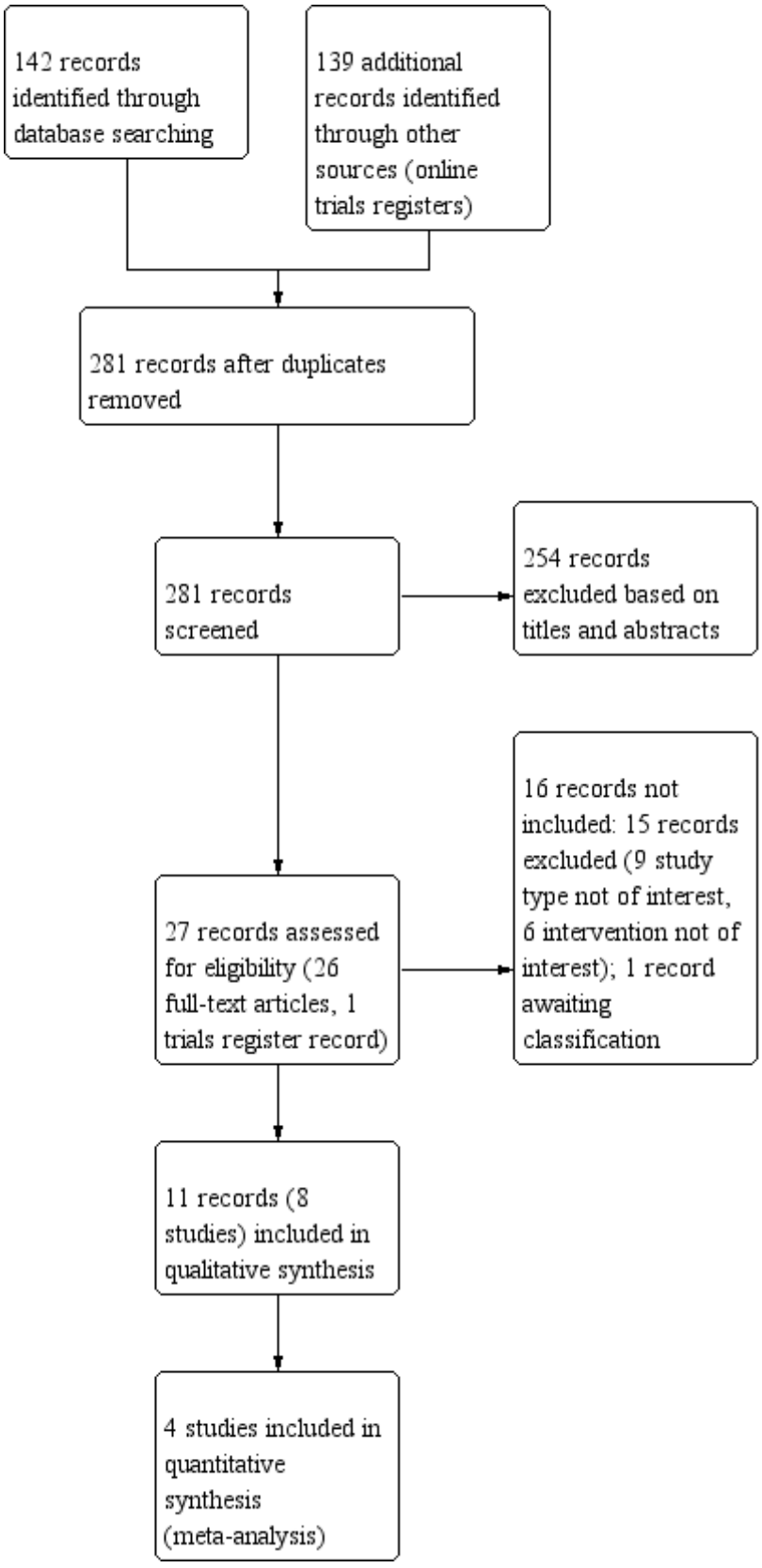
Data collection and analysis

Some parts of the methods section of this Cochrane Review used text that was originally published in other Cochrane publications co-authored by FP and protocol contributor Doreen Tushabe (predominantly Peinemann 2013a and Peinemann 2013b), as well as using text that was originally published in the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011).

Selection of studies

While preparing this systematic review, we endorsed the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) statement, adhered to its principles and conformed to its checklist (Moher 2009). We downloaded all titles and abstracts retrieved by electronic searching to an Excel spreadsheet (Microsoft Corp 2011), and removed any duplicates. Two review authors (FP, SP) independently examined any remaining references. We included a study selection flow chart in the review (Figure 1).

Figure 1. Study flow diagram.



We excluded those studies that clearly did not meet the inclusion criteria and obtained copies of the full text of potentially relevant references. Two review authors (FP, SP) independently assessed the eligibility of retrieved papers. We resolved any disagreements by discussion between the two review authors; no third party arbitration was necessary. We documented reasons for exclusion in the Characteristics of excluded studies tables. If we identified multiple reports of one study we used the most-up-to-date full-text results. We checked the multiple reports for possible duplicate data, addressed the issue and did not include duplicate data in the analysis.

Data extraction and management

For each included study, two review authors (FP, SP) extracted study characteristics and outcomes independently onto a data extraction form. The data included: information on study design, participant characteristics (such as inclusion criteria, age, disease severity, comorbidity, previous treatment, number enrolled in each arm), interventions (such as type of irradiation, type of bath, dose applied, duration of therapy, control treatment), risk of bias, follow-up duration, outcome measures, and deviations from the study protocol. We pilot tested *The Cochrane Editorial Resources Committee's data collection form for intervention reviews* (for RCTs only) available from the Cochrane Skin Group website: www.skin.cochrane.org/resources, then used this for data extraction. We resolved differences between review authors by discussion.

Assessment of risk of bias in included studies

Two review authors (FP, SP) independently appraised the risk of bias in the included studies. We resolved differences between review authors by discussion. We used the items listed within Cochrane's tool for assessing risk of bias (Higgins 2011):

- random sequence generation (selection bias);
- allocation concealment (selection bias);
- blinding of participants and personnel (performance bias);
- blinding of outcome assessment (detection bias);
- incomplete outcome data such as missing data (attrition bias);
- selective reporting such as not reporting pre-specified outcomes (reporting bias); and
- other sources of bias such as bias related to the specific study design (other bias).

In general, a judgement of "low risk" of bias was given if plausible bias is unlikely to seriously alter the results, for example, if the participants and investigators enrolling those participants could not foresee the assignment. A judgement of "high risk" of bias was given if plausible bias seriously weakens confidence in the results, for example, if the participants or investigators enrolling those participants could possibly foresee the assignments. A judgement of "unclear" risk of bias was given if plausible bias raises some doubt about the results, for example, the method of concealment is not described or not described in sufficient detail to allow a definite judgement.

To draw conclusions about the overall risk of bias for an outcome, it was necessary to summarise the results of the 'Risk of bias' assessments performed for each individual study. We assessed the risk of bias at study level, not by outcome. We aligned the summary assessment to the Cochrane 'Possible approach for summary assessments of the risk of bias for each important outcome (across domains) within and across studies', as shown in Table 8.7a in the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011). We assessed whether the risk of bias for a single outcome was low, unclear, or high, then we interpreted whether the plausible bias was unlikely to seriously alter the results, raises some doubts about the results, or seriously weakened the confidence in the results. We assessed within a study whether there was a low risk of bias for all key domains, an unclear risk of bias for one or more domains, or a high risk of bias for one or more key domains. We assessed across studies whether most information was from studies at low risk of bias or at high or unclear risk of bias, and we assessed across studies whether the proportion of information from studies at high risk of bias was sufficient to affect the interpretation of results.

Measures of treatment effect

For time-to-event data such as survival, we planned to extract the hazard ratio (HR) and its standard error or confidence interval (CI) from trial reports; if these were not reported, we planned to estimate the logHR and its standard error using the methods of Parmar 1998 and using the tool provided by Tierney 2007.

For dichotomous data, such as PASI-75 and treatment-related adverse events requiring withdrawal, we estimated the proportion of events among the assessed participants. We pooled the data and estimated a risk ratio (RR) and a P value for overall effect by using the Mantel-Haenszel statistic and a fixed-effect model. If the P value was not reported by the study, then we estimated the P value by using the web-based Easy Fisher Exact Test Calculator (Social Science Statistics 2018). In case of rare events, we planned to use Peto odds ratios instead, but this was not applied.

For continuous outcomes (e.g. PASI), we planned to extract the final value or change from baseline and corresponding standard deviation (SD) of the outcome of interest and the number of people or limbs assessed at endpoint in each treatment arm at the end of follow-up. This was in order to estimate the mean difference (MD) or standardised mean difference (SMD) between treatment arms. We planned to analyse and present continuous data using the MD if all results were measured on the same scale (e.g. PASI). If this was not the case (e.g. fear, or quality of life), we planned to use the SMD. Eligible continuous outcomes were not reported.

We planned to extract the proportion of participants who reached the 50% reduction of the respective psoriatic lesion score compared to the baseline value at a fixed time point to allow pooling of data. If this was not possible, we planned to extract the time necessary to reach 50% reduction compared to baseline value. To calculate a mean difference, the number of people at risk and the probability of an event at a given time is required. Where studies did not provide that information, we chose to describe the individual results and not to pool the data. If data were given in a chart, we deduced the numbers from the chart.

Where possible, all data that we extracted were those relevant to an intention-to-treat (ITT) analysis in which all data were analysed in groups to which they were assigned. We stated if this was not possible. We noted the time points at which outcomes were collected and reported. We reported the 95% CIs for all analyses.

Unit of analysis issues

We included between-participant data as well as within-participant data. In general, within-participant studies apply the intervention to a body part such as a limb and the comparator to a different body part such as the opposite limb (e.g. right arm versus left arm). Those data are distinct. Consequently, we separately analysed and reported information on between-participant data and within-participant data. PASI-75 is the primary efficacy outcome for both data types.

If studies reported multiple intervention groups, we designated the intervention group and each different comparator group.

Dealing with missing data

We conformed to Cochrane's principal options for dealing with missing data (Higgins 2011). If data were missing, or only imputed data were reported, we planned to contact trial authors to request data on the outcomes of the people or limbs of the study. When relevant data regarding study selection, data extraction, and 'Risk of bias' assessment were missing, we planned to contact study authors to retrieve the missing data. If data remained missing after contact with authors, we analysed only the available data and addressed the potential impact on the findings in the Discussion.

Assessment of heterogeneity

We planned to assess heterogeneity (composed of dissimilar parts) between studies by visual inspection of forest plots; by estimation of the percentage heterogeneity between trials that could not be ascribed to sampling variation (I^2 statistic) (Higgins 2003); and if possible, by subgroup analyses. If there was evidence of substantial heterogeneity, we planned to investigate and report the possible reasons for this. An I^2 statistic greater than 50% was considered to indicate substantial heterogeneity, demonstrating a considerable variation in results. In this case, we planned to present the graphical display of a forest plot, but we did not plan to report an average value for the intervention effect.

Assessment of reporting biases

We planned to assess study protocols to see if the planned outcomes have been reported, but did not identify any. We planned to assess reporting bias, such as publication bias, by constructing a funnel plot if there were a sufficient number of included studies for a particular outcome (that is, at least 10 studies included in a meta-analysis).

Data synthesis

We analysed the data using the Review Manager 5.3 software (Review Manager 2014); one review author entered the data (FP) and another review author checked it (SP). If sufficient clinically similar studies were available, we deemed it feasible to pool data. We planned to consider clinical homogeneity and statistical heterogeneity before pooling the data. If the I^2 statistic value was greater than 50%, we did not combine studies in order to report an average value for the intervention effect. We planned to use random-effects models with inverse variance weighting for all analyses (DerSimonian 1986).

Concerning the dichotomous events of PASI-75 and treatment-related adverse events requiring withdrawal, we pooled the data and estimated a risk ratio and a P value for overall effect by using the Mantel-Haenszel statistic and a fixed-effect model.

Where possible, all data that we extracted were those relevant to an intention-to-treat (ITT) analysis in which all data were analysed in groups to which they were assigned. We stated if this was possible. We noted the time points at which outcomes were collected and reported. We reported the 95% confidence intervals (CIs) for all analyses.

We planned to use ordinal data from people who answered the Dermatology Life Quality Index (DLQI) questionnaire (Table 2) (Melilli 2006) or the visual analogue scale (VAS) on pruritus (itching), as well as from people who achieved a remission and people who experienced secondary malignancy. However, these data were not reported.

In the protocol, we addressed a problem that might arise if we included only a single study in an analysis of dichotomous data. In this instance, the confidence intervals around risk ratios calculated in Review Manager 2014 are unreliable. Where results were estimated for individual studies with low numbers of outcomes (less than 10 in total), or where the total sample size was less than 30 people, or limbs and a risk ratio was used, we planned to report the proportion of outcomes in each treatment group together with a P value from a Fisher's exact test. But this problem did not arise.

The analysis should be in intention-to-treat and all missing data were considered as failure.

Results on outcomes that were not predefined were also reported in Effects of interventions as additional information, though, the results were not relevant for the conclusion of the present review.

'Summary of findings' tables and GRADE assessments

We prepared one 'Summary of findings' table using the GRADE profiler software (GRADEpro GDT 2014) concerning the comparison of between-participant data: salt bath + UVB compared with other treatment + UVB. We listed the predefined two primary outcomes: PASI-75 and treatment-related adverse events requiring withdrawal. For each outcome, two review authors (FP, SP) independently assessed the certainty of the evidence by using the five GRADE considerations, that is, study limitations, inconsistency, indirectness, imprecision, and publication bias as described in the *Cochrane Handbook for Systematic Reviews of Interventions* (Schünemann 2011). Due to lack of data, we did not prepare other 'Summary of findings' tables, which might be possible for comparison type one regarding between-participant data and for both comparison types regarding within-participant data.

Subgroup analysis and investigation of heterogeneity

We did not undertake any subgroup analyses.

Sensitivity analysis

We planned to conduct a sensitivity analysis removing studies at high or uncertain risk of bias. However, we did not undertake any sensitivity analyses due to the limited number of studies included in this review.

RESULTS

Description of studies

Results of the search

The Electronic searches of databases and online trials registers retrieved 281 records (142 from databases and 139 from online trials registries) once duplicates were removed (Figure 1). We screened the title and abstract of 281 records and excluded 254 records. We screened the full texts of the remaining 27 records and included 11 records and did not include 16 records. The exclusion reasons for 15 records (Excluded studies) are shown in the Characteristics of excluded studies. One record is listed in Studies awaiting classification, and described in Characteristics of studies awaiting classification. The latter record (NCT02713711) could be an eligible study for inclusion in a future update. The results and full description of the methods of the study were not available. We included eight studies (Arnold 2001; Brockow 2007a; Brockow 2007b; Dawe 2005; Gambichler 2001; Klein 2011; Leaute-Labreze 2001; Schiener 2007) associated with 11 records. For a full description of our screening process, see Figure 1.

Included studies

Of the 27 potentially relevant records, we included 11 records (Included studies), which are associated with eight different studies (Figure 1). The characteristics of the eight included studies are described in the Characteristics of included studies tables.

Design and sample sizes

We included eight randomised controlled trials (RCTs) (2105 participants; 1976 analysed) in this review. Six studies were parallel RCTs (2035 participants; 1908 analysed) that randomised patients to an intervention or comparator group (Arnold 2001; Brockow 2007a; Brockow 2007b; Klein 2011; Leaute-Labreze 2001; Schiener 2007). Leaute-Labreze 2001 randomised participants to an intervention group (24 analysed), or two different comparator groups (22 and 21 analysed). Schiener 2007 randomised participants to an intervention group (299 analysed), or three different comparator groups (270, 285, and 305 analysed). Two studies (70 participants; 68 analysed) were within-participants studies (140 limbs; 136 analysed) (Dawe 2005; Gambichler 2001). Dawe 2005 randomised arms or legs to an intervention or comparator group (120 limbs; 116 analysed), and Gambichler 2001 randomised elbows to an intervention or comparator group (20 limbs; 20 analysed). The majority of studies did not report the recruitment periods. The earliest reported recruitment happened in the year 2001.

Assessment at the end of treatment was reported by seven studies: up to eight weeks (Arnold 2001), six weeks (Brockow 2007a), six weeks (Brockow 2007b), eight weeks (Gambichler 2001), seven weeks (Klein 2011), three weeks (Leaute-Labreze 2001), and eight weeks (Schiener 2007) after start of treatment. In one study (Dawe 2005), we did not identify a clear reporting of treatment duration. Assessment at the end of follow-up was reported by six studies: up to eight months (Arnold 2001), six months (Brockow 2007a), six months (Brockow 2007b), 12 months (Dawe 2005), six months (Klein 2011), 12 months (Leaute-Labreze 2001) after end of treatment. In two studies (Gambichler 2001; Schiener 2007), we did not identify a clear reporting of follow-up duration. The duration of trials in total (start of treatment to end of follow-up) was roughly: up to four months (Arnold 2001), up to eight months (Brockow 2007a), up to eight months (Brockow 2007b), at least 12 months (Dawe 2005), at least two months (Gambichler 2001), up to eight months (Klein 2011), up to 13 months (Leaute-Labreze 2001), and at least two months (Schiener 2007).

Setting

Five of the eight included studies were set in Germany (Brockow 2007a; Brockow 2007b; Gambichler 2001; Klein 2011; Schiener 2007), and a single study was set in the Netherlands (Arnold 2001), the UK (Dawe 2005), and France (Leaute-Labreze 2001), respectively. Four studies were conducted in a single centre (Arnold 2001; Dawe 2005; Gambichler 2001; Leaute-Labreze 2001), and the remaining four studies (Brockow 2007a; Brockow 2007b; Klein 2011; Schiener 2007) were conducted in more than one centre. Five studies reported the recruitment of outpatients (Arnold 2001; Brockow 2007a; Brockow 2007b; Gambichler 2001; Schiener 2007), and the other three studies did not report any information on recruitment (Dawe 2005; Klein 2011; Leaute-Labreze 2001). One single-centre study was conducted in the Psoriasis Day Care Centre at Ede, the Netherlands. Another single-centre study was conducted in a spa centre at Salies-de-Bearn, France. Two other single-centre studies were conducted; one in Germany and one in the UK. Four multi-centre studies were conducted in spa centres or outpatient clinics in Germany. Three of eight studies were sponsored by commercial spa or salt companies (German Spas Association (Deutscher Heilbäderverband); Mavena Healthcare AG, Switzerland, the commercial spa facility La Compagnie Fermiere de Salies de Bearn), one by health insurance companies ("primary" health insurance companies in Bavaria, Germany), one by an association of dermatologists (Berufsverband der Deutschen Dermatologen, Germany), and three did not report on funding.

Participants

The study participants were diagnosed with psoriasis by a dermatologist. Six studies reported a mean age range from 41 to 49 years of age in the intervention group, and from 45 to 50 years of age in the control group (Arnold 2001; Brockow 2007a; Brockow 2007b; Klein 2011; Leaute-Labreze 2001; Schiener 2007). One study reported a mean age of 36 years in the intervention group and 46 years of age in the comparator group (Gambichler 2001). One study did not report information on age (Dawe 2005). Four studies reported male gender from 56% to 74% in the intervention group and from 60% to 62% in the control group (Brockow 2007a; Brockow 2007b; Klein 2011; Schiener 2007). Two studies reported male gender in 40% and 57% for all people or limbs, respectively (Arnold 2001; Gambichler 2001). Two studies did not report information on gender (Dawe 2005; Leaute-Labreze 2001).

All eight included studies reported on assessing the skin type by using the Fitzpatrick phototyping scale (Fitzpatrick 1988), which results in six categories. Most participants were categorised type III, in some studies, a considerable fraction of participants were also categorised II and IV. According to the Australian Radiation Protection and Nuclear Safety Agency (ARPANSA): "The Fitzpatrick skin phototype is a commonly used system to describe a person's skin type in terms of response to ultraviolet radiation (UVR) exposure." The various types correspond to pale white skin (I), white skin (II), light brown skin (III), moderate brown skin (IV), dark brown skin (V), and deeply pigmented dark brown to black skin (VI).

As a measure of severity of disease, the PASI score ranging from 0 to 72 points was assessed at the beginning of the study in five studies (Brockow 2007a; Brockow 2007b; Klein 2011; Leaute-Labreze 2001; Schiener 2007). In the test arm versus control arms, the median PASI score was 17 versus 16 (Brockow 2007a), 17 versus 18 (Brockow 2007b), 15.1 versus 15.3 (Klein 2011), 15.0 versus 15.7 (Leaute-Labreze 2001), and 16 versus 16 versus 17 versus 17 (Schiener 2007). Concerning baseline PASI score, there was no imbalance between treatment arms. Three studies (Arnold 2001; Dawe 2005; Gambichler 2001) did not report the PASI score.

Four of the studies reporting between-participant data (Brockow 2007a; Brockow 2007b; Klein 2011; Schiener 2007) stated the proportion of participants who had any experience of former phototherapy, which was balanced across the treatment groups. Three studies (Brockow 2007a; Brockow 2007b; Schiener 2007) reported that between 80% and 90% of included participants had previous phototherapy, while one study (Klein 2011) reported a smaller proportion between 10% and 15%. One of the studies reporting within-participant data (Dawe 2005) reported a proportion of 75%.

Four of the studies reporting between-participant data (Brockow 2007a; Brockow 2007b; Klein 2011; Schiener 2007) stated the proportion of participants who had previous systematic therapy due to psoriasis, which was balanced across the treatment groups. Three studies (Brockow 2007a; Brockow 2007b; Schiener 2007) reported that between 20% and 40% of included participants had previous systematic therapy, while one study (Klein 2011) reported a smaller proportion between 1% and 3%. One of the studies reporting within-participant data (Dawe 2005) reported a proportion of 12%.

Three of the studies reporting between-participant data (Brockow 2007a; Brockow 2007b; Schiener 2007) stated the proportion of participants who had previous inpatient care due to psoriasis, which was balanced across the treatment groups. These studies reported that between 40% and 60% of included participants had previous inpatient care. Klein 2011 reported that about 55% of participants had previous topical treatment due to psoriasis.

Three studies reported on the duration of disease. Two of the studies reporting between-participant data (Leaute-Labreze 2001; Schiener 2007) reported a mean or median duration of 15 to 20 years. One of the studies reporting within-participant data (Gambichler 2001) reported a mean duration of 2.5 years.

Interventions and comparisons

To make various salt concentrations comparable, we converted the information on salt solutions into the unit g/L (Table 3).

Comparison 1: salt bath + UVB versus other treatment without UVB

We identified one comparison in one of the studies reporting between-participant data (Schiener 2007). Schiener 2007 randomised 310 participants to the intervention group salt water + UVB and randomised 321 participants to the comparator group psoralen bath + UVA.

- Schiener 2007: salt bath + UVB versus psoralen bath + UVA

We did not identify comparisons in the studies reporting within-participants data

Comparison 2: salt bath + UVB versus other treatment + UVB or UVB only

We identified seven comparisons in the six studies reporting between-participant data (Arnold 2001; Brockow 2007a; Brockow 2007b; Klein 2011; Leaute-Labreze 2001; Schiener 2007). UVB was applied in addition to another treatment, such as psoralen bath or tap water bath in two comparator groups. UVB only was applied in five comparator groups. Arnold 2001 randomised 20 participants to the intervention group salt water + UVB and 20 participants to the comparator group psoralen bath + UVB. Schiener 2007 randomised 310 participants to the intervention group salt bath + UVB, randomised 301 participants to the comparator group UVB only, and randomised 301 participants to tap water + UVB. The other studies (Brockow 2007a; Brockow 2007b; Klein 2011; Leaute-Labreze 2001) randomised participants to the intervention group salt bath + UVB, and to the comparator group UVB only.

- Arnold 2001: salt bath + UVB versus psoralen bath + UVB
- Brockow 2007a: salt bath **+** UVB versus UVB only
- Brockow 2007b: salt bath **+** UVB versus UVB only
- Klein 2011: salt bath **+** UVB versus UVB only
- Leaute-Labreze 2001: salt bath **+** UVB versus UVB only
- Schiener 2007: salt bath **+** UVB versus UVB only
- Schiener 2007: salt bath **+** UVB versus tap water + UVB

We identified two comparisons in the two studies reporting within-participants data (Dawe 2005; Gambichler 2001). Both studies randomised body parts to salt water + UVB versus UVB only.

- Dawe 2005: salt bath + UVB versus UVB only
- Gambichler 2001: salt bath + UVB versus UVB only

Salt bath

People, legs, arms, or elbows were soaked for 15 to 30 minutes in salt water with a sodium chloride salt concentration ranging from 0.8 g/L to 250 g/L. The sources were natural springs in three studies (Brockow 2007a; Brockow 2007b; Leaute-Labreze 2001), dissolved sodium chloride in tap water in three studies (Arnold 2001; Gambichler 2001; Schiener 2007), and dissolved commercial Dead Sea salt in tap water in two studies (Dawe 2005; Klein 2011). In general, salt bath + UVB was applied once a day, three to five days a week, for up to eight weeks, and reaching a maximum number of 15 to 35 applications.

UVB

For irradiation with UVB light, the studies used devices such as Philips (Eindhoven, the Netherlands) 100 Watts TL-01 lamps. Four studies used only 311 nm narrowband UVB (Arnold 2001; Dawe 2005; Klein 2011; Leaute-Labreze 2001), two studies used only 280 nm to 320 nm broadband UVB (Brockow 2007b; Gambichler 2001), and two studies used both (Brockow 2007a; Schiener 2007). Schiener 2007 reported a 300 nm to 320 nm 'selective phototherapy', which represents a part of the broadband UVB and which has been predominantly in German phototherapy centres. Some studies assessed a so-called minimal erythema dose (MED) before treatment to determine a starting dose, which might be set at 50% of the MED. The MED was defined as the dose to produce a just-detectable erythema with sharp borders within 24 hours in some uninvolved and untanned skin areas of 2 cm^2. The authors of four studies reported mean starting doses from 0.02 J/cm^2 to 0.4 J/

cm^2 (Brockow 2007b; Gambichler 2001; Klein 2011; Leaute-Labreze 2001). In general, UVB was applied once a day, three to five days a week, for up to eight weeks, and reaching a maximum number of 15 to 35 applications.

Cumulative UVB doses

Regarding the intervention (salt water bath + UVB), the authors of five studies (Brockow 2007a; Dawe 2005; Klein 2011; Leaute-Labreze 2001; Schiener 2007) reported mean cumulative doses for primarily or only using narrowband UVB from 11.8 J/cm^2 to 50.7 J/cm^2 and the authors of two studies (Brockow 2007b; Gambichler 2001) reported mean cumulative doses for only using broadband UVB from 2.7 J/cm^2 to 7.2 J/cm^2. Regarding the comparator (UVB alone), the authors of seven studies reported mean cumulative doses for narrowband UVB from 12.5 J/cm^2 to 41.3 J/$cm^2$and for broadband UVB from 2.8 J/cm^2 to 7.2 J/cm^2 (Brockow 2007a; Brockow 2007b; Dawe 2005; Gambichler 2001; Klein 2011; Leaute-Labreze 2001; Schiener 2007). One study did not report UVB doses (Arnold 2001).

Outcomes

Primary outcomes

Psoriasis area and severity index (PASI)-75

Between-participant data

Two of six studies (Brockow 2007a; Brockow 2007b) reported PASI-75.

Four of six studies (Arnold 2001; Klein 2011; Leaute-Labreze 2001; Schiener 2007) reported aggregate data on PASI, such as mean PASI and PASI-50, but did not report PASI-75 as defined in the inclusion criteria. It is not possible to deduce PASI-75 from mean PASI or PASI-50, but it is possible to calculate PASI-75 if individual data are available. Therefore, we sent e-mail requests to the authors of the respective studies to send us individual data on PASI. We used the e-mail addresses provided by recent papers of the authors. If an e-mail address was no longer active, we sent the request to an e-mail address provided by the institution that was involved in the study. We sent enquiries to authors of all included studies. Detailed information is provided in Appendix 6. We asked for individual patient data on PASI of the studies by Arnold 2001, Brockow 2007a, Brockow 2007b, Klein 2011, Leaute-Labreze 2001, and Schiener 2007 to enable a calculation of PASI-75. We did not receive the requested information.

Within-participant data

Two of two studies (Dawe 2005, Gambichler 2001) reported individual severity scores which are different from PASI, and they consequently did not report PASI-75. We sent enquiries to authors of all included studies. Detailed information is provided in Appendix 6. We asked for individual patient data on PASI of the studies by Dawe 2005 and Gambichler 2001 to enable a calculation of PASI-75. We did not receive the requested information.

Treatment-related adverse events requiring withdrawal

Between-participant data

Two of six studies reported treatment-related adverse events requiring withdrawal (Klein 2011; Leaute-Labreze 2001). Four of six studies did not report this outcome.

Within-participant data

One study (Dawe 2005) reported this outcome.

Secondary outcomes

The included studies did not report outcomes that were predefined as secondary by the present review including Dermatology Life Quality Index (DLQI), Pruritus severity using a visual analogue scale (VAS) from 0 ('no itching') to 100 ('severe itching'), Time to relapse, and Secondary malignancies.

Excluded studies

Of 25 potentially relevant records, we excluded 15 records (Figure 1). One record (Studies awaiting classification) is awaiting classification and is described in the Characteristics of studies awaiting classification table. The reason for exclusion of 15 records (Excluded studies) are described in the Characteristics of excluded studies table and are based on:

- not intervention of interest (n = 6): Dead Sea bathing and sun exposure; geothermal sea bathing + UVB; sulphurous thermal spring water, bath not followed by UVB consistently; lagoon bathing followed by UVB; oral retinoid added to bath and UVB; and UVB but not salt water baths;
- not study type of interest (n = 9): systematic review (n = 5); single-arm study (n = 2); nonsystematic review (n = 2).

Studies awaiting classification

NCT02713711 randomised 24 adult participants with psoriasis in a single-centre study in Chile. The number of participants correspond to the two treatment groups of interest. The intervention was salt bath followed by artificial UVB. The comparator was artificial UVB only. The study was sponsored by Universidad Catolica del Maule, Chile. This study is completed and the authors have submitted the manuscript. At the present time, the manuscript has not been accepted for publication. Thus, the results of the outcomes are not available yet (correspondence with study author shown in Appendix 6).

Risk of bias in included studies

The risk of bias table in Characteristics of included studies provides details of each item of the risk of bias tool for randomised controlled trials. Figure 2 and Figure 3 provide an overview.

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

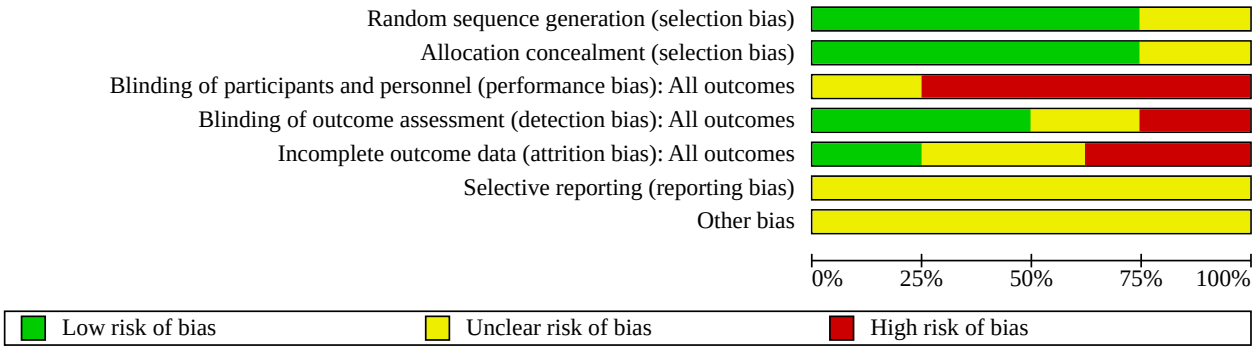
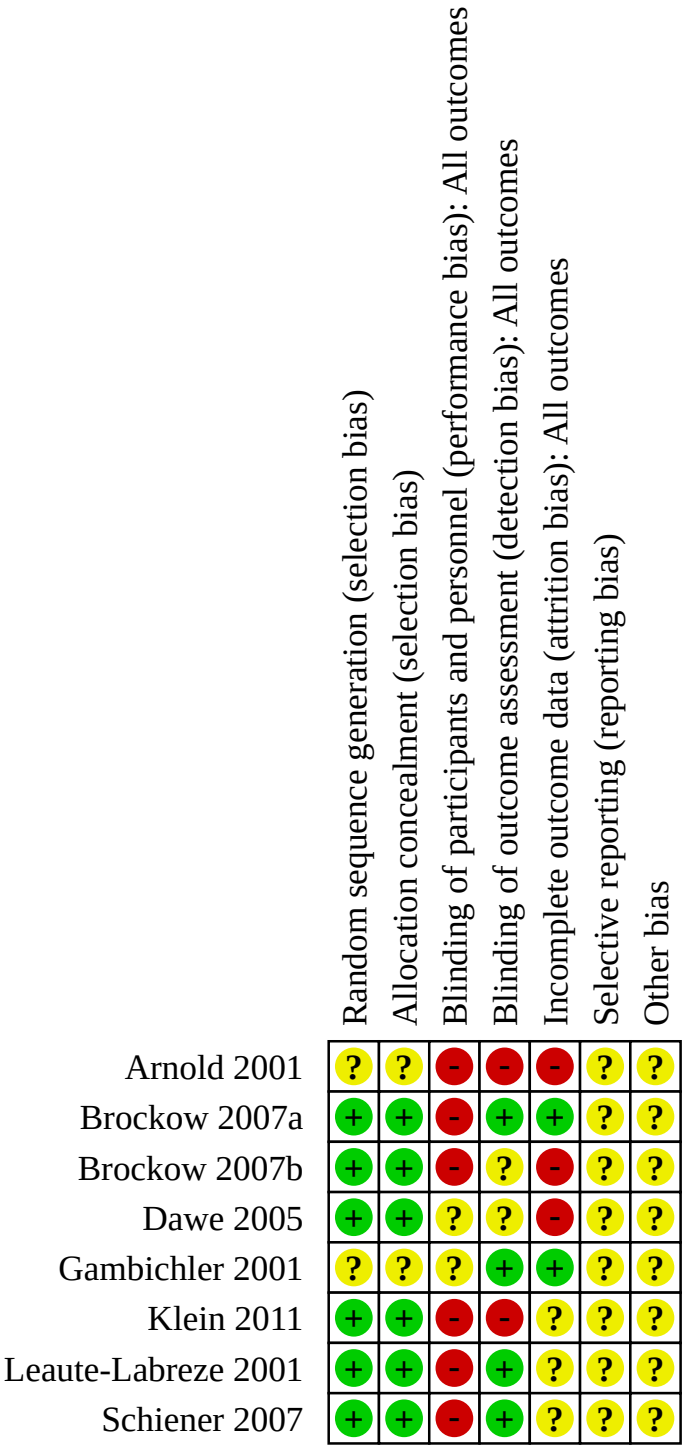


Figure 3. 'Risk of bias' summary: review authors' judgements about each risk of bias item for each included study.



Allocation

The authors of six studies clearly described an adequate random sequence generation and an adequate concealment of the allocation, which was judged as low risk of bias (Brockow 2007a; Brockow 2007b; Dawe 2005; Klein 2011; Leaute-Labreze 2001; Schiener 2007). In the other two studies, selection bias from random sequence generation and an adequate concealment of the allocation was judged as unclear risk of bias (Arnold 2001; Gambichler 2001).

Blinding

The authors of five studies reported that they did not blind investigators and patients and we judged a high risk of performance bias (Brockow 2007a; Brockow 2007b; Klein 2011; Leaute-Labreze 2001; Schiener 2007). A further study did not report this topic so we also judged it as high risk of performance bias (Arnold 2001). One study reported the issue of blinding, but patients and nurses were not blinded (Dawe 2005). As physicians may have been blinded, we judged an unclear risk of performance bias. One other study reported partial blinding of people or limbs, and we judged an unclear risk of bias (Gambichler 2001).

Most of the studies tried to blind the persons involved in outcome assessment, but this could not be achieved in all cases. We judged a low risk of detection bias in four studies as the assessors were presumably unaware of patients' treatment assignments (Brockow 2007a; Gambichler 2001; Leaute-Labreze 2001; Schiener 2007). We judged an unclear risk in two studies as the blinding was tried but was not achieved (Brockow 2007b; Dawe 2005). The authors of one study did not report this topic so we considered it high risk of detection bias (Arnold 2001) . In addition, one study was considered at high risk as blinding was not implemented (Klein 2011).

Incomplete outcome data

Concerning three studies, we were unsure whether a rather low proportion of dropouts or a high proportion of dropouts but the application of an intention-to-treat analysis may have affected the outcome (Klein 2011; Leaute-Labreze 2001; Schiener 2007). Therefore, we judged them at unclear risk of attrition bias. We judged attrition bias as high risk in three studies (Arnold 2001; Brockow 2007b; Dawe 2005) as a considerable number of patient data could not be used in the analysis. In two studies, we did not identify attrition bias and they were judged low risk of bias (Brockow 2007a; Gambichler 2001).

Selective reporting

No protocol was available for any included study. Thus, we searched for inconsistencies within the reporting of the article. We did not identify a selective reporting issue and judged all eight studies at unclear risk of reporting bias (Arnold 2001; Brockow 2007a; Brockow 2007b; Dawe 2005; Gambichler 2001; Klein 2011; Leaute-Labreze 2001; Schiener 2007).

Other potential sources of bias

We did not identify a substantial source of other bias from the information available in the reports; hence, we judged all eight included studies at unclear risk of other sources of bias due to insufficient information available to make a full assessment (Arnold 2001; Brockow 2007a; Brockow 2007b; Dawe 2005; Gambichler 2001; Klein 2011; Leaute-Labreze 2001; Schiener 2007).

Effects of interventions

See: **Summary of findings 1** Salt bath + UVB compared with UVB alone for chronic plaque psoriasis

Comparison 1: Salt bath plus UVB versus other treatment without UVB

Primary outcomes

PASI-75 response

We did not identify appropriate data.

Treatment-related adverse events requiring withdrawal

We did not identify appropriate data.

Secondary outcomes

Dermatology Life Quality Index (DLQI)

We did not identify appropriate data.

Pruritus severity using a visual analogue scale (VAS) from 0 ('no itching') to 100 ('severe itching')

We did not identify appropriate data.

Time to relapse

We did not identify appropriate data.

Secondary malignancies

We did not identify appropriate data.

Not predefined outcomes

We identified outcomes reported in the eight included studies that were not predefined by the current review. These outcomes should not have an impact on the conclusion. Nevertheless, the respective results should be reported to provide a broader picture of the results reported in the various studies.

PASI-50 response (between-participant data)

Schiener 2007 reported the proportion of participants who achieved a 50% or more reduction in their Psoriasis Area and Severity Index score (PASI-50) from baseline (Table 4). Schiener 2007 reported proportions of PASI-50 of the intervention group salt bath + UVB that were similar to those of the comparator group psoralen bath + UVA (Table 4). The difference between treatment groups was not statistically significant.

PASI (between-participant data)

We did not identify appropriate data.

Clearance of psoriatic lesions (within-participant data)

We did not identify appropriate data.

Treatment-related adverse events

All eight included studies reported on treatment-related adverse events (Table 5) such as dermatitis solaris, phototoxic reaction, erythema, burning, stinging, itching, itchy papular eruption, edema, and blisters. The relationship of adverse events with study interventions was classified as definitive, possible, or unlikely by the study authors. We extracted only adverse events which were

classified as definitive or possible. We limited the reporting on statistically significant results.

Between-participant data

Schiener 2007 reported 33 events in 284 assessed participants after exposure of salt water + UVB versus 16 events in 297 participants after psoralen bath + UVA. The difference between the treatment groups was statistically significant (P = 0.0072) in favour of psoralen bath + UVA. The 49 events were phototoxic reactions.

Within-participant data

We did not identify statistically significant results.

Treatment-related severe adverse events

Between-participant data

Schiener 2007 reported zero events in the intervention group salt bath + UVB and three events (photodermatitis, photodermatitis, and malignant melanoma) and three events in the comparator group psoralen bath + UVA (Table 6). The difference between the treatment groups was not statistically significant.

Within-participant data

We did not identify appropriate data.

Patient-reported outcomes

The authors of four studies (Brockow 2007b; Klein 2011; Leaute-Labreze 2001; Schiener 2007) reported patient-reported outcomes (Table 7). We did not consider the self-administered Psoriasis Area and Severity Index (S-PASI), the patients' self-rated analogue to the clinician-rated PASI, which is scored and interpreted as the PASI (Brockow 2007a). We did not consider the short form of the questionnaire on experience with skin complaints (SF-QES) reported by Schiener 2007, because the test of statistical significance on change scores were applied across four different treatment groups only.

Between-participant data

Schiener 2007 reported global ratings on disease severity, treatment effect, and tolerability using 100-mm visual analogue scales (VAS) (Table 7). The numbers of assessed participants in the intervention group salt bath + UVB versus the comparator group psoralen bath + UVA were not specified. Statistical significance was not tested.

Within-participant data

We did not identify appropriate data.

Comparison 2: Salt bath plus UVB versus other treatment with UVB or UVB only

Please see Summary of findings 1.

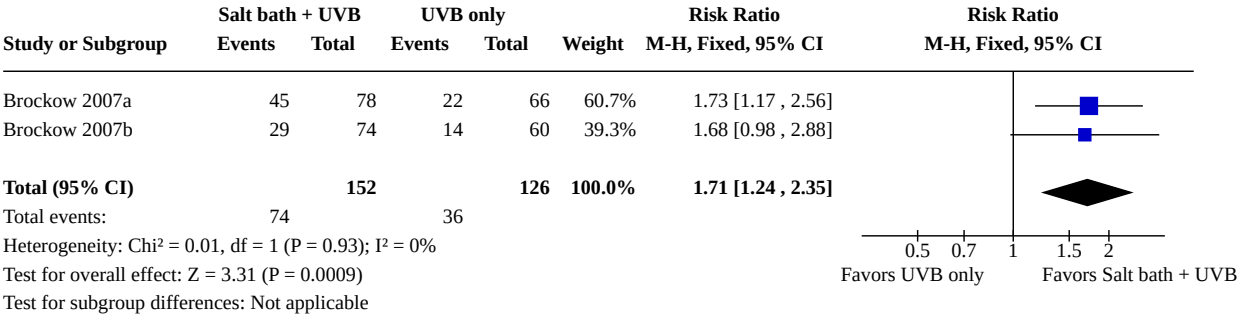
Primary outcomes

PASI-75 response

Between-participant data

Brockow 2007a and Brockow 2007b stated the proportion of participants who achieved PASI-75 at time points between six to eight weeks after start of treatment (Table 8). Brockow 2007a found a higher proportion of PASI-75 in the intervention group salt bath + UVB versus the comparator group UVB only. The difference between treatment groups was statistically significant (P = 0.0044) in favour of salt bath. Brockow 2007b also found a higher proportion of PASI-75 with salt bath + UVB versus UVB only. However, the difference between treatment groups was not statistically significant (P = 0.0632). We pooled the data of both studies and estimated a risk ratio of 1.71 (95% CI 1.24 to 2.35; P = 0.0009; 278 participants; two studies; low-certainty evidence); Analysis 1.1; Figure 4) which favours salt bath + UVB. Please note that due to the nature of this measurement (that is, the number of patients with a PASI-75), a high event rate is favourable.

Figure 4. Forest plot of comparison: 1 Saline+UVB versus UVB, outcome: 1.1 PASI-75 response.



Within-participant data

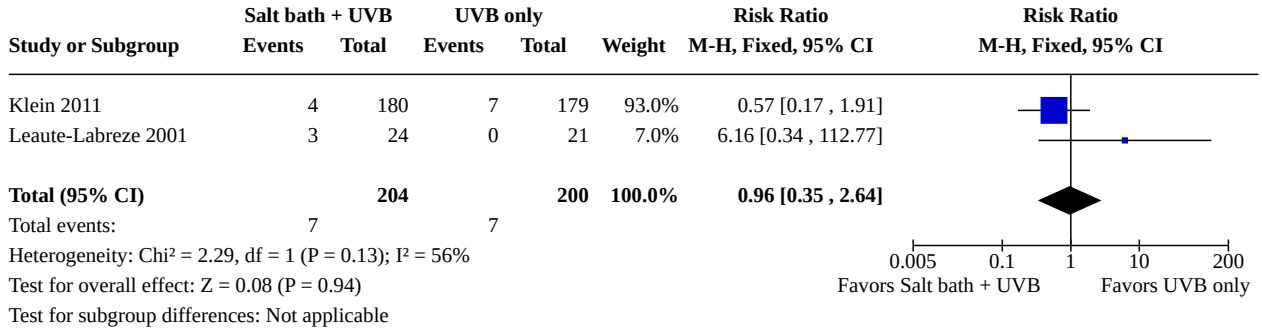
We did not identify appropriate data.

Treatment-related adverse events requiring withdrawal

Between-participant data

Klein 2011 and Leaute-Labreze 2001 stated the proportion of participants who had treatment-related adverse events requiring withdrawal (Table 9). The differences between treatment groups in both studies were not statistically significant. We pooled the data of the two studies and calculated a risk ratio of 0.96 (95% CI 0.35 to 2.64; P = 0.94; 404 participants; two studies; low-certainty evidence); Analysis 1.2; Figure 5). The result did not favour any treatment.

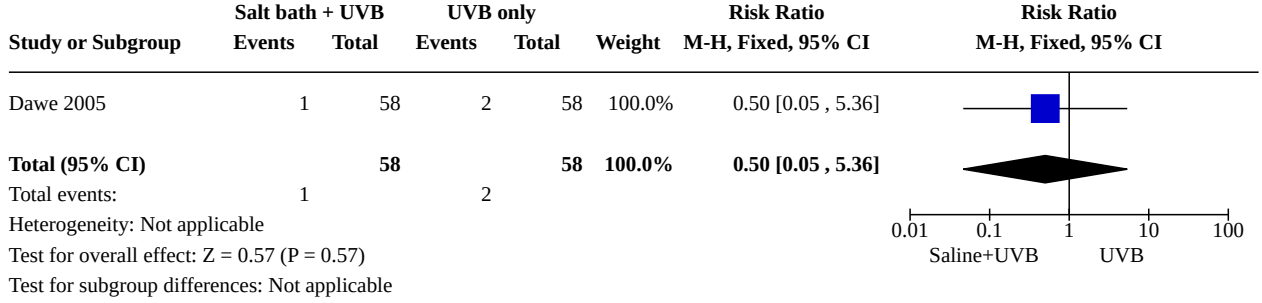
Figure 5. Forest plot of comparison: 1 Saline + UVB versus UVB, outcome: 1.2 Treatment-related adverse events requiring withdrawal (between participants).



Within-participant data

Dawe 2005 reported one event with salt bath + UVB and two events with UVB only (Analysis 1.3; Figure 6). The result did not favour any treatment; low-certainty evidence.

Figure 6. Forest plot of comparison: 1 Saline + UVB versus UVB, outcome: 1.3 Treatment-related adverse events requiring withdrawal (within participants).



Secondary outcomes

Dermatology Life Quality Index (DLQI)

We did not identify appropriate data.

Pruritus severity using a visual analogue scale (VAS) from 0 ('no itching') to 100 ('severe itching')

We did not identify appropriate data.

Time to relapse

We did not identify appropriate data.

Secondary malignancies

We did not identify appropriate data.

Not predefined outcomes

We identified outcomes reported in the eight included studies that were not predefined by the current review. These outcomes should not have an impact on the conclusion. Nevertheless, the respective results should be reported to provide a broader picture of the results reported in the various studies.

PASI-50 response (between-participant data)

Brockow 2007a, Brockow 2007b and Schiener 2007 reported PASI-50 (Table 4). Brockow 2007a found a higher proportion of PASI-50 in the intervention group bath + UVB versus the comparator group UVB only. The difference between treatment groups was statistically significant (P < 0.001) in favour of salt bath + UVB. Brockow 2007b found also a higher proportion of PASI-50 in the intervention group salt bath + UVB versus the comparator group UVB only. The difference between treatment groups was also statistically significant (P < 0.0053) in favour of salt bath + UVB. Schiener 2007 found a higher proportion of PASI-50 in the intervention group salt bath + UVB versus the comparator group tap water + UVB. The difference between treatment groups was again statistically significant (P < 0.0003) in favour of salt bath + UVB.

PASI (between-participant data)

Arnold 2001, Klein 2011, Leaute-Labreze 2001 reported the change of PASI score from baseline ((day 21 to day 0)/day 0) (Table 10). Klein 2011 found a greater reduction of PASI in the intervention group salt bath + UVB versus the comparator group UVB only. The difference between treatment groups was statistically significant (P < 0.0001) in favour of salt bath + UVB. Arnold 2001 and Leaute-Labreze 2001 reported data on percentage change in PASI for each

group with both groups showing a reduction in PASI; however, no formal statistical comparison of the two groups were presented.

Clearance of psoriatic lesions (within-participant data)

Gambichler 2001 and Dawe 2005 reported various clearance of psoriatic lesions scores (Table 11). In both studies, differences in change of scores from baseline were not statistically significant between treatment groups.

Treatment-related adverse events

Between-participant data

We did not identify statistically significant results.

Within-participant data

Dawe 2005 reported six events in 41 assessed arms or legs after exposure of salt bath + UVB versus zero events after exposure of UVB only. The difference between the treatment groups was statistically significant (P < 0.0257) in favour of no treatment. The six events in the intervention arm included three times itching, two times stinging, and one time itchy papular eruption.

Treatment-related severe adverse events

Between-participant data

Schiener 2007 reported zero events in the intervention group salt bath + UVB and three events (photodermatitis, exacerbation as guttate psoriasis, and alcohol problem) in the comparator group tap water + UVB (Table 6). Schiener 2007 also reported zero events in the comparator group UVB only. The difference between the treatment groups was not statistically significant.

Within-participant data

We did not identify appropriate data.

Patient-reported outcomes

The authors of four studies (Brockow 2007b; Klein 2011; Leaute-Labreze 2001; Schiener 2007) reported patient-reported outcomes (Table 7). We did not consider the self-administered Psoriasis Area and Severity Index (S-PASI), the patients' self-rated analogue to the clinician-rated PASI, which is scored and interpreted as the PASI (Brockow 2007a). We did not consider the short form of the questionnaire on experience with skin complaints (SF-QES) reported by Schiener 2007, because the test of statistical significance on change scores were applied across four different treatment groups only.

Between-participant data

Brockow 2007b reported global ratings on disease severity, treatment effect, and tolerability using 100 mm visual analogue scales (Table 7). The numbers of assessed participants in the intervention group salt water + UVB versus the comparator group UVB only were not specified. Statistical significance was not tested.

Klein 2011 reported a change of the Freiburg Life Quality Assessment for the three parts physical complaints, global health total, and global health skin only (Table 7). The data showed improvement in both treatment groups with analyses conducted at the time point session 35 equivalent to six weeks after start of treatment. The results showed statistically significantly better improvement in the intervention group salt bath + UVB versus the comparator group UVB only, which favours salt bath + UVB.

Klein 2011 reported a change from baseline for the psoriasis disability index and the sickness impact profile for the intervention group salt bath + UVB group versus the comparator group UVB only (Table 7). Statistical significance was not tested.

Klein 2011 reported the proportion of global impression of therapy (very good or good) as well as global impression of therapy (very bad or bad) (Table 7). The differences between the intervention group salt bath + UVB versus the comparator group UVB only were statistically significant, which favours salt bath + UVB.

Leaute-Labreze 2001 reported a change from baseline for the quality of life index for the intervention group salt bath + UVB versus the comparator group UVB only (Table 7). Statistical significance was not tested.

Schiener 2007 reported global ratings on disease severity, treatment effect, and tolerability using 100-mm visual analogue scales (Table 7). The numbers of assessed participants in the intervention group salt bath + UVB versus the comparator group tap water + UVB versus the comparator group UVB only were not specified. Statistical significance was not tested.

Within-participant data

We did not identify appropriate data.

DISCUSSION

Summary of main results

Our review evaluated the current state of evidence on the efficacy of the following:

- Indoor salt bath + ultraviolet B (UVB) versus other treatment without UVB (comparison one);
- Indoor salt bath + UVB versus other treatment + UVB or UVB only (comparison two).

We included eight randomised controlled trials (RCTs) on chronic plaque psoriasis. With respect to predefined outcomes, comparison one was not reported by any included study. With respect to predefined outcomes, comparison two was reported by five included studies.

Concerning the primary outcome Psoriasis Area and Severity Index (PASI-75) response, two between-participant studies randomised participants to the intervention group salt bath + UVB or to the comparator group UVB only and found that salt bath + UVB may improve psoriasis (low-certainty evidence) (Summary of findings 1).

Concerning the primary outcome treatment-related adverse events requiring withdrawal, two other between-participant studies also randomised participants to the intervention group salt bath + UVB or to the comparator group UVB only and found that there may be little to no difference between the groups with regard to this outcome (low-certainty evidence) (Summary of findings 1). One of the studies reported skin irritation; the other did not specify the type of adverse events reported by the participants. One within-participant study (paired right/left comparison) randomised skin areas to the intervention group salt bath + UVB or to the comparator group UVB only and found that there may be little to no difference between the groups with regard to this outcome (low-certainty

evidence). The study reported one event with the salt bath + UVB group (severe itch immediately after Dead Sea salt soaks), and two events with the UVB only group (inadequate response to phototherapy and conversion to psoralen bath + ultraviolet A (UVA)).

None of the predefined secondary outcomes of this review were reported in any of the included studies (Dermatology Life Quality Index (DLQI), pruritus severity using a visual analogue scale (VAS), time to relapse, or secondary malignancies).

The reporting of our pre-specified outcomes was either non-existent or limited, with a maximum of two studies reporting a given outcome. The two trials that contributed data for the primary efficacy outcome did not blind their outcome assessors and were conducted by the same group: one of the two trials was funded by the German Spas Association, but the other trial did not state a funding source.

Overall completeness and applicability of evidence

Seven of the eight included studies were published in 2007 or earlier, and we can assume that the majority of patients were treated 10 to 20 years ago. Nonetheless, we presume that the principle treatment procedures might not deviate considerably from the current practice.

The primary outcome PASI-75 was reported in two out of six between-participant studies (Brockow 2007a; Brockow 2007b), but not in the two within-participant studies.

The primary outcome treatment-related adverse events requiring withdrawal was reported in two other between-participant studies (Klein 2011; Leaute-Labreze 2001), and in one within-participant study (Dawe 2005). Out of eight studies, the primary efficacy outcome (PASI-75 for two different data types) was reported by only two studies.

Out of eight studies, the primary adverse event outcome (treatment-related adverse events requiring withdrawal for two different data types) were reported by only two between-participant studies and only one within-participant study. None of the predefined secondary outcomes were reported, so there were no patient-reported outcomes. For one of the two comparisons, none of the predefined outcomes were reported, so there is no evidence to assess at all for half of what was of interest.

Ultraviolet B phototherapy might pose a risk of carcinogenesis, especially of squamous cell carcinoma, and thus the cumulative exposure time should be controlled (Chang 2014; de Gruijl 2002). The studies included in the present review lack long-term observation and secondary neoplasia was not addressed.

All studies were conducted by non-academic institutions that build their business on the evaluated treatments. Therefore, a financial conflict of interest might be present in most, if not all of the included studies. Five of the eight studies were conducted in Germany. This preference might be the result of a lasting culture-specific increase of supply in the past or of a supplier-induced demand in recent times.

Key issues are that most trials conducted did not contribute data to the primary outcomes and the primary efficacy outcome data all come from two small unblinded trials conducted by a single group of investigators. There was no information for the primary or secondary outcomes on salt water baths + UVB versus no UVB, which is a key comparison.

Quality of the evidence

To accommodate events in the analysis of the primary outcome PASI-75, we used the number of people that reached PASI-75. We downgraded the certainty of evidence by two levels for this outcome (low certainty of evidence). We downgraded one level because of study limitations (risk of bias). Due to lack of blinding, we judged a high risk of performance bias. We downgraded one level because of high probability of publication bias. Six studies included in the review did not contribute to the primary outcome. The two studies that did contribute data (Brockow 2007a; Brockow 2007b) were conducted by the same sponsor. It should be acknowledged that some studies tried to blind outcome assessment and assessed if the blinding could be realised. In general, lack of blinding of outcome assessment contributed to a high risk of bias in most studies.

Treatment-related adverse events requiring withdrawal was also used as primary outcome. We downgraded the certainty of evidence by two levels for this outcome (low certainty of evidence). We downgraded one level because of study limitations (risk of bias). Due to lack of blinding, we judged a high bias of performance bias. We downgraded one level because of high probability of publication bias. Five studies included in the review did not contribute to the primary outcome. Three studies did contribute data, two between-participant studies (Klein 2011; Leaute-Labreze 2001) and one within-participant study (Dawe 2005).

In general, the reporting did not facilitate a clear and instant understanding. The variety in outcome reporting reduced the pooling of data considerably. Many data are not eligible for meta-analysis, which may create a selection bias within the review. The authors of four studies (Arnold 2001; Dawe 2005; Gambichler 2001; Leaute-Labreze 2001) did not report a participant flow diagram. Acknowledging the study limitations in the reporting of the two primary outcomes, we judge an unclear internal validity. Secondary outcomes of this review were not measured by any of the included studies; therefore, we were unable to determine the certainty of evidence for these outcomes.

Potential biases in the review process

We conducted a comprehensive search for studies including a search for ongoing studies. The search was broad and sensitive; thus, the risk of not detecting a relevant study is very small. We did not make any post-hoc analysis decisions after seeing the data. Only two studies reported PASI-75, and only two studies reported treatment-related adverse events requiring withdrawal, but we retained the predefined primary outcomes. We tried to access individual study data to complement missing information. Although, we rephrased the name of both outcomes, this did not actually affect the planned concept, but enabled clarification. Subsequently, we assume that there were no relevant departures from protocol that could be potential sources of bias. The restriction to treatment-related adverse events instead of extracting all adverse events probably reduced the number of events included in the analyses. It is not fully clear if this modification caused or prevented bias.

Agreements and disagreements with other studies or reviews

The Ontario Health Technology Assessment (Health Quality Ontario 2009) included four RCTs in a systematic review that are also included in the present review (Brockow 2007a; Brockow 2007b; Leaute-Labreze 2001; Schiener 2007): quote "The purpose of this evidence based analysis was to determine the effectiveness and safety of ultraviolet phototherapy for moderate-to-severe plaque psoriasis. " The authors concluded that quote "Spa salt water baths prior to phototherapy did increase short term clinical response of moderate-to-severe plaque psoriasis but did not decrease cumulative ultraviolet irradiation dose" and judged that there was high-quality and adequate study evidence for this statement. Clinical response was defined as an improvement in physical signs and secondary psychological effects as well as reduction in inflammation and control of skin shedding.

In 2004, the Institute for Quality and Efficiency in Health Care (Institut für Qualität und Wirtschaftlichkeit im Gesundheitswesen, IQWiG) was commissioned by the Federal Joint Committee (Gemeinsamer Bundesausschuss; G-BA) to conduct an evaluation of the benefits and harms of different types of balneophototherapy. The systematic literature search was conducted separately for asynchronous and synchronous balneophototherapy in the databases MEDLINE, Embase and CENTRAL (in each case: coverage until March 2006). In the final report (full report in German: IQWiG 2006a; executive summary in English: IQWiG 2006b), three types of balneophototherapy were evaluated.

1. Asynchronous bath-PUVA (psoralen plus UVA) compared with UVB only (or tap water bath + UVB)

- Intervention and comparator do not match the inclusion criteria of the present review (not intervention of interest)

2. Asynchronous salt bath + UVB compared with UVB only (or tap water bath + UVB)

- Intervention and comparator match comparison 2
- Three included RCTs: the so-called "BP-BVDD-Studie 2004", Dawe 2005, and Leaute-Labreze 2001
- Conclusion: Salt bath + UVB has an additional benefit compared to UVB only (and also compared to tap water bath + UVB)

3. Synchronous balneophototherapy (Dead Sea salt bath + UVB) compared with UVB only

- Intervention and comparator match comparison 2
- A single RCT: the so-called "TOMESA_PV-Studie 2006"
- Conclusion: Dead Sea salt bath + UVB has an additional benefit compared to UVB only

The two studies BP-BVDD-Studie 2004 and TOMESA_PV-Studie 2006 are not publicly available. Thus, of the eight studies included in the present review, only two published studies were considered by IQWiG 2006a. The Federal Joint Committee (Gemeinsamer Bundesausschuss, G-BA), the highest decision-making body concerning the distribution of the Statutory Health Insurance funds in Germany, decided that indoor salt water baths followed by artificial ultraviolet B (UVB) light for patients with severe and medium severe chronic plaque psoriasis can be reimbursed not only by hospitals, but also by practices (G-BA 2008).

Roos 2010 suggested in a nonsystematic review to offer also natural balneophototherapy (Dead Sea climatotherapy) to patients though it would include additional travel and accommodation costs. Chen 2013 did not detect a difference in the effect between those phototherapy variations in a Cochrane Review. These results supported our decision that we did not differentiate between broad-band ultraviolet B, narrow-band ultraviolet B, mixed type irradiations, and psoralen bath + UVA in the present review. In a systematic review on ultraviolet based therapy for psoriasis, Almutawa 2013, in contrast, did report some differences among the phototherapy variations: quote "As a monotherapy, PUVA was more effective than NB-UVB, and NB-UVB was more effective than BB-UVB and bath PUVA in the treatment of adults with moderate to severe plaque-type psoriasis, based on clearance as an end point."

AUTHORS' CONCLUSIONS

Implications for practice

Low-certainty evidence indicates that people with chronic plaque psoriasis may see a reduction in psoriasis severity after treatment with indoor salt bath + ultraviolet B light (UVB) compared against UVB alone.

Low-certainty evidence for the same comparison indicates that people with chronic plaque psoriasis may experience little to no difference in risk of treatment-related adverse events requiring withdrawal.

As the evidence is based on data from a limited number of studies, which provided low-certainty evidence, we cannot draw a clear conclusion regarding the benefit or harm of indoor (artificial) salt water baths followed by exposure to artificial UVB for treating chronic plaque psoriasis in adults. The two trials which contributed data for the primary efficacy outcome were conducted by the same group, and one of the two trials was funded by the German Spas Association, although the other trial did not report any funding source. Neither trial blinded the outcome assessors.

Of our two comparisons of interest, one (Indoor salt bath + UVB versus other treatment without UVB) was assessed by a single study, which did not report any of our pre-specified outcomes. The other comparison (Indoor salt bath + UVB versus other treatment + UVB or UVB only) was assessed by all eight included studies, but their reporting of our pre-specified outcomes was either non-existent or limited, with a maximum of two studies reporting a given outcome.

Implications for research

We recommend further randomised controlled trials (RCTs) that assess Psoriasis Area and Severity Index (PASI-75), with detailed reporting of the outcome, as well as treatment-related adverse events requiring withdrawal. Future studies should be independently funded, and should ensure blinding of assessment and should enable blinding of performance. The time points of assessing any outcome should be specified. We think that 'end of treatment' might not be sufficiently clear. Several time points should be used to allow matching with other studies. The number of people or limbs available for analysis should be given for every time point. The included studies lacked data on all secondary outcomes. These outcomes should be considered in future studies.

The limited number of trials and centres suggest a need for increased generalisability in the evidence base for this treatment. Future studies should consider potential harm by UVB exposure. Thus, it is important to keep contact with patients, general practitioners, and dermatologists and inform about the well-being of the participants on a regular basis. In this context it seems meaningful to develop core outcomes for psoriasis treatment trials through the Cochrane Skin **C**ore **Ou**tcome **S**et **In**itiative (CS-COUSIN; http://cs-cousin.org). To consider any potential harm by UVB exposure, future study protocols should include long-term observations. Future studies should clarify the reporting according to the CONSORT statement (Schulz 2010).

Future comparisons should include less logistically-complicated types of phototherapy, such as oral psoralen plus UVA (PUVA). Secondary malignancies are uncommon, and differences very unlikely to be detected in future RCTs. Observational studies are more likely to provide evidence on this topic.

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* Indicates the major publication for the study

CHARACTERISTICS OF STUDIES

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

Arnold 2001

Study characteristics	
Methods	Two-group parallel, phase III randomised controlled trial • Setting: single-centre study with participants from the Psoriasis Day Care Centre at Ede, the Netherlands • Duration of enrolment: not reported • Follow-up time: within the 8-weeks treatment period
Participants	**Inclusion criteria of the trial** • Patients with psoriasis. • All patients were allowed to use an emollient cream if necessary. **Exclusion criteria of the trial** • Pregnancy.

Arnold 2001 *(Continued)*

- Age younger than 18 years.
- Use of systemic photosensitising agents.
- Treatment with UVB, psoralen bath + UVA, systemic immunosuppressants or antimetabolites within 6 weeks, and topically administered antipsoriatics within 2 weeks before entering the study. All patients were allowed to use an emollient cream if necessary

Characteristics (intervention versus control)

- Age: mean age in years (range): 41 (18 to 86) versus 49 (18 to 77)
- Skin type (N): II (15 versus 14), III (3 versus 4), IV (2 versus 2)
- Severity: not reported
- Previous treatment: not reported
- Duration of condition: not reported

Interventions

Intervention (n = 20)

- Saline water bath prior to irradiation with narrow-band 311 nm UVB.
- *Baths* : concentration: 6.7 g/L NaCl dissolved in tap water. Patients were immersed for 15 to 20 minutes in the salt bath, gently dried and immediately irradiated.
- *Artificial UVB* : 32 Philips TL01/1000 W tubes in a Waldmann UV 1000 unit (Waldmann, Villingen- Schwenningen, Germany) were used for narrow-band 311 nm UVB irradiation. Radiation measurements were taken with a Waldmann UV meter. The irradiance was 7.3 mW/cm^2. To convert from mW/cm^2 to J/cm^2, we need to know the time duration of irradiation, which was not reported.

Control intervention (n = 20)

- *Baths* : concentration: 5.7 mg/L psoralen in tap water. Authors dissolved 0.5% ethanolic solution of crystalline 8-methoxypsoralen (8-MOP) in tap water. Patients were immersed for 15 to 20 minutes in the psoralen bath, gently dried and immediately irradiated. Psoralen bath prior to irradiation with narrow-band 311 nm UVB.
- *Artificial UVB* : the same conditions as reported for the intervention

The interventions were applied once a day, three days a week, for up to eight weeks, and reaching a maximum number of 24 applications. Duration of UV irradiation was not reported.

Outcomes

Primary outcomes of the trial

1. Change of PASI, which was assessed at baseline, at 2, 4, 6, and 8 weeks after treatment.

Secondary outcomes of the trial

1. Adverse events (burning erythema)

Notes

Publication type is a letter to the editor.

Conflicts of interest: issue not reported.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Not reported
Allocation concealment (selection bias)	Unclear risk	Not reported
Blinding of participants and personnel (performance bias)	High risk	Not reported, so assume not blinded.

Arnold 2001 *(Continued)*
All outcomes

Blinding of outcome assessment (detection bias) All outcomes	High risk	Not reported, so assume not blinded.
Incomplete outcome data (attrition bias) All outcomes	High risk	Quote (page 353): "In the salt-UVB group, four patients dropped out: one had been included while on methotrexate medication, one had been given a prescription for calcipotriol ointment during the study and in two cases the PASI was lost or incorrectly entered into the computer." Quote (page 353): "In the psoralen-UVB group, three patients dropped out: one had to be hospitalized during the study for a non-psoriasis-related disease, for unknown reasons one did not show up after six treatments and in one the PASI was lost (as above)." Comment: we judged a high risk of bias as a considerable number of patient data could not be used in the analysis.
Selective reporting (reporting bias)	Unclear risk	Comment: we did not identify a selective reporting issue and judged an unclear risk of bias.
Other bias	Unclear risk	Comment: we did not identify other bias such as design-specific risks of bias, baseline imbalance, blocked randomisation in unblinded trials, and differential diagnostic activity. Publication type is a letter to the editor. As a result, the description of patients and methods, especially statistical approaches is limited. Tables and figures are completely absent. The number of enrolled patients is unclear. The type of analysis, such as per protocol, as treated, or per intention to treat is not reported.

Brockow 2007a

Study characteristics	
Methods	Two-group parallel, phase III pragmatic randomised controlled trial • setting: multi-centre study (4 centres) with outpatients living in the respective spa town or within a radius of 50 km from the spa centres located in Germany • Duration of enrolment: August 2001 to April 2005 • Follow-up time: 3 to 6 months
Participants	**Inclusion criteria of the trial** • Patients with psoriasis without substantial changes during the last month • Psoriasis Area and Severity Index (PASI) of >10 and/or an involvement of >15% of the total body surface area **Exclusion criteria of the trial** • Patients younger than 18 years • Pregnant or breast-feeding women • Persons with malignant hypertension, coronary heart disease, heart failure, arrhythmia, or a history of malignancies • Patients currently on photosensitising agents or on medications negatively affecting psoriasis • Patients who received phototherapy 4 weeks prior to study entry

Brockow 2007a *(Continued)*

Characteristics (intervention versus control): balanced

- Age: mean age in years (SD): 47.5 (14.2) versus 49.0 (13.7), number assessed: 79 versus 73
- Gender (M/F, %): 47 (59%) / 33 (41%) versus 45 (62%) / 28 (38%), number assessed: 80 versus 73
- Skin type (N, %): I: 2 (3%) versus 2 (3%); II: 4 (5%) versus 8 (11%); III: 59 (76%) versus 49 (66%); IV: 13 (17%) versus 15 (20%); number assessed: 78 versus 74
- Severity: median (interquartile range) PASI score (0 to 72): 17 (13 to 22) versus 16 (13 to 21), number assessed: 80 versus 73
- Previous treatment:
  - any experience of former phototherapy: 83% (66 of 80) versus 81% (60 of 74);
  - previous systematic antipsoriatic agents: 38% (30 of 80) versus 22% (16 of 74);
  - history of inpatient care because of psoriasis: 56% (42 of 75) versus 49% (36 of 73).
- duration of condition: not reported

Interventions

Intervention (n = 81)

- Highly concentrated saline spa water baths followed by artificial ultraviolet B (UVB). Patients took a 20-minute whole body saline spa water bath with a temperature of 37°C prior to UVB irradiation. Patients were allowed to dab off but not to wipe their skin after bathing. Within 10 minutes after bathing, patients were irradiated with UVB.
- *Highly concentrated saline spa water baths* : sodium chloride concentrations of local springs varied between 25% and 27% and magnesium ions should not exceed 2.9 g/L. Concentration: 250 g/L to 270 g/L NaCl present in spring water.
- *Artificial UVB* : two spa centres provided narrowband UVB (311 nm), while the remainder provided selective ultraviolet phototherapy (300 nm to 320 nm) or broadband UVB (280 nm to 320 nm). Minimal erythema dose (MED) was assessed before the start of treatment to determine the starting dose. Starting dose was 50% of MED (visit 1). For broadband UVB or ultraviolet phototherapy UVB, the dose was increased by 25% of MED from visit 2 to 10, afterward by 10% of MED. For narrow-band UVB, the dose was uniformly increased by 10% of MED. For broadband or selective UVB, the mean cumulative dose was 2.7 J/cm^2. For narrowband UVB, the mean cumulative dose was 20.7 J/cm^2.

Control intervention (n = 79)

- *Artificial UVB alone* : for broadband or selective UVB, the mean cumulative dose was 2.8 J/cm^2. For narrowband UVB, the mean cumulative dose was 19.1 J/cm^2. Other conditions equal those reported for the intervention.

The interventions were applied once a day, three days a week, for up to six weeks, and reaching a maximum number of 18 applications. Duration of UV irradiation was not reported.

Outcomes

Primary outcomes of the trial

1. PASI-50: reduction of ≥ 50% of the Psoriasis Area and Severity Index (PASI) or the involved body surface area. PASI was assessed at baseline, after 2 weeks, after 4 weeks, at the end of the intervention period (maximum: 6 weeks).

Secondary outcomes of the trial

1. PASI-75: Reduction of ≥75% of the PASI or the involved body surface area. PASI was assessed at baseline, after 2 weeks, after 4 weeks, at the end of the intervention period (maximum: 6 weeks).
2. S-PASI: self-administeredPASI by the patients. S-PASI was assessed at baseline, after 2 weeks, after 4 weeks, at the end of the intervention period (maximum: 6 weeks), after 3 months, and after 6 months.

Notes

Quote (page 731): "This study was funded by the German Spas Association (Deutscher Heilbäderverband)."

Conflicts of interest: issue not reported.

Risk of bias

Brockow 2007a *(Continued)*

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote (page 726): "Study participants were externally randomized [...] via a central telephone hotline. One computer-generated randomization list with blocks of 12 masked to the site investigators was prepared for each of the participating spa centres." Comment: the authors clearly described an adequate random sequence generation, which was judged as low risk of bias.
Allocation concealment (selection bias)	Low risk	Quote (page 726): "Allocation concealment was broken just before the first intervention was administered." Comment: the authors clearly described an adequate concealment of the allocation, which was judged as low risk of bias.
Blinding of participants and personnel (performance bias) All outcomes	High risk	Quote (page 727): "Blinding of the participants was not possible due to the nature of the interventions." Comment: the authors reported that they did not blind investigators and patients and we judged a high risk of performance bias.
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote (page 727; page 729): "Blinding of PASI raters was intended. The study centre did not inform the dermatological clinics about treatment allocation. Only the phototherapists at the spa centres knew the treatment allocation. Both patients and phototherapists were instructed not to inform the PASI raters about treatment allocation. Success of observer blinding was evaluated at the end of the intervention period by a questionnaire. [...] PASI raters stated that they knew the treatment allocation in 42% of cases (60/142)." Comment: we judged a low risk of detection bias in four studies as the assessors were presumably unaware of patients' treatment assignments.
Incomplete outcome data (attrition bias) All outcomes	Low risk	2 of 81 patients of the intervention group withdrew early and did not attend follow-up visits. 8 of 79 patients of the control group withdrew early and did not attend follow-up visits; 3 further patients were lost to follow-up but were included in the analysis. Comment: we think that the proportion of dropouts is low and may not affect the outcome. Thus, we judged a low risk of attrition bias.
Selective reporting (reporting bias)	Unclear risk	Comment: we did not identify a selective reporting issue and judged an unclear risk of bias.
Other bias	Unclear risk	Comment: we did not identify other bias such as design-specific risks of bias, baseline imbalance, blocked randomisation in unblinded trials, and differential diagnostic activity.

Brockow 2007b

Study characteristics	
Methods	Two-group parallel, phase III pragmatic randomised controlled trial • Setting: multi-centre study (five centres) with outpatients living in the respective spa town or within a radius of 50 km from the spa centres located in Germany • Duration of enrolment: August 2001 to April 2005

Brockow 2007b *(Continued)*

- Follow-up time: 3 to 6 months

Participants	**Inclusion criteria of the trial**
	• Patients with psoriasis without substantial changes during the last month
	• Psoriasis Area and Severity Index (PASI) of > 10 and/or an involvement of > 15% of the total body surface area
	
	Exclusion criteria of the trial
	• Persons with erythrodermic, pustular or isolated palmoplantar psoriasis
	• Patients younger than 18 years
	• Pregnant or breast-feeding women
	• Persons with malignant hypertension, coronary heart disease, heart failure, arrhythmia, or a history of malignancies
	• Patients currently on photosensitising agents or on medications negatively affecting psoriasis
	• Patients who were not legally competent
	• Patients who received phototherapy 4 weeks prior to study entry
	
	Characteristics (intervention versus control): balanced except gender
	• Age: mean age in years (SD): 49.8 (13.8) versus 50.0 (12.7), number assessed: 78 versus 77
	• Gender (M/F, %): 58 (74%) / 20 (26%) versus 44 (57%) / 33 (43%), number assessed: 78 versus 77, significantly more females with control
	• Skin type (N, %): I: 4 (5%) versus 1 (1%); II: 12 (15%) versus 10 (13%); III: 51 (65%) versus 52 (68%); IV: 10 (13%) versus 14 (18%); V: 1 (1%) versus 0 (0%)
	• Severity: median (interquartile range) PASI score (0 to 72): 17 (12 to 24) versus 18 (12 to 23), number assessed: 77 versus 75
	• Pprevious treatment:
	  ◦ any experience of former phototherapy: 87% (68 of 81) versus 87% (67 of 83);
	  ◦ previous systematic antipsoriatic agents: 23% (18 of 78) versus 27% (21 of 78);
	  ◦ history of inpatient care because of psoriasis: 56% (39 of 70) versus 49% (32 of 66).
	• Duration of condition: not reported

Interventions	**Intervention (n = 81)** • Low concentrated saline spa water baths followed by artificial ultraviolet B (UVB). Patients took a 20-minute whole body saline spa water bath with a temperature of 37°C prior to UVB irradiation. Patients were allowed to dab off but not to wipe their skin after bathing. Within 10 minutes after bathing, patients were irradiated with UVB. • *Low concentrated saline spa water baths* : sodium chloride concentrations varied between 4.5% and 12% depending on the local source. Concentration: 45 g/L to 120 g/L NaCl present in spring water. • *Artificial UVB* : either broadband UVB (280 nm to 320 nm) or selective UVB phototherapy (300 nm to 320 nm) were used as irradiation sources. Narrowband UVB (311 nm) was also admitted, but no spa centre provided it. Minimal erythema dose (MED) was assessed before the start of treatment to determine the starting dose. Starting dose was 50% of MED (visit 1). From visit 2 to 10 UVB dose was increased by 25% of MED, afterwards by 10% of MED. If an erythema occurred, UVB dose was adjusted depending on the severity of erythemal response. 18 Patients were treated three times a week until remission or for a maximum of 6 weeks (18 sessions). Remission was defined as a reduction of PASI below a score of 5. Mean starting dose was 0.044 J/cm^2. Average dose per visit was 0.27 J/cm^2. Cumulative dose was 4.74 J/cm^2. **Control intervention (n = 83)** • *Artificial UVB alone* : mean starting dose was 0.044 J/cm^2. Average dose per visit was 0.25 J/cm^2. Cumulative dose was 4.30 J/cm^2. Other conditions equal those reported for the intervention.

Brockow 2007b *(Continued)*

	The interventions were applied once a day, three days a week, for up to six weeks, and reaching a maximum number of 18 applications. Duration of UV irradiation was not reported.
Outcomes	**Primary outcomes of the trial** 1. PASI-50: Reduction of ≥ 50% of the Psoriasis Area and Severity Index (PASI) or the involved body surface area. PASI was assessed at baseline, after 2 weeks, after 4 weeks, at the end of the intervention period (maximum: 6 weeks). **Secondary outcomes of the trial** 1. PASI-75: reduction of ≥75% of the Psoriasis Area and Severity Index (PASI) or the involved body surface area. PASI was assessed at baseline, after 2 weeks, after 4 weeks, and at the end of the intervention period (maximum: 6 weeks). In the conclusion of the abstract, the authors used the phrase "at the end of a 6-week treatment course". In the protocol adherence of the results, the authors used the phrase "Average treatment period was 6.6 weeks (SD 1.2)." Therefore, we assume that the expression 'end of treatment' can is consistent with the time point of six weeks after start of treatment. 2. S-PASI: self-administered PASI by the patients. S-PASI was assessed at baseline, after 2 weeks, after 4 weeks, at the end of the intervention period (maximum: 6 weeks), after 3 months, and after 6 months.
Notes	Funding not reported Conflicts of interest: issue not reported.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote (page 1028): "Study participants were externally randomized [...] via a central telephone hotline. One computer-generated randomization list with blocks of 12 masked to the site investigators was prepared for each of the participating spa centres by the responsible biometrician of the study." Comment: the authors clearly described an adequate random sequence generation, which was judged as low risk of bias.
Allocation concealment (selection bias)	Low risk	Quote (page 1028): "Allocation concealment was broken shortly before the first intervention was administered by the responsible phototherapists at the spa centres." Comment: the authors clearly described an adequate concealment of the allocation, which was judged as low risk of bias.
Blinding of participants and personnel (performance bias) All outcomes	High risk	Quote (page 1029): "Blinding of the participants was not possible due to the nature of the interventions." Comment: the authors reported that they did not blind investigators and patients and we judged a high risk of performance bias.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote (page 1029; page 1030): "Blinding of PASI raters was intended. The study center did not inform the trial sites (dermatological clinics) about treatment allocation. Only the phototherapists at the spa centers knew the treatment allocation. Both patients and phototherapists were instructed not to inform the PASI raters or other staff at the trial sites about treatment allo- cation. Success of observer blinding was evaluated at the end of the intervention period. A questionnaire asked the PASI raters to state whether they knew treatment allocation or not. [...] At the end of the intervention period PASI raters stated that they knew the treatment allocation in 50% of cases (65/129)." Comment: we judged an unclear risk as blinding was tried but was not achieved.

Brockow 2007b *(Continued)*

Incomplete outcome data (attrition bias) All outcomes	High risk	2 of 81 patients of the intervention group withdrew early and did not attend follow-up visits. 19 of 83 patients of the control group withdrew early and did not attend follow-up visits. Comment: we think that the proportion of dropouts is high and may affect the outcome. Thus, we judged a high risk of attrition bias.
Selective reporting (reporting bias)	Unclear risk	Comment: we did not identify a selective reporting issue and judged an unclear risk of bias.
Other bias	Unclear risk	Comment: we did not identify other bias such as design-specific risks of bias, baseline imbalance, blocked randomisation in unblinded trials, and differential diagnostic activity.

Dawe 2005

Study characteristics	
Methods	Two-group parallel split-body, phase III randomised controlled trial with paired comparison of right versus left limb • Setting: single-centre study located in Scotland, UK • Duration of enrolment: February 2002 to February 2003 • Follow-up time: until relapse or up to 12 months

Participants	**Inclusion criteria of the trial**
	
	• Chronic plaque psoriasis; chronic was defined as a history of psoriasis present, or recurring, for at least 1 year
	
	Exclusion criteria of the trial
	
	• Not reported
	
	Characteristics
	
	• Skin type (N, %): I: 9 (15%), II: 30 (50%), III: 21 (35%)
	• Severity: not reported
	• Previous treatment:
	  ○ any experience of former phototherapy: UVB: 62% (36 of 60), psoralen bath + UVA: 13% (8 of 60);
	  ○ previous systematic antipsoriatic agents: 12% (7 of 60).
	• Duration of condition: not reported

Interventions	**Intervention (n = 60 lower extremity)** • Dead Sea salt bath followed by narrow-band UVB was allocated randomly to the right or left limb of each patient. The allocated limb was soaked in a solution of Dead Sea salt for 15 min (see treatment regimens) and whole-body phototherapy then given according to our standard departmental protocol. On completion of the treatment course, patients were followed up every 8 weeks until relapse or for up to 1 year. • *Dead Sea salt soaks* : Mavena Healthcare Mg 46 DS salt ('Sea of Life') was used. The composition of this was $MgCl_2$ 46% minimum, $CaCl_2$ 2.2% maximum, NaCl 0.8% maximum, KCl 0.5% maximum, and water of crystallisation. A 15% by weight solution of this (3.6 kg in 24 L tap water) was used for soaking arms or legs. The salt solution was at 37 °C at the start of the 15-minutes soak. The soaked limb was gently towel dried and UV administration was commenced within 10 min of the soak. The soaked limb was rinsed under tap water after UV exposure. Concentration: 150 g/L Dead Sea salt dissolved in tap water.

Dawe 2005 *(Continued)*

- *Artificial narrowband UVB* : a standard regimen, with starting dose based on minimal erythemal dose (MED) determination, then three times weekly treatment with dose increments of 20% (reducing to 10%, adjusted according to individual erythemal responses to each treatment) was used. The first 20 patients (with sufficiently clear forearm skin) recruited had a MED assessment carried out on a soaked forearm and an unsoaked forearm. For MED determination in patients with skin phototypes I and II, doses administered were 25, 50, 70, 100, 140, 200, 280 and 390 mJ cm^{-2}. For patients with skin phototype III, the first two doses were omitted and doses of 550 and 770 mJ cm^{-2} added. The MED was defined as the lowest dose to produce just perceptible erythema at 24 hours. There were no consistent differences between the paired MED assessments, so patients recruited thereafter received a MED assessment on back skin only. The phototherapy cubicles used were either Waldman UV5000, fitted with 24 Philips 100 W TL-01 lamps, or a Ninewells Medical Physics Department cubicle, fitted with 50 Philips 100 W TL-01 lamps. Irradiance was measured monthly using an IL1400A meter (International Light Inc., Newburyport, MA, U.S.A.) calibrated for TL-01 irradiation in the Photobiology Unit's optical radiation laboratory (traceable to the U.K. National Standards maintained by the National Physical Laboratory). The mean cumulative UVB dose was 24.4 J/cm^2.

Control intervention (n = 60 lower extremity other side)

- *Artificial narrowband UVB alone* : the same conditions as reported for the intervention. The mean cumulative UVB dose was 24.4 J/cm^2.

Both both legs received the same number of treatments with a mean of 25 applications. Duration of UV irradiation was not reported.

Outcomes

Primary outcomes of the trial

1. Change in psoriasis severity (Scaling, Erythema and Induration (SEI) score). The sum of Scaling, Erythema and Induration (SEI) scores, each on a 0–4 scale, was used as a psoriasis severity measure for each of the selected site symmetrical plaques.
2. Duration of psoriasis remission

Secondary outcomes of the trial

1. Comparison of minimal erythemal dose
2. Erythemal intensity with and without Dead Sea salt soaking prior to narrow-band UVB in the first 20 study participants in whom MED testing was performed on both Dead Sea salt soaked and not soaked forearms

Scaling, erythema, and induration score measured at 8 months after end of treatment.

Notes

Quote (page 615): "The sum of Scaling, Erythema and Induration (SEI) scores, each on a 0–4 scale, was used as a psoriasis severity measure for each of the selected site symmetrical plaques. This is a modification of the Psoriasis Area and Severity Index we used in other studies."
Comment: not defined as outcome.

Quote (page 615): "Adverse effects were documented as in standard practice. Erythema was recorded as grade 1 (mild and asymptomatic), grade 2 (well-demarcated, not painful), grade 3 (painful) and grade 4 (severe with blistering)."

Comment: not defined as outcome.

Quote (page 615): "Blinding was achieved by: (i) randomization as above."

Comment: blinding cannot be achieved by randomisation.

Conflicts of interest:

Quote "We are grateful to Mavena Healthcare AG, Switzerland who funded this study and provided the Dead Sea salt used. Mavena was not involved in the design, conduct or analysis of the study."

Risk of bias

Dawe 2005 *(Continued)*

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote (page 615): "The study treatment administered to each side was allocated randomly, both as a measure to ensure successful assessor blinding and also to avoid allocation bias. A blocked random allocation list (variably sized blocks) was generated with user-written software ('ralloc' command) for Stata (Stata 7.0; Stata Corporation, College Station, TX, U.S.A., 2001)." Comment: the authors clearly described an adequate random sequence generation, which was judged as low risk of bias.
Allocation concealment (selection bias)	Low risk	Quote (page 615): "Allocated treatments for each successive entrant to the study were placed in sealed, opaque envelopes which were opened by a nonblinded research nurse only after each patient had signed the informed consent form." Comment: the authors clearly described an adequate concealment of the allocation, which was judged as low risk of bias.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote (page 615): "Blinding was achieved by: (i) randomization as above; (ii) ensuring assessments were always performed before soaks; and (iii) reminders by the nonblinded study nurse to patients not to tell the assessing doctor which limb was receiving the soaks. Patients were not blinded." Comment: patients and nurse were not blinded, while physicians appeared to be blinded. Thus, we judged an unclear risk of bias.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote (page 615): "Those assessing psoriasis severity (SEI) scores were kept unaware of which side was receiving Dead Sea salt soaks. Blinding was achieved by reminders by the nonblinded study nurse to patients not to tell the assessing doctor which limb was receiving the soaks." Comment: we judged an unclear risk as blinding was tried but was not achieved. Blinding effects were not evaluated.
Incomplete outcome data (attrition bias) All outcomes	High risk	Quote (page 615): "Forty-one (68%) participants remained in the study throughout their UVB course. The 19 study withdrawals were because of: [...]" Comment: 32% of patients withdrew. We think that the proportion of dropouts is high and may affect the outcome. Thus, we judged a high risk of attrition bias
Selective reporting (reporting bias)	Unclear risk	Quote (page 616): "For the 41 patients who reached clearance or minimal residual activity while participating in the study there was no detectable difference [...]" Comment: we are not positive if this may considerably affect the outcome and we judged an unclear risk of bias.
Other bias	Unclear risk	Comment: we did not identify other bias such as design-specific risks of bias, baseline imbalance, blocked randomisation in unblinded trials, and differential diagnostic activity.

Gambichler 2001

Study characteristics

Gambichler 2001 *(Continued)*

Methods	Two-group parallel split-body, randomised controlled trial with paired comparison of right versus left elbow • Setting: single-centre study located in Germany recruiting out-patients during autumn and winter • Duration of enrolment: not reported • Follow-up time: not reported
Participants	**Inclusion criteria of the trial** • Psoriasis patients of both sexes, over 18 years of age, with skin types II and III and symmetric psoriasis plaques of equal severity on both elbows **Exclusion criteria of the trial** • Patients with antipsoriatic therapy within the last 2 months prior to the study and patients using photosensitising and psoriasis-provoking agents. **Characteristics** • Age: mean age in years (range): 36 (28 to 49) • Gender (M/F, %): 4 (40%) / 6 (60%) • Skin type (N, %): I: 0, II: 6 (60%), III: 4 (40%) • Severity: PASI not reported • Previous treatment: not reported • Duration of condition: mean duration of 2.5 years ranging from 1 to 4.5 years
Interventions	**Intervention (n = 10, one elbow)** • *Saline salt bath* : one elbow of each patient was soaked in 24% NaCl solution. Concentration: 240 g/L NaCl dissolved in tap water. • *Artificial broadband UVB* : irradiation was applied using the following device: TL/12, Philips, Hamburg, Germany. The spectrum of this UV source ranges from 280 nm to 365 nm, with a peak at 306 nm. UVB intensity was 2 mW/cm^2 at a lamp-to-site distance of 30 cm. The initial UVB dose for skin type II was 0.02 J/cm^2 and for skin type III, 0.03 J/cm^2. The UVB doses were gradually increased up to 50% to 75% of the initial UVB doses after each treatment session. The mean maximal UVB dose was 0.4 J/cm^2 and the mean cumulative UVB dose was 7.2 J/cm^2. **Control intervention (n = 10, the other elbow)** • *Tap water bath* : the other elbow of each patient was soaked in tap water containing 0.02% sodium chloride • *Artificial broadband UVB alone* : the same conditions as reported for the intervention. Both elbows were simultaneously exposed to the solution by bandaging the sites with soaked cotton wool. The interventions were applied to both elbows once a day, three to five days a week, for up to eight weeks, and reaching a maximum number of 30 applications. Duration of UV irradiation was not reported.
Outcomes	**Outcomes of the trial not classified as primary or secondary** 1. The clinical evaluation was based on a severity score with respect to desquamation, erythema, and infiltration of the psoriatic target plaques of the elbows. Severity was assessed on a 5-point scale and graded as follows: severest possible (4); severe (3); moderate (2); slight (1); none (0). The assessment was performed before commencing treatment and after 10, 20, and 30 treatments (end of treatment at 8 weeks after start of treatment).
Notes	Funding not reported Conflicts of interest: issue not reported.

Gambichler 2001 *(Continued)*

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote (page 22): "A prospective, randomized, one-blind, right/left comparison, investigating the efficacy of BPT in psoriasis with highly concentrated salt water versus tap water, was performed in an out-patient setting during autumn and winter." Comment: sequence generation not clear
Allocation concealment (selection bias)	Unclear risk	Comment: allocation concealment not clear
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote (page 22): "A prospective, randomized, one-blind, right/left comparison, investigating the efficacy of BPT in psoriasis with highly concentrated salt water versus tap water, was performed in an out-patient setting during autumn and winter." "Both elbows were simultaneously exposed to these liquids (30°C) by bandaging the sites with soaked cotton wool." Comment: partially blinding of people or limbs
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote (page 23): "To avoid interobserver variation, all patients were clinically assessed by one physician who was not informed which pretreatment had been used prior to phototherapy." Comment: blinding of outcome assessment achieved
Incomplete outcome data (attrition bias) All outcomes	Low risk	Comment: we did not identify a noteworthy proportion of dropouts and judged a low risk of attrition bias.
Selective reporting (reporting bias)	Unclear risk	Comment: we did not identify a selective reporting issue and judged an unclear risk of bias.
Other bias	Unclear risk	Comment: we did not identify other bias such as design-specific risks of bias, baseline imbalance, blocked randomisation in unblinded trials, and differential diagnostic activity.

Klein 2011

Study characteristics	
Methods	Two-group parallel, phase III randomised controlled trial • Setting: multi-centre study (30 centres) located in Germany • Duration of enrolment: not reported • Follow-up time: 6 months
Participants	**Inclusion criteria of the trial** • Psoriasis vulgaris proved by a dermatologist, age ≥ 18 years, Caucasian, having PASI at baseline > 5 **Exclusion criteria of the trial** • Pregnancy/lactation, incompatibility to treatment interventions, erosions, ulcers, viral or bacterial superinfection, generalised psoriasis pustulosa, severe general disease, intake of medication with ef-

Klein 2011 *(Continued)*

fects on photosensitivity, concomitant or previous malignant skin tumours, violation against washout criteria (topical treatment excluding emollients within the last week, systemic treatment within the last 4 weeks, UV-treatment within the last 4 months, intake of medication inducing psoriasis within the last 4 weeks)

Characteristics (intervention versus control): balanced

- Age: mean age in years (SD): 45.0 (14.4) versus 45.8 (14.7), number assessed: 179 versus 177
- Gender (M/F, %): 100 (56%) / 79 (44%) versus 107 (60.5%) / 70 (39.5%), number assessed: 179 versus 177
- Skin type (N, %): I: 9 (5.0%) versus 10 (5.6%); II: 68 (37.8%) versus 64 (35.8%); III: 72 (40.0%) versus 72 (40.2%); IV: 28 (15.6%) versus 32 (17.9%); V: 3 (1.7%) versus 1 (0.6%)
- Severity: median (interquartile range) PASI score (0 to 72): 15.1 (10.9 to 24.3) versus 15.3 (10.0 to 23.7), number assessed: 179 versus 177
- Previous treatment:
  - any experience of former phototherapy: 13.5% (28 of 179) versus 13% (26 of 177);
  - previous systematic antipsoriatic agents: 2.4% (5 of 179) versus 1% (2 of 177);
  - topical treatment: 55.8% (116 of 179) versus 55% (110 versus 177).
- duration of condition: not reported

Interventions

Intervention (n = 183)

- *Dead Sea salt soaks* : a 10% Dead Sea salt solution was used as analogue to the ion-formation of the Dead Sea. Concentration: 100 g/L NaCl dissolved in tap water.
- *Artificial narrowband UVB* : using a continuously adjustable and individually dispensable light console with a reflector system located above the tub using TL-01 UVB lamps including a gauged dosimeter (311 nm, Philips). The mean starting UVB dose was 0.38 J/cm^2. After increasing doses according to skin type, the mean UVB dose at the 35th session was 2.74 J/cm^2. The total mean dosage of irradiation was 50.7 J/cm^2 at the 35th treatment session. Irradiation was performed in mean 31.9 sessions.

Control intervention (n = 184)

- *Artificial narrowband UVB alone* : the same divide as reported for the intervention. The mean starting UVB dose was 0.38 J/cm^2. After increasing doses according to skin type, the mean UVB dose at the 35th session was 2.96 J/cm^2. The total mean dosage of irradiation was 41.3 J/cm^2 at the 35th treatment session. Irradiation was performed in mean 26.8 sessions.

The interventions were applied once a day, three to five days a week, and reaching a maximum number of 35 applications. Duration of UV irradiation was not reported.

Outcomes

Primary outcomes of the trial

1. Primary outcome parameter was the PASI. PASI score was evaluated during the therapy period at baseline, after 10, 15, 20, 25, 30 and 35 treatment sessions by the trial physicians and during follow-up 1 and 6 months after treatment session 35. Primary endpoint was the relative improvement of PASI from baseline to the end of therapy period (session 35 or clearance). Clearance was defined as PASI improvement of at least 75% from baseline to the end of therapy period.

Secondary outcomes of the trial

1. Psoriasis Disability Index (PDI)
2. Freiburg Life Quality Assessment (FLQA-d)
3. Sickness Impact Profile (SIP)
4. Willingnes to pay
5. Adverse events were coded according to the Medical Dictionary for Regulatory Activities

The authors reported early withdrawal before treatment session 35, which might be projected to a time point of about eight weeks after start of treatment. The authors also reported that some people or limbs had an early withdrawal because of adverse events.

Klein 2011 *(Continued)*

Notes	Figure 1 states that 137 patients participated in the follow-up six months after treatment. However, figure 1 also states that only 106 participants were treated through to the end of treatment at session 35 which equals eight weeks after start of treatment. We suppose that this might be a spelling error. The trial was sponsored by the primary health insurance companies in Bavaria, Germany, and completely independent from the producers of any of the medical devices used. The Bavarian ministry of social affairs approved and supervised all procedures. Conflicts of interest: the authors declared that there are none.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote (page 571): "Randomization was performed by an independent organization so that trial physicians had no influence on the allocated treatment strategy." Quote (page 572): "Randomization was performed centrally by an independent organization (central telephone randomization). Randomization was stratified by centre and skin type. Treatments were randomly assigned in a 1: 1 ratio with a block size of 6." Comment: the authors clearly described an adequate random sequence generation, which was judged as low risk of bias.
Allocation concealment (selection bias)	Low risk	Quote (page 572): "Allocation concealment was assured until the end of the study phase. Allocation concealment was broken before realizing the statistical analysis." Comment: the authors clearly described an adequate concealment of the allocation, which was judged as low risk of bias.
Blinding of participants and personnel (performance bias) All outcomes	High risk	Quote (page 571): "Blinding of patients was not possible." Comment: the authors reported that they did not blind investigators and patients and we judged a high risk of performance bias.
Blinding of outcome assessment (detection bias) All outcomes	High risk	Quote (page 577): "This study was not conducted at special skilled PT departments of university institutions, but at private practices of single dermatologists. Patients and evaluator were unblinded. Therefore, we categorised the trial as effectiveness study." Comment: the authors reported that they did not blind outcome assessors and we judged a high risk of detection bias.
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Quote (page 574, figure 1): "Intervention group: 3 did not start treatment; 1 no second PASI available; 35 early withdrawal, 6 with clearance; follow-up 6 months after treatment: 136 of 183 randomized (179 included in ITT analysis)" Quote (page 574, figure 1): "Control group: 5 did not start treatment; 2 no second PASI available; 71 early withdrawal, 1 with clearance; follow-up 6 months after treatment: 137 of 184 randomized (177 included in ITT analysis)" Comment: the authors reported a considerable proportion of dropouts. However, they including the data of almost all randomised participants in an intention-to-treat analysis. We are unsure if the dropouts may affect the outcome and therefore we judged an unclear risk of attrition bias.

Klein 2011 *(Continued)*

Selective reporting (reporting bias)	Unclear risk	Quote (page 576, table 4): "Patients with adverse events with an incidence of ≥5%" Patients with adverse events with an incidence of <5% were not reported. Comment: we are not positive if this may considerably affect the outcome and thus we judged an unclear risk of bias.
Other bias	Unclear risk	Comment: we did not identify other bias such as design-specific risks of bias, baseline imbalance, blocked randomisation in unblinded trials, and differential diagnostic activity. spelling error.

Leaute-Labreze 2001

Study characteristics	
Methods	Three-group parallel, phase III randomised controlled trial • Setting: single-centre study located at Salies de Bearn, a saline spa water centre located in the southwest of France • Duration of enrolment: not reported • Follow-up time: 12 months
Participants	**Inclusion criteria of the trial** • Patients older than 15 years with stable psoriasis vulgaris of more than 1 years' duration and a Psoriasis Area and Severity (PASI) index of more than 10; treatment with other modalities had to be stopped 2 weeks before the start of treatment **Exclusion criteria of the trial** • Patients undergoing active treatment; patients receiving systemic drugs usually responsible for worsening psoriasis, such as lithium carbonate or beta-adrenergic blocking agents; patients with erythrodermic or pustular forms of psoriasis including palmoplantar pustulosis; patients with contraindications to phototherapy (i.e. previous cutaneous carcinoma or photosensitivity) or balneotherapy (i.e. serious heart conditions or contagious disease) and pregnant women **Characteristics (intervention versus control): balanced** • Age: mean age in years (SD): 44.5 versus 48.5, number assessed: 24 versus 21 • Gender (M/F, %): not reported • Skin type (N, %): I: 0 versus 0; II: 3 (12.5%) versus 3 (14.3%); III: 11 (45.8%) versus 15 (71.4%); IV: 9 (37.5%) versus 2 (9.5%); V: 1 (4.2%) versus 1 (4.8%) • Severity: median PASI score: 15.0 versus 15.7, number assessed: 24 versus 21 • Previous treatment: not reported • Median duration of condition: 16.5 years versus 17.5 years
Interventions	**Intervention (n = 24, group C)** • *Saline salt water* : Salies de Bearn is located in the southwest of France; its thermal water is naturally saline (sodium concentration, 250 g/L). The spa water is also magnesium rich (980 mg/L) and contains 26 chemical elements, including bromine and lithium. Concentration: 250 g/L NaCl present in spring water. • *Artificial UVB* : applying UVB 311 nm phototherapy with a UVB lamp (Philips TL 01/100W, Waldman Eclairage, Reichstett, France). Starting dosage ranging from 0.1 to 0.4 J/cm^2 according to the patient's

Leaute-Labreze 2001 *(Continued)*

	phototype, treatment 5 days a week with progressive increments of 0.05 to 0.1 J/cm^2 to a maximum of 1.4 J/cm^2 for phototype 2 and 3 J/cm^2 for phototype 5. The mean total UVB dose was 11.8 /cm^2. **Control intervention (n = 21, group B)** • *Artificial UVB alone* : the same device, starting and increment doses as reported for the intervention. The mean total UVB dose was 12.5 /cm^2. The interventions were applied once a day, five days a week, for up to three weeks, and reaching a maximum number of 15 applications. Duration of UV irradiation was not reported. Group A (n = 22): saline salt water only.
Outcomes	**Primary outcomes of the trial** 1. The main criterion for judgement was the change in PASI score between days 0 and 21 determined by the blinded investigator. **Secondary outcomes of the trial** 1. Change in body surface 2. Change in quality of life index determined on a 10-cm analogue scale 3. Pruritus 4. Adverse event The patients were evaluated during the treatment at days 0, 7, 14, and 21 (end of treatment). The patients were evaluated 1 year after the treatment.
Notes	Funding: this study was supported in part by la Compagnie Fermiere de Salies de Bearn. Conflicts of interest: issue not reported.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote (page 1036): "Randomization was centrally controlled by the Dermatology Department in Bordeaux." Comment: the authors clearly described an adequate random sequence generation, which was judged as low risk of bias.
Allocation concealment (selection bias)	Low risk	Quote (page 1036): "Randomization was centrally controlled by the Dermatology Department in Bordeaux." Comment: the authors clearly described an adequate concealment of the allocation, which was judged as low risk of bias.
Blinding of participants and personnel (performance bias) All outcomes	High risk	Comment: no blinding of patients and staff
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote (page 1036): "A second investigator, blinded for randomization, examined the patient at days 0 and 21. The lesions were photographed before and after the study." Comment: we assume that the assessment of the primary outcome was blinded.

Leaute-Labreze 2001 *(Continued)*

Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Quote (page 1037): "Four patients dropped out early and were excluded from the statistical analysis: 3 had rapidly occurring adverse effects (skin irritation with saline spa water) and 1 had contracted a pulmonary infection." Quote (page 1037): "Only 40 patients (60% of those included) could be reexamined 1 year after their stay." Comment: the authors reported a considerable proportion of dropouts. However, they including the data of almost all randomised participants in an intention-to-treat analysis. We are unsure if the dropouts may affect the outcome and therefore we judged an unclear risk of attrition bias.
Selective reporting (reporting bias)	Unclear risk	Quote (page 1036): "The statistical analysis was based on the intention-to-treat principle." Quote (page 1037): "Data for the 67 remaining patients are summarized in table 2." Data of 4 patients were excluded from the analysis, though, 3 patients had adverse events such as skin irritation. Comment: we are not positive if this affected the outcome, thus, we judged an unclear risk of bias.
Other bias	Unclear risk	Quote (page 1036): "A sample containing 90 patients was selected." Quote (page 1036): "The inclusions started January 1996, and an intermediary analysis was conducted in April 1996, as 71 patients were included. The results of this analysis showed that additional inclusions could not add sufficient power to change its conclusions, and the trial's investigators decided to stop the inclusions." Comment: deviation from the protocol and potentially result-orientated analysis

Schiener 2007

Study characteristics	
Methods	Four-group parallel, phase III randomised controlled trial • Setting: multi-centre study (102 outpatient dermatologic clinics) located in Germany • Duration of enrolment: not reported • Follow-up time: not reported
Participants	**Inclusion criteria of the trial** • Patients with psoriasis without substantial changes during the past month and a Psoriasis Area and Severity Index (PASI) of greater than 7 or an involvement of the total body surface area of 15% or more **Exclusion criteria of the trial** • Patients with erythrodermic, pustular, or isolated palmoplantar psoriasis, patients younger than 18 years, pregnant or breastfeeding women, patients with malignant hypertension, coronary heart disease, heart failure, arrhythmia, or a history of malignancies. Furthermore, patients currently using photosensitising agents or medications negatively affecting psoriasis, e.g. beta-blockers, angiotensin-converting enzyme inhibitors, lithium carbonate, or indomethacin, and patients who were not legally competent.

Schiener 2007 *(Continued)*

Characteristics (intervention versus control 1 versus control 2 versus control 3): balanced

- Age: mean age in years (SD): 46 (14) versus 47 (13) versus 47 (14) versus 47 (14)
- Gender (M/F, %): 169 (57.5%) / 125 (42.5%) versus 155 (58.5%) / 110 (41.5%) versus 158 (57.0%) / 119 (43.0%) versus 195 (65.2%) / 105 (35.0%)
- Skin type (N, %): I: 7 (2.4%) versus 9 (3.64%) versus 7 (2.6%) versus 2 (0.7%); II: 35 (12.1%) versus 23 (8.7%) versus 36 (13.2%) versus 36 (12.2%); III: 184 (63.7%) versus 172 (65.4%) versus 170 (62.3%) versus 181 (61.4%); IV: 63 (21.8%) versus 56 (21.3%) versus 55 (20.1%) versus 71 (24.1%); V: 0 versus 3 (1.1%) versus 5 (1.8% versus 5 (1.7%)
- Severity: median (interquartile range) PASI score (0 to 72): 16 (12 to 22) versus 16 (12 to 22) versus 17 (13 to 22) versus 17 (13 to 24), number assessed: 299 versus 270 versus 285 versus 305
- Previous treatment: not reported
  - any experience of former phototherapy: 87.7% (257 of 299) versus 87.9% (232 of 270) versus 83.9% (229 of 285) versus 86.3% (258 of 305);
  - previous systematic antipsoriatic agents: 29.9% (88 of 299) versus 34.2% (90 of 270) versus 27.6% (76 of 285) versus 29.1% (87 of 305);
  - inpatient care due to psoriasis: 44.1% (126 of 299) versus 43.1% (112 of 270) versus 39.2% (107 of 285) versus 39.9% (118 of 305).
- Mean (standard deviation) duration of condition: 20 (13) years versus 21 (13) years versus 22 (13) years versus 20 (13) years

Interventions

Intervention (n = 299, SW-UVB)

- *Salt water bath* : concentration 25% NaCl. Concentration: 250 g/L NaCl dissolved in tap water.
- *Artificial UVB* : the following irradiation sources were accepted
  - broadband UV-B (280 nm to 320 nm), mean cumulative dose 5.2 J/cm^2,
  - selective UV phototherapy (SUP) (300 nm to 320 nm), mean cumulative does 5.2 J/cm^2, and
  - narrowband UV-B (311 nm), mean cumulative does 31.5 J/cm^2

Control intervention 1 (n = 270, UVB)

- *Artificial UVB only* : the following irradiation sources were accepted
  - broadband UV-B (280 nm to 320 nm), mean cumulative dose 5.4 J/cm^2,
  - selective UV phototherapy (SUP) (300 nm to 320 nm), mean cumulative does 5.4 J/cm^2, and
  - narrowband UV-B (311 nm), mean cumulative does 33.3 J/cm^2.

Control intervention 2 (n = 285, TW-UVB)

- *Tap water bath*
- *Artificial UVB* : the following irradiation sources were accepted
  - broadband UV-B (280 nm to 320 nm), mean cumulative dose 5.6 J/cm^2,
  - selective UV phototherapy (SUP) (300 nm to 320 nm), mean cumulative does 5.6 J/cm^2, and
  - narrowband UV-B (311 nm), mean cumulative does 29.3 J/cm^2.

Control intervention 3 (n = 305, psoralen bath + UVA)

- *Methoxsalen bath* : concentration, 0.5 mg/L
- *Artificial UVA* : broadband UVA (320 nm to 400 nm) was the only accepted irradiation source, mean cumulative dose 63.6 J/cm^2.

The UV doses were individually adapted to erythemal response.

- For patients allocated to UVB, TW-UVB, or SW-UVB, minimal erythemal dose (MED) was assessed. The MED was defined as the dose to produce a just-detectable erythema with sharp borders within 24 hours. The MED was tested by exposing 6 uninvolved and untanned body sites of an area of 2 cm^2 to increasing UVB doses.
- For patients allocated to bath psoralen bath + UVA, minimal phototoxic dose (MPD) was assessed. The MPD was defined as the dose to produce a just-detectable erythema with sharp borders within

Schiener 2007 *(Continued)*

	72 hours. The MPD was tested similarly to MED. The MPD was judged visually immediately and 48 and 72 hours after irradiation. • The starting dose for all UV-B spectra was 50% of MED, and for UVA, 30% of MPD. The interventions were applied once a day, four days a week, for up to eight weeks, and reaching a maximum number of 32 applications. Duration and mechanism (device) of UV irradiation were not reported.
Outcomes	**Primary outcomes of the trial** 1. Reduction of PASI or involved body surface area by 50% or more during the intervention period **Secondary outcomes of the trial** 1. Self-administered PASI (S-PASI): The S-PASI was operationalised in the same way as the PASI (reduction of S-PASI or involved body surface area by 50% or more). The S-PASI proved to be a reliable, valid, and responsive outcome measure.22 The S-PASI is scored and interpreted in the same way as the PASI. 2. The short form of the Questionnaire on Experience With Skin Complaints (SF-QES): The SF-QES consists of 4 subscales scored from 0 to 4. One scale has an inverse effect on the underlying construct. Total score, defined as the sum of all subscales, can range from −4 to +12. Higher scores indicate a higher level of stigmatisation feelings. 3. Global ratings of disease severity, treatment effect, and tolerability both by patients and observers: Global ratings were assessed by 100 mm visual analogue scales, higher scores indicating a more severe disease status, better treatment effect, and higher tolerability. The patients were evaluated during the treatment at baseline and after 2, 4, 6 and 8 (end of treatment) weeks.
Notes	This study was supported in part by the Berufsverband der Deutschen Dermatologen, a professional, noncommercial association of German dermatologists. Conflicts of interest: Issue not reported.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote (page 587): "One computer-generated randomization list with block lengths of 12 was prepared for each trial site by the responsible biometrician of the study. Patients were centrally randomized to receive UV-B, TW UV-B, SW UV-B, or psoralen bath + UVA." Comment: the authors clearly described an adequate random sequence generation, which was judged as low risk of bias.
Allocation concealment (selection bias)	Low risk	Quote (page 587): "Allocation was concealed until eligibility was checked and informed consent was given." Comment: the authors clearly described an adequate concealment of the allocation, which was judged as low risk of bias.
Blinding of participants and personnel (performance bias) All outcomes	High risk	Quote (page 589): "Patients were not told to which intervention they were randomized. Nevertheless, only patients assigned to TW UV-B or psoralen bath + UVA could in fact be considered to be blinded. The bath solutions of TW UV-B and psoralen bath + UVA do not differ in physical appearance, taste, or color. Patients assigned to SW UV-B or UV-B could not be blinded. A highly concentrated salt-water bath can be easily identified by taste or buoyancy." Comment: the authors reported that they did not blind patients and we judged a high risk of performance bias.

Schiener 2007 *(Continued)*

Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote (page 589): "Blinding of PASI raters was intended. Both the staff and the patients were instructed not to inform PASI raters about the treatment allocation. Success of rater blinding was evaluated at the end of the intervention period. [...] At the end of the intervention period, PASI raters stated that they knew the treatment assignment in 58.2% of cases (587/1008)." Comment: we judged a low risk of detection bias as the assessors were presumably unaware of patients' treatment assignments.
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Intervention (SW-UVB) 310 randomised - 84 not assigned intervention, lost, or discontinued = 226, but 299 included in analysis (11 excluded) Intervention (UVB alone) 301 randomised - 116 not assigned intervention, lost, or discontinued = 185, but 270 included in analysis (31 excluded) Intervention (TW-UVB) 301 randomised - 123 not assigned intervention, lost, or discontinued = 178, but 285 included in analysis (24 excluded) Intervention (psoralen bath + UVA) 321 randomised - 88 not assigned intervention, lost, or discontinued = 233, but 305 included in analysis (16 excluded) Comment: the authors reported a considerable proportion of dropouts. However, they including the data of almost all randomised participants in an intention-to-treat analysis. We are unsure if the dropouts may affect the outcome and therefore we judged an unclear risk of attrition bias.
Selective reporting (reporting bias)	Unclear risk	Comment: we did not identify a selective reporting issue and judged an unclear risk of bias.
Other bias	Unclear risk	Comment: we did not identify other bias such as design-specific risks of bias, baseline imbalance, blocked randomisation in unblinded trials, and differential diagnostic activity.

$CaCl_2$: calcium chloride;**KCl:** potassium chloride; **MED:** minimal erythema dose; **$MgCl_2$:** magnesium chloride; **MPD:** minimal phototoxic dose; **NaCl:** sodium chloride; **PASI:** Psoriasis Area and Severity Index; **SD:** standard deviation; **UV:** ultra violet.

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

Study	Reason for exclusion
Bailey 2012	Study type not of interest: systematic review
Browne 2017	Study type not of interest: nonsystematic review
Cattaneo 2012	Study type not of interest: single-arm study
Chen 2013	Study type not of interest: systematic review
Claes 2006	Study type not of interest: systematic review
Even 1996	Intervention not of interest: Dead Sea bathing and sun exposure
Eysteinsdottir 2014	Intervention not of interest: geothermal sea bathing + UVB
Gambichler 2000b	Study type not of interest: systematic review
Gawlik 2001	Study type not of interest: nonsystematic review

Study	Reason for exclusion
Guan 2017	Study type not of interest: systematic review
Hollo 2004	Study type not of interest: single-arm study
Morri 2012	Intervention not of interest: sulphurous thermal spring water, bath not followed by UVB consistently
Olafsson 2002	Intervention not of interest: lagoon bathing followed by UVB
Scholl 1981	Intervention not of interest: oral retinoid added to bath and UVB
Werfel 2015	Intervention not of interest: UVB but not salt water baths

UV: ultra violet

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

NCT02713711

Methods	Four-group parallel, phase III randomised controlled trial • Setting: single-centre study located in Chile • Duration of enrolment: not reported • Randomisation: not reported • Blinding: not reported • Follow-up time: 4 weeks • Groups: balneophototherapy, balneotherapy, phototherapy, no treatment
Participants	**Inclusion criteria of the trial** • Patients older than 18 years with medically diagnosed psoriasis more than 1 year ago, with more than one plaque on the skin, and with concurrent topical treatment for psoriasis **Exclusion criteria of the trial** • Pregnancy, skin carcinoma, severe diabetes mellitus, uncontrolled pathologies and/or cardiac/renal insufficiency and/or acute infections **Characteristics (intervention versus control)** • Age: not reported • Gender (M/F, %): not reported • Phototype (N, %): not reported
Interventions	**Intervention (artificial balneophototherapy group)** • *Saline salt water*: 12 sessions of 15 minutes balneotherapy in warm water (32°C) and dissolved natural sea salt (250g/L) • *UVB*: 12 sessions of phototherapy (UVB) **Comparator (artificial balneotherapy group)** • *Saline salt water*: 12 sessions of 15 minutes balneotherapy in warm water (32°C) and dissolved natural sea salt (250g/L)*Artificial UVB alone*: the same conditions as reported for the intervention. **Comparator (phototherapy group)** • *UVB alone*: the same conditions as reported for the intervention.

NCT02713711 *(Continued)*

	Control (no treatment group) • The control group plaques did not receive any treatment.
Outcomes	**Primary outcomes of the trial** 1. Per cent change in psoriatic plaque area from day 1 before first session until day 26 after 12 sessions **Secondary outcomes of the trial** 1. Change in psoriatic plaque erythema from day 1 to day 26 2. Change of individual perception of psoriasis severity assessed by psoriasis area and severity index (PASI) score from day 1 to day 26 3. Change of individual perception of quality of life index assessed by short form 36 health survey (SF-36) score from day 1 to day 26 4. Individual change of psoriasis disability assessed by psoriasis disability index (PDI) from day 1 to day 26 The patients were evaluated during the treatment at days 1, 12, and 26 (end of treatment).
Notes	Sponsor: Universidad Catolica del Maule, Chile. Study start date December 2013; study completion data 2014; first registered with ClinicalTrials.gov in March 2016. No study results posted. No publication available. Thus, risk of bias cannot be assessed and results cannot be presented. Official title: "Comparison of the effectiveness of artificial balneotherapy, phototherapy, and artificial balneophototherapy in the treatment of psoriasis: A randomized controlled trial"

DATA AND ANALYSES

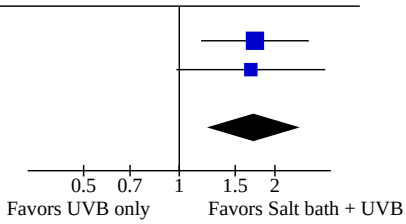
Comparison 1. Saline+UVB versus UVB

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1.1 PASI-75 response	2	278	Risk Ratio (M-H, Fixed, 95% CI)	1.71 [1.24, 2.35]
1.2 Treatment-related adverse events requiring withdrawal (between participant)	2	404	Risk Ratio (M-H, Fixed, 95% CI)	0.96 [0.35, 2.64]
1.3 Treatment-related adverse events requiring withdrawal (within participant)	1	116	Risk Ratio (M-H, Fixed, 95% CI)	0.50 [0.05, 5.36]

Analysis 1.1. Comparison 1: Saline+UVB versus UVB, Outcome 1: PASI-75 response

Study or Subgroup	Salt bath + UVB Events	Total	UVB only Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Brockow 2007a	45	78	22	66	60.7%	1.73 [1.17 , 2.56]
Brockow 2007b	29	74	14	60	39.3%	1.68 [0.98 , 2.88]
Total (95% CI)		**152**		**126**	**100.0%**	**1.71 [1.24 , 2.35]**
Total events:	74		36			

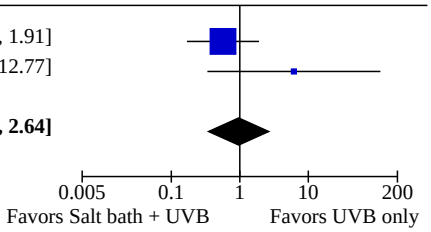
Heterogeneity: Chi² = 0.01, df = 1 (P = 0.93); I² = 0%
Test for overall effect: Z = 3.31 (P = 0.0009)
Test for subgroup differences: Not applicable



Analysis 1.2. Comparison 1: Saline+UVB versus UVB, Outcome 2: Treatment-related adverse events requiring withdrawal (between participant)

Study or Subgroup	Salt bath + UVB Events	Total	UVB only Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Klein 2011	4	180	7	179	93.0%	0.57 [0.17 , 1.91]
Leaute-Labreze 2001	3	24	0	21	7.0%	6.16 [0.34 , 112.77]
Total (95% CI)		**204**		**200**	**100.0%**	**0.96 [0.35 , 2.64]**
Total events:	7		7			

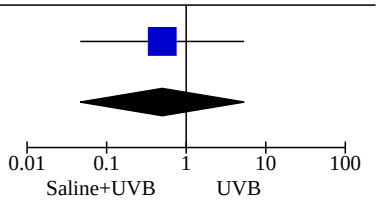
Heterogeneity: Chi² = 2.29, df = 1 (P = 0.13); I² = 56%
Test for overall effect: Z = 0.08 (P = 0.94)
Test for subgroup differences: Not applicable



Analysis 1.3. Comparison 1: Saline+UVB versus UVB, Outcome 3: Treatment-related adverse events requiring withdrawal (within participant)

Study or Subgroup	Salt bath + UVB Events	Total	UVB only Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Dawe 2005	1	58	2	58	100.0%	0.50 [0.05 , 5.36]
Total (95% CI)		**58**		**58**	**100.0%**	**0.50 [0.05 , 5.36]**
Total events:	1		2			

Heterogeneity: Not applicable
Test for overall effect: Z = 0.57 (P = 0.57)
Test for subgroup differences: Not applicable



ADDITIONAL TABLES

Table 1. Psoriasis Area and Severity Index (PASI)

Section		Area involved		Severity		
Item	**Factor**	**Item**	**Factor**	**Item**	**Clinical signs**	**Factor**
Head	0.1	-	0, 1, 2, 3, 4, 5, or 6	Sum of clinical signs	-	0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, or 12

Table 1. Psoriasis Area and Severity Index (PASI) *(Continued)*

-	-	0%	0	-	Erythema (redness)	0, 1, 2, 3, or 4
-	-	< 10%	1	-	Induration (thickness)	0, 1, 2, 3, or 4
-	-	10% to < 30%	2	-	Desquamation (scaling)	0, 1, 2, 3, or 4
-	-	30% to < 50%	3	-	-	-
-	-	50% to < 70%	4	-	-	-
-	-	70% to < 90%	5	-	-	-
-	-	90% to 100%	6	-	-	-
Arms	0.2	-	-	-	-	-
Trunk	0.3	-	-	-	-	-
Legs	0.4	-	-	-	-	-
Subtotal	Section factor *area factor* sum of clinical signs factor					
Total	Sum of subtotals; range 0 to 72					

According to Fredriksson 1978. Online calculator available (Corti 2009). Instructions: multiply section factor with area involved factor and multiply with sum of clinical signs factor; repeat for all four sections and add up all four subtotals. The items and corresponding factors regarding the area involved and the severity are exemplified for the section item 'head' and are not shown for the other section items 'arms', 'trunk', and 'legs'. Severity of clinical signs range from none (zero) to maximum (four).

Table 2. Dermatology Life Quality Index (DLQI) questionnaire

Number	Question	Answer options
1	Over the last week, how itchy, sore, painful, or stinging has your skin been?	Very much A lot A little Not at all
2	Over the last week, how embarrassed or self-conscious have you been because of your skin?	Very much A lot A little Not at all
3	Over the last week, how much has your skin interfered with you going shopping or looking after your home or garden?	Very much A lot A little Not at all

Table 2. Dermatology Life Quality Index (DLQI) questionnaire *(Continued)*

		Not relevant
4	Over the last week, how much has your skin influenced the clothes you wear?	Very much A lot A little Not at all Not relevant
5	Over the last week, how much has your skin affected any social or leisure activities?	Very much A lot A little Not at all Not relevant
6	Over the last week, how much has your skin made it difficult for you to do any sport?	Very much A lot A little Not at all Not relevant
7	Over the last week, has your skin prevented you from working or studying? (If "No", over the last week, how much has your skin been a problem at work or studying?)	Yes No Not relevant
8	Over the last week, how much has your skin created problems with your partner or any of your close friends?	Very much A lot A little Not at all Not relevant
9	Over the last week, how much has your skin caused any sexual difficulties?	Very much A lot A little Not at all Not relevant
10	Over the last week, how much of a problem has the treatment for your skin been, for example, by making your home messy or by taking up time?	Very much A lot A little Not at all

Table 2. Dermatology Life Quality Index (DLQI) questionnaire *(Continued)*

	Not relevant

The aim of the Dermatology Life Quality Index (DLQI) questionnaire is to measure how much the life of adults has been affected by their skin problem over the last week. The DLQI is calculated by summing the score of each question, resulting in a maximum of 30 and a minimum of zero. The higher the score, the more quality of life is impaired. The scoring of each question is as follows: Very much (three), A lot (two), A little (one), Not at all (zero), Not relevant (zero); question seven = Yes (three) to unanswered (zero).
Meaning of the total DLQI score: zero to one = no effect at all on patient's life; two to five = small effect on patient's life; six to 10 = moderate effect on patient's life; 11 to 20 = very large effect on patient's life; 21 to 30 = extremely large effect on patient's life. Minimal Clinically Important Difference (MCID) of the DLQI: a change in DLQI score of at least four points is considered clinically important (Basra 2008).
Finlay 1994 developed the DLQI. The following website provides further information and interpretation: www.dermatology.org.uk.

Table 3. Salt concentrations

Study	Intervention	Comparator
Arnold 2001	6.7 g/L NaCl dissolved in tap water	5.7 mg/L psoralen dissolved in tap water
Brockow 2007a	250 to 270 g/L NaCl present in natural spring water	no bath
Brockow 2007b	45 to 120 g/L NaCl present in natural spring water	no bath
Dawe 2005	150 g/L Dead Sea salt dissolved in tap water	no bath
Gambichler 2001	240 g/L NaCl dissolved in tap water	0.2 g/L present in tap water
Klein 2011	100 g/L Dead Sea salt dissolved in tap water	no bath
Leaute-Labreze 2001	250 g/L NaCl present in natural sping water	no bath
Schiener 2007	250 g/L NaCL dissolved in tap water	0.5 mg/L psoralen dissolved in tap water

NaCl: sodium chloride

Table 4. PASI-50 (between-participant data)

Study	Time point	Intervention			Comparators			P value[1]
		Description	A/R	Proportion	Description	A/R	Proportion	
Brockow 2007a	Session 18 (six weeks)	Salt bath + UVB	79/81	86% (68 of 79)	UVB only	71/79	54% (38 of 71)	**< 0.001**
Brockow 2007b	Session 18 (six weeks)	Salt bath + UVB	79/81	73% (58 of 79)	UVB only	64/83	50% (32 of 64)	**0.0053**
Schiener 2007	Eight weeks	Salt bath + UVB	299/310	74.9% (224 of 299)	Tap water + UVB	285/301	60.7% (173 of 285)	**0.0003**
					Psoralen bath + UVA	305/321	78.4% (239 of 305)	0.3369

[1]: Estimated by review authors using Easy Fisher Exact Test Calculator (Social Science Statistics 2018); statistically signifiant P values (P < 0.05) in bold font.
A/R: number of analysed/randomised people; n.r.: not reported; PASI-50: Participants have achieved a 50% or more reduction in their Psoriasis Area and Severity Index score from baseline; UVB: artificial ultraviolet B light

Table 5. Treatment-related adverse events

Study	Interven-tion				Comparators				P value[1]
	Description	A/R	Type	Events	Description	A/R	Type	Events	
Arnold 2001	Salt bath + UVB	16/20	Burning erythema	2	Psoralen bath + UVA	17/20	Burning erythema	2	1.0
Brockow 2007a	Salt bath + UVB	79/81	Dermatitis solaris	2	UVB	71/79	Dermatitis solaris	1	1.0
Brockow 2007b	Salt bath + UVB	76/81	3 x phototoxic reaction 1 × burning/stinging	4	UVB	53/83	2x phototoxic reaction 3x dermatitis solaris	5	0.4861
Dawe 2005	Salt bath + UVB	41/60 arms or legs	3 x itching, 2 x stinging 1 x itchy papular eruption	6	UVB	41/60 arms or legs	n.a.	0	**< 0.0257**

Table 5. Treatment-related adverse events *(Continued)*

Gambichler 2001	Salt bath + UVB	10/10 elbows	n.a.	0	Tap water + UVB	10/10 elbows	n.a.	0	1.0
Klein 2011	Salt bath + UVB	180/183	'Definite' or 'probable' events	21	UVB	179/184	'Definite' or 'probable' events	11	0.0943
Leaute-Labreze 2001	Salt bath + UVB	24/24	Itching and burning in most cases	12	UVB	21/21	Itching and burning in most cases	7	0.3661
Schiener 2007	Salt bath + UVB	284/310	Phototoxic reactions	33	UVB	252/301	Phototoxic reactions	31	0.894
					Tap water + UVB	266/301	Phototoxic reactions	19	0.0809
					Psoralen bath + UVA	297/321	Phototoxic reactions	16	**0.0072**
			Grade IV or V erythemas	3	UVB	252/301	Grade IV or V erythemas	1	0.6263
					Tap water + UVB	266/301	Grade IV or V erythemas	2	1.0
					Psoralen bath + UVA	297/321	Grade IV or V erythemas	5	0.7252
			Oedema[2]	n.r.	n.r.	n.r.	Oedema[2]	n.r.	n.a.
			Blisters[2]	n.r.	n.r.	n.r.	Blisters[2]	n.r.	n.a.

[1]: Estimated by review authors using Easy Fisher Exact Test Calculator (Social Science Statistics 2018); statistically signifiant P values (P < 0.05) in bold font.
[2]: Schiener 2007 reported seven patients who developed edema and four who developed blisters, but the adverse events were not linked to a treatment group.
A/R: number of analyzed/randomized people or limbs; n.a.: not applicable; n.r.: not reported; UVA: artivicial ultraviolet A light; UVB: artificial ultraviolet B light

Table 6. Treatment-related serious adverse events

Study	Intervention				Comparators				P value[1]
	Description	A/R	Type	Events	Description	A/R	Type	Events	

Table 6. Treatment-related serious adverse events *(Continued)*

Schiener 2007	Salt bath + UVB	284/310	n.a.	0	UVB only	252/301	n.a.	0	1.0
					Tap water + UVB	266/301	1 x photodermatitis; 1 x exacerbation as guttate psoriasis; 1 alcohol problem	3	0.1125
					Psoralen bath + UVA	297/321	2 x photodermatitis; 1 x malignant melanoma[2]	3	0.2491

[1]: Estimated by review authors using Easy Fisher Exact Test Calculator (Social Science Statistics 2018); statistically signifiant P values (P < 0.05) in bold font.
[2]: Schiener 2007 provided detailed information on the malignant melanoma case: "A malignant melanoma was diagnosed after the eighth irradiation. Queries at the trial site disclosed that an 'atypical nevus' had already been detected by a dermatologist 17 months before study enrollment. Furthermore, it is very unlikely that the tumor had progressed during the short period of 2 weeks." Though, a relationship between study intervention and event was judged as possible, we did not separately include the case as a secondary malignancy.
A/R: number of analysed/randomised people; n.a.: not applicable; UVA: artificial ultraviolet A light; UVB: artificial ultraviolet B light

Table 7. Patient-reported outcomes

Study	HRQL	Intervention			Comparators			P value[1]
	Measure	Description	A/R	Change of index	Description	A/R	Change of index	
Brockow 2007b [2]	Global rating of disease severity by patients. Mean change of score (standard deviation) baseline to end of treatment (maximum 6 weeks).	Salt bath + UVB	n.r./81	29.9 (24.7)	UVB only	n.r./83	12.4 (24.6)	n.r.
Brockow 2007b [2]	" baseline to 3 months	Salt bath + UVB	n.r./81	32.2 (27.6)	UVB only	n.r./83	22.5 (25.5)	n.r.
Brockow 2007b [2]	" baseline to 6 months	Salt bath + UVB	n.r./81	22.5 (27.9)	UVB only	n.r./83	24.3 (27.6)	n.r.

Table 7. Patient-reported outcomes *(Continued)*

Brockow 2007b [2]	Global rating of treatment effect by patients. Mean (standard deviation) score at end of treatment (maximum 6 weeks).	Salt bath + UVB	n.r./81	81.2 (19.2)	UVB only	n.r./83	64.5 (27.7)	n.r.
Brockow 2007b [2]	Global rating of tolerability by patients. Mean (standard deviation) score at end of treatment (maximum 6 weeks).	Salt bath + UVB	n.r./81	87.4 (12.3)	UVB only	n.r./83	87.4 (12.3)	n.r.
Brockow 2007b [2]	Self-administered PASI (S-PASI). Number of participants with reduction of S-PASI by 50% or more (%) at end of treatment (maximum 6 weeks).	Salt bath + UVB	77/81	45 (58)	UVB only	61/83	24 (39)	**0.04**
Brockow 2007b [2]	" at 3 months.	Salt bath + UVB	72/81	40 (56)	UVB only	54/83	24 (44)	0.28
Brockow 2007b [2]	" at 6 months.	Salt bath + UVB	67/81	30 (45)	UVB only	46/83	24 (50)	0.70
Klein 2011	Psoriasis disability index at eight weeks on session 35	Salt bath + UVB	144/183[3]	-18.3% ((22.3 - 27.3) / 27.3)[5]	UVB only	106/184[4]	-15.2%% ((25.6 - 30.2) / 30.2)[5]	n.r.
Klein 2011	" at one month	Salt bath + UVB	n.r./183	-26.1% ((20.2 - 27.3) / 27.3)[5]	UVB only	n.r./184	-20.5%% ((24.0 - 30.2) / 30.2)[5]	n.r.
Klein 2011	" at six months	Salt bath + UVB	n.r./183	-30.0% ((19.1 - 27.3) / 27.3)[5]	UVB only	n.r./184	-23.5%% ((23.1 - 30.2) / 30.2)[5]	n.r.
Klein 2011	Sickness impact profile at eight weeks on session 35	Salt bath + UVB	144/183	-19.0% ((4.7 - 5.8) / 5.8)[5]	UVB only	106/184	-10.7% ((5.0 - 5.6) / 5.6)[5]	n.r.
Klein 2011	" at one month	Salt bath + UVB	n.r./183	-20.7% ((4.6 - 5.8) / 5.8)[5]	UVB only	n.r./184	-8.9% ((5.1 - 5.6) / 5.6)[5]	n.r.

Table 7. Patient-reported outcomes *(Continued)*

Klein 2011	" at six months	Salt bath + UVB	n.r./183	-31.0% ((4.0 - 5.8) / 5.8)[5]	UVB only	n.r./184	-21.4% ((4.4 - 5.6) / 5.6)[5]	n.r.
Klein 2011	Improvement of physical complaints of Freiburg Life Quality Assessment on session 35 (eight weeks)	Salt bath + UVB	144/183	+16.7% ((2.8 - 2.4) / 2.4)	UVB only	106/184	+8.3% ((2.6 - 2.4) / 2.4)	**<0.001**
Klein 2011	Global health total of Freiburg Life Quality Assessment on session 35 (eight weeks)	Salt bath + UVB	144/183	+37.5% ((3.3 - 2.4) / 2.4)	UVB only	106/184	+8.3% ((2.6 - 2.4) / 2.4)	**0.007**
Klein 2011	Global health skin only of Freiburg Life Quality Assessment on session 35 (eight weeks)	Salt bath + UVB	144/183	+100.0% ((4.8 - 2.4) / 2.4)	UVB only	106/184	+54.2% ((3.7 - 2.4) / 2.4)	**0.001**
Klein 2011	Global impression of therapy: very good or good on session 35 (eight weeks)	Salt bath + UVB	144/183	64.8%	UVB only	106/184	32.8%	**<0.001**
Klein 2011	Global impression of therapy: very bad or bad on session 35 (eight weeks)	Salt bath + UVB	144/183	5.3%	UVB only	106/184	30.4%	**<0.001**
Leaute-Labreze 2001	Quality of life index determined on a 10-cm analog scale on day 21 (three weeks)	Salt bath + UVB	24/24	-60%[6]	UVB only	21/21	-50%[6]	n.r.
Schiener 2007 [2]	Global rating of disease severity by patients. Mean change of score (standard deviation) baseline to 2, 4, and 6 weeks or to end of treatment (maximum 8 weeks).	Salt bath + UVB	299/310	36.3 (26.4)	UVB only	270/301	21.5 (26.3)	n.r.
Schiener 2007 [2]	"	Salt bath + UVB	299/310	36.3 (26.4)	Tap water + UVB	285/301	28.1 (29.9)	n.r.
Schiener 2007 [2]	"	Salt bath + UVB	299/310	36.3 (26.4)	Psoralen bath + UVA	305/321	43.2 (27.5)	n.r.
Schiener 2007 [2]	Global rating of treatment effect by patients. Mean (standard deviation) score at 2, 4, and 6 weeks or at end of treatment (maximum 8 weeks).	Salt bath + UVB	299/310	77.8 (21.3)	UVB only	270/301	59.0 (27.0)	n.r.

Table 7. Patient-reported outcomes *(Continued)*

Schiener 2007 [2]	"	Salt bath + UVB	299/310	77.8 (21.3)	Tap water + UVB	285/301	65.3 (29.4)	n.r.
Schiener 2007 [2]	"	Salt bath + UVB	299/310	77.8 (21.3)	Psoralen bath + UVA	305/321	82.9 (22.5)	n.r.
Schiener 2007 [2]	Global rating of tolerability by patients. Mean (standard deviation) score at 2, 4, and 6 weeks or at end of treatment (maximum 8 weeks).	Salt bath + UVB	299/310	85.1 (16.7)	UVB only	270/301	75.8 (21.3)	n.r.
Schiener 2007 [2]	"	Salt bath + UVB	299/310	85.1 (16.7)	Tap water + UVB	285/301	82.3 (19.6)	n.r.
Schiener 2007 [2]	"	Salt bath + UVB	299/310	85.1 (16.7)	Psoralen bath + UVA	305/321	88.6 (16.1)	n.r.
Schiener 2007 [7]	Short Form of the Questionnaire on Experience with Skin complaints (SF-QES). Change scores did not differ significantly between groups (P = 0.47). Overall median improvement was -0.14 (25th to 75th percentile, -1.27 to 0.00; n = 1107 participants). Assessment at 2, 4, and 6 weeks or at end of treatment (maximum 8 weeks).	no data	no data	no data	no data	no data	no data	0.47
Schiener 2007 [8]	Self-administered PASI (S-PASI). Number of participants with reduction of S-PASI by 50% or more (%) at 2, 4, and 6 weeks or at end of treatment (maximum 8 weeks).	Salt bath + UVB	286/310	217 (75.9)	UVB	258/301	134 (51.9)	**<0.001**
Schiener 2007 [8]	"	Salt bath + UVB	286/310	217 (75.9)	Tap water + UVB	266/301	174 (65.4)	**0.009**
Schiener 2007 [8]	"	Salt bath + UVB	286/310	217 (75.9)	Psoralen bath + UVA	292/321	237 (81.2)	0.13

[1]: P values reported by study

[2]: Brockow 2007b and Schiener 2007. Global ratings on on disease severity, treatment effect, and tolerability using 100-mm visual analog scales. Positive change scores indicated improvement, higher scores at the end of treatment indicated better effectivenes or tolerability.

[3]: 183 patients were randomised to Salt bath + UVB. Data from 144 people were analysed and the data from the following 39 patients were not analysed: Three people did not start treatment; one person was not available for second PASI; early withdrawal concerned 35 people; see figure 1 of the article by Klein 2011.

[4]: 184 patients were randomised to UVB only. Data from 106 patients were analysed and the data from the following 78 patients were not analysed: Five people did not start treatment; two people were not available for second PASI; early withdrawal concerned 71 patients; see figure 1 of the article by Klein 2011. This figure states that 137 patients participated in the follow-up six months after treatment. However, the same figure also states that only 106 participants were treated through to the end of treatment at session 35 which equals eight weeks after start of treatment. We suppose that this might be a spelling error.
[5]: *Psoriasis disability index* or *Sickness impact profile* change from baseline as a proportion from baseline as reported by Klein 2011 and calculated by review authors using the following formula: ((session 35 - baseline) / baseline). The data show a better improvement in the Salt bath + UVB group compared to the UVB group for all six analyses, though, it is not clear whether the differences are statistically significant.
[6]: Quality of life index change from baseline as a proportion from baseline as reported and calculated by Leaute-Labreze 2001 using the following formula: ((day 21 - day 0) / day 0). The data show a decrease of quality of life index for both treatment groups, however, the quality of life index was not defined by the study and it is not clear whether the changes actually mean impairment or improvement.
[7]: Schiener 2007: The Short Form of the Questionnaire on Experience with Skin complaints (SF-QES) consists of 4 subscales scored from 0 to 4. One scale has an inverse effect on the underlying construct. Total score, defined as the sum of all subscales, can range from −4 to +12. Higher scores indicate a higher level of stigmatisation feelings.
[8]: Schiener 2007: The Self-administered PASI (S-PASI) was operationalized in the same way as the PASI (reduction of S-PASI or involved body surface area by 50% or more). The S-PASI proved to be a reliable, valid, and responsive outcome measure. The S-PASI is scored and interpreted in the same way as the PASI.
A/R: number of analysed/randomised people; n.r.: not reported; not stat signif: not statistically significant; PUVA: psoralen and ultraviolet A light; UVB: artificial ultraviolet B light

Table 8. PASI-75 (between-participant data)

Study	Time point	Intervention			Compara-tors			P value[1]
		Description	A/R	Achieved; Failed	Description	A/R	Achieved; Failed	
Brockow 2007a [2,3]	session 18 (six weeks)	Salt bath + UVB	78/81	58% (45 of 78); 42% (33 of 78)	UVB only	66/79	33% (22 of 66); 67% (44 of 66)	0.0044
Brockow 2007b [2]	session 18 (six weeks)	Salt bath + UVB	74/81	39% (29 of 74); 1% (45 of 74)	UVB only	60/83	23% (14 of 60); 77% (46 of 60)	0.0632

[1]: Estimated by review authors using Easy Fisher Exact Test Calculator (Social Science Statistics 2018); statistically signifiant P values (P < 0.05) in bold font.
[2]: Brockow 2007a and Brockow 2007b classified the data as results from secondary analysis.
[3]: We identified a spelling error Brockow 2007a: the spelling concerning the heading 'PASI-75' in table 2 should be 'PASI-75' instead of 'PASI-50'.
A/R: number of analysed/randomised people or limbs; UVA: artificial ultraviolet A light; UVB: artificial ultraviolet B light

Table 9. Treatment-related adverse events requiring withdrawal

Study	Time point	Intervention			Compara-tors			P value[1]
		Description	A/R	Type and (number) of events	Description	A/R	Type and (number) of events	

Table 9. Treatment-related adverse events requiring withdrawal *(Continued)*

Dawe 2005	eight weeks	Salt bath + UVB	58/60	severe itch immediately after Dead Sea salt soaks (1)	UVB only	58/60	inadequate response to phototherapy and conversion to psoralen bath + UVA (2)	1.0
Klein 2011	session 35 (eight weeks)	Salt bath + UVB	180/183	n.sp. (4)	UVB only	179/184	n.sp. (7)	0.3795
Leaute-Labreze 2001	three weeks	Salt bath + UVB	24/24	skin irritation (3)	UVB only	21/21	skin irritation (0)	0.2364

[1]: Estimated by review authors using Easy Fisher Exact Test Calculator (Social Science Statistics 2018); statistically signifiant P values (P < 0.05) in bold font.
A/R: number of analysed/randomised people or limbs; n.r.: not reported; n.sp.: not specified; UVA: artificial ultraviolet A light; UVB: artificial ultraviolet B light

Table 10. PASI (between-participant data)

Study	Time point	Intervention			Comparators			P value[1]
		Description	A/R	Change of PASI[2]	Description	A/R	Change PASI[2]	
Arnold 2001	Session 24 (eight weeks)	Salt bath + UVB	16/20	-90% ((1.5 to 14.6)/14.6)	Psoralen bath + UVA	17/20	-74% ((3.1 to 11.9)/11.9)	n.r.
Klein 2011	Session 35 (eight weeks)	Salt bath + UVB	179/183	-82% ((2.7 to 15.1)/15.1)	UVB only	177/184	-44% ((8.6 to 15.3)/15.3)	< 0.0001
Leaute-Labreze 2001	Session 15 (three weeks)	Salt bath + UVB	24/24	-55%	UVB only	21/21	-64%	n.r.

[1]: P value calculated by study authors.
[2]: Calculation takes use of the values measured on the following days: (day 21 - day 0)/day 0.
A/R: number of analysed/randomised people; n.r.: not reported; PASI: Psoriasis Area and Severity Index score; UVA: artificial ultraviolet B light; UVB: artificial ultraviolet B light

Table 11. Clearance of psoriatic lesions scores (within-participant data)

Study	Score	Body parts	Intervention	Comparators	P value[1]

Table 11. Clearance of psoriatic lesions scores (within-participant data) *(Continued)*

			Description	BL	Change of score[2]	Descrip-tion	BL	Change of score[2]	
Dawe 2005	scaling, erythema, and induration score measured at 8 months[3]	arms or legs	Salt bath + UVB	6.8	-63% ((2.5 to 6.8)/6.8)	UVB	6.8	-63% ((2.5 to 6.8)/6.8)	"not sig-nificant"
Gambich-ler 2001	five-point severity score measured after 30 treatments (time point n.r.)	elbows	Salt bath + UVB	7.9	-68% ((2.5 to 7.9)/7.9)	Tap water + UVB	7.8	-69% ((2.4-7 to 8)/7.8)	"not sig-nificant"

[1]: statistical significance reported by study authors
[2]: Calculation takes use of the values measured on the following weeks: (week 8 - week 0)/week 0.
[3]: Dawe 2005: numerals deduced from the line chart shown in figure 1 of the article.
A/R: number of analysed/randomised units; BL: baseline score; n.r.: not reported

APPENDICES

Appendix 1. Skin Group Specialised Register (CRS) search strategy

Psoria* and (((balneotherapy or balneo-therapy or soak* or bath* or salt* or dead sea or sole$ or saline) and (phototherapy* or ultraviolet or UVB or uv-b or uv light)) or balneophototherapy or balneo-phototherapy)

Appendix 2. CENTRAL (Cochrane Library) search strategy

#1 MeSH descriptor: [Psoriasis] explode all trees
#2 psoria*:ti,ab,kw
#3 #1 or #2
#4 soak*:ti,ab,kw
#5 (balneotherapy or balneo-therapy):ti,ab,kw
#6 bath*:ti,ab,kw
#7 (salt* or dead sea or saltwater or sole* or saline):ti,ab,kw
#8 MeSH descriptor: [Baths] explode all trees
#9 {or #4-#8}
#10 MeSH descriptor: [Phototherapy] explode all trees
#11 phototherap*:ti,ab,kw
#12 MeSH descriptor: [Ultraviolet Therapy] explode all trees
#13 (ultraviolet or UVB or uv-b):ti,ab,kw
#14 uv light:ti,ab,kw
#15 MeSH descriptor: [Ultraviolet Rays] explode all trees
#16 (TL01 or TL-01 or 311-nm):ti,ab,kw
#17{ or #10-#16}
#18 #9 and #17
#19 balneophototherapy:ti,ab,kw
#20 balneo-phototherapy:ti,ab,kw
#21 #18 or #19 or #20
#22 #3 and #21

Appendix 3. MEDLINE (Ovid) search strategy

1. exp Psoriasis/
2. psoria$.mp.
3. 1 or 2
4. soak$.mp.
5. (balneotherapy or balneo-therapy).mp.
6. bath$.mp.
7. (salt$ or dead sea or saltwater or sole$ or saline).mp.
8. Baths/
9. or/4-8
10. exp Phototherapy/
11. phototherap$.mp.
12. exp Ultraviolet Therapy/
13. (ultraviolet or UVB or uv-b).mp.
14. uv light.mp.
15. Ultraviolet Rays/
16. (TL01 or TL-01 or 311-nm).mp.
17. or/10-16
18. 9 and 17
19. balneophototherapy.mp.
20. balneo-phototherapy.mp.
21. 18 or 19 or 20
22. randomized controlled trial.pt.
23. controlled clinical trial.pt.
24. randomized.ab.
25. placebo.ab.
26. clinical trials as topic.sh.
27. randomly.ab.
28. trial.ti.

29. 22 or 23 or 24 or 25 or 26 or 27 or 28
30. exp animals/ not humans.sh.
31. 29 not 30
32. 3 and 21 and 31

[22-31: Cochrane Highly Sensitive Search Strategy for identifying randomized trials in MEDLINE: sensitivity- and precision-maximizing version (2008 revision)]

Appendix 4. Embase (Ovid) search strategy

1. exp psoriasis/
2. psoria$.mp.
3. 1 or 2
4. soak$.mp.
5. (balneotherapy or balneo-therapy).mp.
6. exp balneotherapy/
7. exp bath/
8. bath$.mp.
9. (salt$ or dead sea or saltwater or sole$ or saline).mp.
10. or/4-9
11. exp phototherapy/
12. phototherap$.mp.
13. (ultraviolet or UVB or uv-b).mp.
14. uv light.mp.
15. exp ultraviolet radiation/
16. (TL01 or TL-01 or 311-nm).mp.
17. or/11-16
18. 10 and 17
19. balneophototherapy.mp.
20. balneo-phototherapy.mp.
21. 18 or 19 or 20
22. crossover procedure.sh.
23. double-blind procedure.sh.
24. single-blind procedure.sh.
25. (crossover$ or cross over$).tw.
26. placebo$.tw.
27. (doubl$ adj blind$).tw.
28. allocat$.tw.
29. trial.ti.
30. randomized controlled trial.sh.
31. random$.tw.
32. or/22-31
33. exp animal/ or exp invertebrate/ or animal experiment/ or animal model/ or animal tissue/ or animal cell/ or nonhuman/
34. human/ or normal human/
35. 33 and 34
36. 33 not 35
37. 32 not 36
38. 3 and 21 and 37

Appendix 5. LILACS search strategy

psoria$ and (balneotherapy or balneo-therapy or balneophototherapy or balneo-phototherapy or salt$ or saline or bath$ or bano)
These terms searched with the Controlled clinical trials topic-specific query filter.

Appendix 6. Inquiries on missing data and inclusion criteria

We sent an e-mail to Karl Ludwig Resch <k.l.resch@d-i-g.org>, sponsor of the so-called 'BD-BVDD 2004' study included by IQWiG 2006b to see if it is linked to the results published by Karl Ludwig Resch as a co-author of Brockow 2007a, Brockow 2007b, and Schiener 2007. We also asked for individual patient data on PASI to enable a calculation of PASI-75. The address was presumed active as we communicated before but we did not receive a response to our inquiry.

We sent an e-mail to Annette Klein <annette.klein@klinik.uni-regensburg.de> and <sekretariat.derma@ukr.de>, first author of Klein 2011. We inquired whether the so-called 'TOMESA-PV 2006' study included by IQWiG 2006b is linked to the results published by the TOMESA-study group of Klein 2011. We also asked for individual patient data on PASI to enable a calculation of PASI-75. TOMESA stands for Dead Sea

salt in German language using the first two letters of each of the following three words 'Totes Meer Salz'. PV stands for Psoriasis vulgaris. We received an automatic reply from <Sekretariat.Derma@klinik.uni-regensburg.de> but did not receive a response to our inquiry.

We sent e-mails to W.P. Arnold <arnoldp@zgu.nl>, Alain Taieb <alain.taieb@chu-bordeaux.fr>, R.S. Dawe <r.s.dawe@dundee.ac.uk>, and Thilo Gambichler <t.gambichler@klinikum-bochum.de> and asked for individual patient data on PASI of the studies by Arnold 2001, Dawe 2005, Gambichler 2001, and Leaute-Labreze 2001 to enable a calculation of PASI-75. We received automatic replies from Ziekenhuis Gelderse Vallei <communicatie@zgv.nl> and <no-reply@chu-bordeaux.fr> but did not receive a response to our inquiry. We received a response from Robert Dawe (Staff) <r.s.dawe@dundee.ac.uk> who kindly reminded us that he did not measure PASI. We received a response from Prof. Dr. med. Thilo Gambichler <t.gambichler@klinikum-bochum.de>, the author of the present review, that study data were no more available.

We contacted Gabriel Nasri Marzuca-Nassr on 16 November 2016 by using the social networking site ResearchGate. His name was posted by ClinicalTrials.gov to indicate as the responsible person of the completed study NCT02713711. This RCT is included in the present review but results are not yet available (08 March 2017). We asked for the proposed publication date and for sharing the data. He replied quickly and told us that the manuscript of the study is submitted but not yet accepted for publication. He confirmed that the patients bathed in the salt water. On 10 May 2018, we sent a request to Gabriel Nasri Marzuca-Nassr, again using ResearchGate. He replied that he is writing the final manuscript and will submit it in a few months. On 7 June 2019, we sent a request to Gabriel Nasri Marzuca-Nassr, again using ResearchGate.

HISTORY

Protocol first published: Issue 11, 2015
Review first published: Issue 5, 2020

CONTRIBUTIONS OF AUTHORS

FP was the contact person with the editorial base.
FP co-ordinated contributions from the co-authors and wrote the final draft of the review.
FP, MH, SP, TC, TG screened papers against eligibility criteria.
FP obtained data on ongoing and unpublished studies.
FP, MH, SP, TG appraised the quality of papers.
FP, MH, SP, TC, TG extracted data for the review and sought additional information about papers.
FP entered data into RevMan.
FP, MH, SP, TG analysed and interpreted data.
FP, MH, SP, AL, TG worked on the methods sections.
FP, MH, SP, TG drafted the clinical sections of the background and responded to the clinical comments of the referees.
FP, MH, SP, AL, TG responded to the methodology and statistics comments of the referees.
DC checked the Plain language summary section.
FP is the guarantor of the update.

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DECLARATIONS OF INTEREST

Frank Peinemann: nothing to declare.

Marco Harari: "I am the Director of the DMZ Medical Center, in which patients are treated with climatotherapy (not artificial UV treatment)."

Sandra Peternel: nothing to declare.

Thalia Chan: nothing to declare.

David Chan: nothing to declare.

Alexander Labeit: nothing to declare.

Thilo Gambichler: "Since 1998, I have been performing research in the field of indoor salt water baths followed by artificial ultraviolet B light. I am an author of the following studies Gambichler 2001 (included study) and Gambichler 2000b (excluded study). In this review, I was not involved in extracting data from these studies."

SOURCES OF SUPPORT

Internal sources

- University of Cologne, Germany

  Provision of the full texts of articles

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 section Types of studies, we specified various subtypes of randomised designs and whether they were planned for inclusion.

Under Types of interventions: We acknowledged the two different comparisons we would be including to ensure it was clear to the reader. Comparison one would be salt bath + UVB versus other treatment + UVB. Comparison two would be salt bath + UVB versus other treatment + UVB or UVB only. The results of both comparisons would be reported separately.

In section Primary outcomes, we distinguished between-participant data from within-participant data. We rephrased the adverse outcome "treatment-related adverse events requiring withdrawal" instead of "serious adverse events requiring withdrawal" to make clear that the adverse outcome is linked with the treatment.

In section Types of outcome measures, we added that we used the web-based Easy Fisher Exact Test Calculator (Social Science Statistics 2018). We also added that we would extract numerical data from graphs where needed.

In section Assessment of risk of bias in included studies, we did not assess detection bias and attrition bias for each outcome separately because of sparse reporting.

In section Unit of analysis issues, we stated that we separately reported the results of between-participant data and within-participant data.We also added how we would handle studies with multiple intervention arms.

We added more details regarding the 'Summary of findings' table we created. We also described the GRADE approach.

Only two studies reported the predefined PASI-75, and six studies reported severity scores which could not be used in the present review. We wanted to report the respective results to provide a broader picture of the results of the various studies. Therefore, we reported outcomes although they were not predefined by the current review and they should not have an impact on the conclusion.

INDEX TERMS

Medical Subject Headings (MeSH)

Baths [adverse effects] [*methods]; Chronic Disease; Combined Modality Therapy [adverse effects] [methods]; Ficusin [therapeutic use]; Mineral Waters [adverse effects] [*therapeutic use]; Photosensitizing Agents [therapeutic use]; Psoriasis [*therapy]; PUVA Therapy [methods]; Randomized Controlled Trials as Topic; Sodium Chloride [therapeutic use]; Ultraviolet Therapy [adverse effects] [*methods]

MeSH check words

Adult; Female; Humans; Male; Middle Aged