Aus der Klinik für Dermatologie, Venerologie und Allergologie der Medizinischen Fakultät Charité – Universitätsmedizin Berlin

DISSERTATION

Topical treatments for scalp psoriasis

zur Erlangung des akademischen Grades

Doctor medicinae (Dr. med.)

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von

Justin Gabriel Schlager

aus Augsburg

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Abstracts

Topical treatments for scalp psoriasis

Background: People with chronic plaque psoriasis often have lesions on the scalp that are difficult to treat. Our objective was to assess the efficacy and safety of topical treatments for scalp psoriasis.

Methods: We searched the following databases up to August 2015: the Cochrane Skin Group Specialised Register, CENTRAL, MEDLINE, EMBASE and LILACS. We also searched five trial registers, screened abstracts of six psoriasis-specific conferences and checked the bibliography of included studies for further references to relevant randomised controlled trials (RCTs). Our quality of evidence assessment was based on the Grading of Recommendations Assessment, Development and Evaluation (GRADE) Working Group approach. We graded the quality of evidence for the following outcomes: 'clearance' or 'response' as assessed by the investigator global assessment (IGA) and 'response' according to the patient global assessment (PGA), improvement in quality of life, and the number of patients with adverse events (AE) requiring withdrawal of treatment. We expressed the results of the individual studies as risk ratios (RR) with 95% confidence intervals (CI) for dichotomous outcomes, and mean differences with 95% CI for continuous outcomes. If studies were sufficiently homogeneous, we meta-analysed the data by using the random-effects model.

Results: We included 59 RCTs, with overall 11.561 participants. Most findings were limited to short-term treatments (< six months). Overall evidence was of moderate quality. According to the clinician and patients' self-assessment a corticosteroid/vitamin D combination (e.g. betamethasone dipropionate plus calcipotriol) and corticosteroids of high and very high potency were more effective than vitamin D. The two-compound combination was superior to the corticosteroid alone, but the additional benefit was small. Reporting of quality of life data was insufficient to be included for meta-analyses and not feasible for quality of evidence assessment. The two-compound combination and corticosteroids caused fewer withdrawals due to AEs than vitamin D. There was no difference between the two-compound combination and corticosteroid monotherapy concerning this outcome. None of the studies stated which AE that caused withdrawal from treatment. However, the risk of withdrawing due to AEs was very small for all three therapies. Due to poor data evaluation of most other topical treatments was limited.

Conclusion: Given the comparable safety profile and only slim benefit of the two-compound combination over the corticosteroid alone, monotherapy with generic topical corticosteroids of high and very high potency may be fully acceptable for short-term therapy. More quality of life data and long-term assessments are needed.

Topische Therapie der Kopfhautschuppenflechte

Hintergrund: Patienten mit Psoriasis vulgaris (Schuppenflechte) weisen häufig Herde im Bereich der Kopfhaut auf. Aufgrund der Behaarung sind die Herde mit topischen Präparaten schwierig zu behandeln. Diese systematische Übersichtsarbeit verglich topische Therapieformen der Kopfhautschuppenflechte im Hinblick auf Wirksamkeit und Verträglichkeit.

Methodik: Die Literaturrecherche erfolgte bis August 2015 in folgenden Datenbanken: Cochrane Skin Group Specialised Register, CENTRAL, MEDLINE, EMBASE und LILACS. Des Weiteren wurden fünf Studienregister, Abstracts sechs Psoriasis spezifischer Konferenzen, als auch die Referenzlisten eingeschlossener Studien untersucht. Es wurden ausschließlich randomisierte kontrollierte Studien eingeschlossen. Die Bewertung der Evidenzqualität erfolgte gemäß der Methodik der Grading of Recommendations Assessment, Development and Evaluation (GRADE) Arbeitsgruppe. Hierbei lag der Hauptfokus auf folgenden Outcomes: „clearance“ und „response“ gemäß des „investigator global assessment“ (IGA) und „response“ gemäß des „patient global assessment“ (PGA), Verbesserung der Lebensqualität, und die Anzahl der Patienten, die aufgrund von Nebenwirkungen die Behandlung unterbrechen mussten. Die Ergebnisse der jeweiligen Studien wurden als relatives Risiko mit 95% Konfidenzintervall (KI) für dichotome Outcomes und als Mittelwertdifferenz mit 95% KI für kontinuierliche Outcomes dargestellt. Ausreichend homogene Studien, wurden mittels Random-Effects-Model metaanalysiert.

Ergebnisse: Insgesamt wurden 59 Studien mit 11561 Patienten eingeschlossen. Nahezu alle Ergebnisse beschränkten sich auf Kurzzeittherapien (kürzer als sechs Monate). Insgesamt war die Evidenzqualität moderat. Untersuchern und Patienten zufolge war das Kortikosteroid/Vitamin D Kombinationspräparat (z.B. Betamethasone Dipropionate plus Calcipotriol), als auch die Monotherapie mit einem Kortikosteroid von hoher und sehr hoher Potenz effektiver als Vitamin D. Das Kombinationspräparat zeigte bessere Ergebnisse als das entsprechende Kortikosteroid als Monotherapie, doch der Unterschied war gering. Daten zur Verbesserung der Lebensqualität wurden nur unzureichend berichtet und konnten keiner Metaanalyse unterzogen werden. Die Bewertung der Evidenzqualität war für dieses Outcome ebenfalls nicht möglich. Patienten mit Kombinationspräparat oder Kortikosteroid Monotherapie mussten seltener die Behandlung aufgrund von Nebenwirkungen abbrechen als mit Vitamin D. In Bezug auf Therapieabbrüche aufgrund von Nebenwirkungen unterschieden sich das Kombinationspräparat und das entsprechende Kortikosteroid als Monotherapie nicht. Keine der Studien berichtete welche Nebenwirkungen für einen Behandlungsabbruch verantwortlich waren. Insgesamt waren Behandlungsabbrüche jedoch sehr selten. Die Datenlage für andere topische Präparate war größtenteils ungenügend.

Schlussfolgerung: In Anbetracht der ähnlich guten Verträglichkeit beider Präparate und des nur marginal effektiveren Kombinationspräparates, wäre die Monotherpie mit einem Kortikosteroid mit hoher oder sehr hoher Potenz für die Kurzzeitbehandlung der Kopfhautschuppenflechte ausreichend. Weitere randomisierte kontrollierte Studien zur Verbesserung der Lebensqualität, als auch zu Langzeittherapien sind allerdings notwendig um eine ausreichende Datenlage für erreichen.

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[Bestandteil der Dissertationen]

Eidesstattliche Versicherung

„Ich, Justin Gabriel Schlager, versichere an Eides statt durch meine eigenhändige Unterschrift, dass ich die vorgelegte Dissertation mit dem Thema: „Topical treatments for scalp psoriasis" selbstständig und ohne nicht offengelegte Hilfe Dritter verfasst und keine anderen als die angegebenen Quellen und Hilfsmittel genutzt habe.
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Ausführliche Anteilserklärung an der erfolgten Publikation

Schlager JG, Rosumeck S, Werner RN, Jacobs A, Schmitt J, Schlager C, Nast A.
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DOI: 10.1002/14651858.CD009687.pub2.

Nach Vorgaben durch die „Cochrane editorial base" wurden die untenstehenden Punkte 4., 6., 7. und 8. von zwei Autoren (Schlager JG und Rosumeck S) jeweils selbstständig und unabhängig voneinander durchgeführt. Die übrigen Punkte wurden durch den Doktoranden eigenständig erbracht:

1. Mitarbeit am Protokoll des Reviews.
2. Kontaktperson für die „editorial base" der Cochrane Skin Group und Koordination der jeweiligen Beiträge der Co-Autoren.
3. Identifizierung geeigneter Artikel bzw. Abstracts aus fünf Studienregistern, sechs Psoriasis-Konferenzen und aus den Referenzlisten der eingeschlossenen Studien.
4. Identifizierung geeigneter Studien aus den Ergebnissen der elektronischen Literatur-Suche, die von der Cochrane „editorial base" vorgegeben und durchgeführt wurde.
5. Besorgung von fehlenden Daten und Informationen eingeschlossener Studien, als auch von noch laufenden oder noch nicht veröffentlichten Studien. Dies geschah durch Kontaktaufnahme mit den Autoren oder Sponsoren der jeweiligen Studie.
6. Überprüfung und Bewertung der Qualität der eingeschlossenen Studien anhand des „Cochrane Collaboration risk of bias assessment-tools".
7. Bewertung der Evidenzqualität anhand der Methodik der Grading of

Recommendations Assessment, Development and Evaluation (GRADE) – Arbeitgruppe.

8. Systematische Datenextraktion aus den 59 eingeschlossenen Studien mithilfe von Review Manager (RevMan) und Microsoft Excel 2011.
9. Inhaltliche Ausarbeitung und schriftliches Verfassen der Einleitung und Beantwortung der Fragen der Cochrane-Gutachter bezüglich des medizinisch-klinischen Inhaltes.
10. Wesentliche Teilnahme an der Ausarbeitung des Methodik Teils. Hierbei insbesondere die Definition der Einschlusskriterien, Definition der zu untersuchenden Outcomes, als auch Planung des methodischen Vorgehens im Falle, dass Studien keine „Intention To Treat" (ITT)-Analyse durchführten. Zudem Beantwortung der Fragen der Cochrane-Gutachter zur Methodik und Statistik. Schreiben von über 80% des Methodikteils.
11. Analyse und Interpretation der extrahierten Daten und Ergebnisse. Schreiben des gesamten Ergebnisteils.
12. Eigenständige Diskussion der Ergebnisse und Schreiben der gesamten Diskussion.

Unterschrift, Datum und Stempel des betreuenden Hochschullehrers

[redacted]

CHARITÉ
UNIVERSITÄTSMEDIZIN BERLIN
Klinik für Dermatologie,
Venerologie und Allergologie
Division of Evidence Based Medicine (dEBM)
Leiter: PD Dr. med. Alexander Nast
Campus Charité Mitte
Charitéplatz 1 | D-10117 Berlin

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☐	1	NEW ENGL J MED	0028-4793	268652	55.873	54.390	13.844	353	8.4	0.67634	24.284
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☐	3	JAMA-J AM MED ASSOC	0098-7484	126479	35.289	31.026	10.189	228	>10.0	0.26099	14.418
☐	4	ANN INTERN MED	0003-4819	48356	17.810	17.469	5.134	157	>10.0	0.10629	8.134
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☐	10	J CACHEXIA SARCOPENI	2190-5991	713	7.315	7.523	2.167	30	2.5	0.00208	1.521
☐	11	MAYO CLIN PROC	0025-6196	9990	6.262	6.211	1.352	145	8.4	0.01972	2.283
☐	12	J INTERN MED	0954-6820	8802	6.063	5.622	2.250	100	8.1	0.01507	1.822
☑	13	COCHRANE DB SYST REV	1469-493X	43592	6.035	6.539	1.007	801	4.8	0.14928	2.365
☐	14	CAN MED ASSOC J	0820-3946	12121	5.959	6.912	2.120	83	8.7	0.02326	2.678
☐	15	MEDICINE	0025-7974	4912	5.723	5.285	0.103	311	>10.0	0.00585	1.910
☐	16	ANN FAM MED	1544-1709	3556	5.434	5.886	2.952	62	5.7	0.01116	2.431
☐	17	TRANSL RES	1931-5244	2112	5.030	4.149	1.468	94	3.2	0.00757	1.244
☐	18	AM J MED	0002-9343	22662	5.003	5.258	1.661	165	>10.0	0.02750	1.975
☐	19	AM J PREV MED	0749-3797	15857	4.527	5.395	1.140	215	6.7	0.04177	2.132
☐	20	MED J AUSTRALIA	0025-729X	10268	4.089	3.445	1.297	158	8.1	0.01780	1.129

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Topical treatments for scalp psoriasis (Review)

Schlager JG, Rosumeck S, Werner RN, Jacobs A, Schmitt J, Schlager C, Nast A

Schlager JG, Rosumeck S, Werner RN, Jacobs A, Schmitt J, Schlager C, Nast A.
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[Intervention Review]

Topical treatments for scalp psoriasis

Justin Gabriel Schlager[1], Stefanie Rosumeck[1], Ricardo Niklas Werner[1], Anja Jacobs[2], Jochen Schmitt[3], Christoph Schlager[4], Alexander Nast[1]

[1]Division of Evidence Based Medicine, Department of Dermatology, Venerology and Allergology, Charité - Universitätsmedizin Berlin, Berlin, Germany. [2]Department of Medical Consulting, Federal Joint Committee (G-BA, Gemeinsamer Bundesausschuss), Berlin, Germany. [3]Center for Evidence-Based Healthcare, Faculty of Medicine Carl Gustav Carus, Technischen Universität (TU) Dresden, Dresden, Germany. [4]c/o Cochrane Skin Group, The University of Nottingham, Nottingham, UK

Contact address: Alexander Nast, Division of Evidence Based Medicine, Department of Dermatology, Venerology and Allergology, Charité - Universitätsmedizin Berlin, Charitéplatz 1, Berlin, 10117, Germany. alexander.nast@charite.de.

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ABSTRACT

Background

People with chronic plaque psoriasis often have lesions on the scalp. Hair makes the scalp difficult to treat and the adjacent facial skin is particularly sensitive to topical treatments.

Objectives

To assess the efficacy and safety of topical treatments for scalp psoriasis.

Search methods

We searched the following databases up to August 2015: the Cochrane Skin Group Specialised Register, CENTRAL (2015, Issue 7), MEDLINE (from 1946), EMBASE (from 1974) and LILACS (from 1982). We also searched five trials registers, screened abstracts of six psoriasis-specific conferences and checked the reference lists of included studies for further references to relevant randomised controlled trials.

Selection criteria

Randomised controlled trials (RCTs) with a parallel-group, cross-over or within-patient design of topical treatments for people of all ages with scalp psoriasis.

Data collection and analysis

Two authors independently carried out study selection, data extraction and 'Risk of bias' assessment. Disagreements were settled by reference to a third author.

To assess the quality of evidence, we focused on the following outcomes: 'clearance' or 'response' as assessed by the investigator global assessment (IGA), improvement in quality of life, adverse events requiring withdrawal of treatment and 'response' as assessed by the patient global assessment (PGA).

We expressed the results of the single studies as risk ratios (RR) with 95% confidence intervals (CI) for dichotomous outcomes, and mean differences (MD) with 95% CI for continuous outcomes. If studies were sufficiently homogeneous, we meta-analysed the data

by using the random-effects model. Where it was not possible to calculate a point estimate for a single study, we described the data qualitatively. We also presented the number needed to treat to benefit (NNTB).

We categorised topical corticosteroids according to the German classification of corticosteroid potency as mild, moderate, high and very high.

Main results

We included 59 RCTs with a total of 11,561 participants. Thirty studies were either conducted or sponsored by the manufacturer of the study medication. The risk of bias varied considerably among the included studies. For instance, most authors did not state the randomisation method and few addressed allocation concealment. Most findings were limited to short-term treatments, since most studies were conducted for less than six months. Only one trial investigated long-term therapy (12 months). Although we found a wide variety of different interventions, we limited the grading of the quality of evidence to three major comparisons: steroid versus vitamin D, two-compound combination of steroid and vitamin D versus steroid monotherapy and versus vitamin D.

In terms of clearance, as assessed by the IGA, steroids were better than vitamin D (RR 1.82; 95% CI 1.52 to 2.18; four studies, 2180 participants, NNTB = 8; 95% CI 7 to 11; moderate quality evidence). Statistically, the two-compound combination was superior to steroid monotherapy, however the additional benefit was small (RR 1.22; 95% CI 1.08 to 1.36; four studies, 2474 participants, NNTB = 17; 95% CI 11 to 41; moderate quality evidence). The two-compound combination was more effective than vitamin D alone (RR 2.28; 95% CI 1.87 to 2.78; four studies, 2008 participants, NNTB = 6; 95% CI 5 to 7; high quality evidence).

In terms of treatment response, as assessed by the IGA, corticosteroids were more effective than vitamin D (RR 2.09; 95% CI 1.80 to 2.41; three studies, 1827 participants; NNTB = 4; 95% CI 4 to 5; high quality evidence). The two-compound combination was better than steroid monotherapy, but the additional benefit was small (RR 1.15; 95% CI 1.06 to 1.25; three studies, 2444 participants, NNTB = 13; 95% CI 9 to 24; moderate quality evidence). It was also more effective than vitamin D alone (RR 2.31; 95% CI 1.75 to 3.04; four studies, 2222 participants, NNTB = 3; 95% CI 3 to 4; moderate quality evidence).

Reporting of quality of life data was poor and data were insufficient to be included for meta-analysis.

Steroids caused fewer withdrawals due to adverse events than vitamin D (RR 0.22; 95% CI 0.11 to 0.42; four studies, 2291 participants; moderate quality evidence). The two-compound combination and steroid monotherapy did not differ in the number of adverse events leading withdrawal (RR 0.88; 95% CI 0.42 to 1.88; three studies, 2433 participants; moderate quality evidence). The two-compound combination led to fewer withdrawals due to adverse events than vitamin D (RR 0.19; 95% CI 0.11 to 0.36; three studies, 1970 participants; high quality evidence). No study reported the type of adverse event requiring withdrawal.

In terms of treatment response, as assessed by the PGA, steroids were more effective than vitamin D (RR 1.48; 95% CI 1.28 to 1.72; three studies, 1827 participants; NNTB = 5; 95% CI 5 to 7; moderate quality evidence). Statistically, the two-compound combination was better than steroid monotherapy, however the benefit was not clinically important (RR 1.13; 95% CI 1.06 to 1.20; two studies, 2226 participants; NNTB = 13; 95% CI 9 to 26; high quality evidence). The two-compound combination was more effective than vitamin D (RR 1.76; 95% CI 1.46 to 2.12; four studies, 2222 participants; NNTB = 4; 95% CI 3 to 6; moderate quality evidence).

Common adverse events with these three interventions were local irritation, skin pain and folliculitis. Systemic adverse events were rare and probably not drug-related.

In addition to the results of the major three comparisons we found that the two-compound combination, steroids and vitamin D monotherapy were more effective than the vehicle. Steroids of moderate, high and very high potency tended to be similarly effective and well tolerated. There are inherent limitations in this review concerning the evaluation of salicylic acid, tar, dithranol or other topical treatments.

Authors' conclusions

The two-compound combination as well as corticosteroid monotherapy were more effective and safer than vitamin D monotherapy. Given the similar safety profile and only slim benefit of the two-compound combination over the steroid alone, monotherapy with generic topical steroids may be fully acceptable for short-term therapy.

Future RCTs should investigate how specific therapies improve the participants' quality of life. Long-term assessments are needed (i.e. 6 to 12 months).

PLAIN LANGUAGE SUMMARY

Topical treatments for psoriasis of the scalp

Background

People with chronic plaque psoriasis often have lesions on the scalp. As well as itching, the reddish, scaly lesions are visible and are often embarrassing. 'Topical' treatments (drugs applied to the skin, e.g. as creams) are usually tried first, but applying them to the scalp is difficult because of the hair. There are a number of topical drugs in use, such as corticosteroids (also known as steroids), vitamin D, tar-based preparations, tacrolimus, dithranol or salicylic acid. Some topical corticosteroids have more potency than others so are categorised into four levels of strength: mild, moderate, high and very high. As psoriasis remains a long-term condition, it is of great importance to know which of the drugs work best, what kind of side effects they may have and how likely they are to occur.

Review question

What are the most effective and safest treatments for psoriasis on the scalp?

Study characteristics

We looked at 59 randomised controlled trials with 11,561 participants. Thirty studies were either conducted or sponsored by the manufacturer of the study medication.

Quality of the evidence

On average, the overall quality of the evidence was moderate for the three most important comparisons that included corticosteroids (e.g. betamethasone dipropionate), vitamin D (e.g. calcipotriol) and their combination product. We looked for a reduction in the severity of the psoriasis, improvement in quality of life and harmful side effects of the treatments. Most findings were based on short-term therapies with a duration of less than six months.

Key results

Prior investigators found that the combination product was more effective than the steroid alone, but clinically the benefit was questionable. Both treatments reduced scalp psoriasis better than vitamin D.

Due to poor information, we could not assess which treatment improved quality of life best. Most studies simply did not measure the improvement in quality of life.

Participants who applied vitamin D stopped treatment more often because of harmful side effects than those who applied a topical steroid or the combination product. Steroids were as likely as the combination product to cause discontinuation of the treatment because of side effects. However, only a few participants who used one of the three medications experienced harmful side effects. No study reported the type of side effect that made participants stop the treatment.

Participants assessed the efficacy of the treatments similarly to the investigator: those who applied a steroid or the combination product responded better to treatment than participants who used vitamin D alone. Statistically, the combination product was more effective than the steroid alone, but clinically the benefit was questionable.

The most common harmful side effects of these treatments were irritation, itching and skin pain at the site of application. Side effects on other sites of the body were very rare and most likely not caused by the drug.

Other findings were the following: steroids, vitamin D and their combination product were more effective than the vehicle preparation (cream, shampoo etc) that did not contain the active drug. Compared to one another, steroids tended to be similarly effective and have similar side effects, even though some were of a higher strength.

We could not sufficiently assess the efficacy and safety of other topical treatments, such as salicylic acid, tar or dithranol.

Conclusion

Steroids and the two-compound combination of a steroid and vitamin D were most effective with the least risk of causing harmful side effects. Given the similar safety profile and only slim benefit of the two-compound combination over the steroid alone, topical steroids on their own may be fully acceptable for short-term therapy.

The following questions remain unanswered and should be investigated by future trials: Is there truly no difference in terms of effectiveness or safety between topical corticosteroids of different strength? Does the vehicle preparation (e.g. cream or shampoo) have any influence on how the active agent works? Which topical treatment leads to disease control over a long time span without risking patient's safety? Finally, there is a strong need for more studies that assess which topical treatments improve quality of life best.

SUMMARY OF FINDINGS FOR THE MAIN COMPARISON *[Explanation]*

Steroid compared to vitamin D for scalp psoriasis

Patient or population: scalp psoriasis
Intervention: steroid
Comparison: vitamin D

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Quality of the evidence (GRADE)	Comments
	Risk with vitamin D	Risk with steroid				
Number of participants achieving 'clearance' by IGA	Study population 159 per 1000	289 per 1000 (241 to 346)	RR 1.82 (1.52 to 2.18)	2180 (4 RCTs)	⊕⊕⊕◯ MODERATE [1]	-
Number of participants achieving 'response' by IGA	Study population 251 per 1000	525 per 1000 (452 to 605)	RR 2.09 (1.80 to 2.41)	1827 (3 RCTs)	⊕⊕⊕⊕ HIGH	-
Quality of life	Study population 0 per 1000	0 per 1000 (0 to 0)	Not estimable	(0 studies)	-	No study addressed this outcome.
Number of participants withdrawing due to adverse events (AE)	Study population		RR 0.22 (0.11 to 0.42)	2291 (4 RCTs)	⊕⊕⊕◯ MODERATE [2]	No study reported the sort of AE that caused withdrawal. In 2 small studies with high risk of bias (Köse 1997, N = 43 participants; Yilmaz 2005, N = 30 participants) no withdrawals occurred.

	53 per 1000	12 per 1000 (6 to 22)				
Number of participants achieving 'response' by PGA	Study population 403 per 1000	596 per 1000 (516 to 693)	RR 1.48 (1.28 to 1.72)	1827 (3 RCTs)	⊕⊕⊕◯ MODERATE [3]	-

***The risk in the intervention group** (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).

AE: adverse event; **CI**: confidence interval; **IGA**: investigator's global assessment; **OR**: odds ratio; **PGA**: patient global assessment; **RCT**: randomised controlled trial; **RR**: risk ratio

GRADE Working Group grades of evidence
High quality: We are very confident that the true effect lies close to that of the estimate of the effect
Moderate quality: 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 quality: Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect
Very low quality: We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect

[1] Downgraded by one level for risk of bias: three out of four studies with unclear blinding of outcome assessment (Klaber 1994; van de Kerkhof 2009; Yilmaz 2005); all studies with unclear allocation concealment.
[2] Downgraded by one level for risk of bias: two out of four studies with unclear blinding of outcome assessment (Klaber 1994; van de Kerkhof 2009); all studies with unclear allocation concealment.
[3] Downgraded by one level for risk of bias: all three studies with unclear allocation concealment; one study with unclear risk of bias in selective reporting (Reygagne 2005); one study with unclear blinding of outcome assessment (van de Kerkhof 2009).

BACKGROUND

An explanation of technical and medical terms is provided in Table 1.

Description of the condition

Psoriasis in general

Psoriasis affects approximately 2% of the population in Western Europe and the US (Barker 1991; Krueger 1984; van de Kerkhof 2001), and 0.2% to 0.6% in Far-Eastern populations such as China, Taiwan or Japan (Chang 2009; Yip 1984). Psoriasis shows two peaks of disease-onset: the first is at around 20 years, and the second at approximately 50 years (Zeljko-Penavic 2010). There are different types including pustular, guttate, inverse, erythrodermic or chronic plaque psoriasis (psoriasis vulgaris), with the latter accounting for 90% of the cases (Griffiths 2007). Clinical signs are characterised by well-demarcated reddish (erythematous) plaques of thickened skin and silvery white scaling. Disease severity can range from a few small plaques to severe cases with up to 90% of the body surface affected (Stern 1997). Typically the plaques are distributed symmetrically on knees and elbows, the trunk or the sacral region. The impairment of quality of life was found to be similar to that of people with other major medical conditions such as cardiovascular diseases, diabetes or even cancer (Rapp 1999). Furthermore, people with psoriasis have a higher risk of experiencing cardiovascular co-morbidities and psychiatric disorders such as depression and anxiety (Devrimci-Ozguven 2000; Dowlatshahi 2014). Around 20% of them also experience inflammation of smaller and major joints or tendons (Reich 2009). Thus, rheumatologists routinely search for psoriatic lesions (e.g. on the scalp) in order to evaluate psoriatic arthritis as a differential diagnosis.

Scalp psoriasis

Regardless of the type of psoriasis, up to 79% of people with the condition present with scalp involvement, which has frequently been the first site to show symptoms of the disease (van de Kerkhof 1998). Psoriatic scalp lesions are characterised by thickened, well-demarcated erythematous plaques, with scaling and frequent itching. The lesions are typically located behind the ear (retro-auricular) and neck, but may appear anywhere on the scalp. The extent varies from fine scaling to thick erythematous crusted plaques on the entire scalp, typically crossing the hair line and affecting a small area of the adjacent facial skin. In severe cases, hair loss due to psoriatic plaques has been reported (Shuster 1972; van de Kerkhof 1992). Compared to sites of the body that can easily be covered by clothes, people with psoriasis on the scalp or face are often troubled, because lesions are difficult to hide. Together with pruritus, this has been shown to be one of the most distressing symptoms (van de Kerkhof 1998a). Embarrassment may lead to social stigmatisation and rejection resulting in reduction of a person's self esteem, social withdrawal and avoidance behaviour (Ginsburg 1993).

Pathophysiology

Psoriasis is a chronic immune-mediated disease. A histological examination of psoriatic plaques reveals hyperproliferation of abnormal keratinocytes, hypervascularisation and infiltration of immune cells, mainly CD4- and CD8-positive T-lymphocytes as well as dendritic cells (Bata-Csorgo 1995; Valdimarsson 1995). Pro-inflammatory cytokines, such as tumour necrosis factor-α (TNF-α), interferon-α (IFN-α), several interleukins (IL-2, IL-6, IL-8, IL-12, IL-17) and vascular endothelial growth factor (VEGF), play a key role in the pathologic interaction between immune cells and keratinocytes (Austin 1999; Prinz 1994). Furthermore, psoriasis shows a close association with autoimmune-associated HLA and DR antigens (Barker 1991; Tagami 1997).

The inheritable component of psoriasis is reflected by a higher incidence of cases in families of affected individuals. Recent studies identified numerous different gene loci and epigenetic alterations that are linked to the predisposition and progression of the disease (Trowbridge 2014; Tsoi 2012).

However, there is evidence indicating that the interaction between genes and certain environmental factors is an important cause of the disease (Dika 2007; Gudjonsson 2008). A wide range of different stimuli, including physical, psychological and chemical, are recognised as being connected to the emergence of psoriasis, irrespective of the actual type. This list includes medication (e.g. beta-blockers, antimalarials, lithium), infections (streptococcus, HIV), smoking, alcohol consumption and stress (Abel 1986; Al'Abadie 1994; Chaput 1985; Li 2012; Setty 2007; Telfer 1992; Tobin 2009). Despite all recent scientific efforts, a complete understanding of all causes of the disease remains a challenge (Trowbridge 2014).

Scalp psoriasis can occasionally be confused with seborrhoeic dermatitis affecting the scalp. Seborrhoeic dermatitis is another inflammatory condition, which commonly affects the entire scalp, resulting in mild inflammation and dandruff. It can also affect the sides of the nose, eyebrows and ears, as well as the chest, armpits and groin. Psoriasis, on the other hand, is usually well demarcated and has a coarser scale, but early diffuse psoriasis of the scalp can sometimes look very similar to seborrhoeic dermatitis. A scalp biopsy may help to distinguish between the two conditions (Del Rosso 2011; Kim 2011; Mashaly 2011). Sometimes, however, both skin conditions coexist, which is commonly called 'seborrhiasis'. A healthy scalp exhibits a physiological colonisation of *Pityrosporum ovale*, a yeast of the *Malassezia* species. However, both conditions can be associated with overgrowth in particular with *Malassezia globosa* and *Malassezia furfur*. This may trigger the disease and lead to exacerbation of inflammation and hyperproliferation of keratinocytes (Baroni 2004; Gomez-Moyano 2014; Rosenberg 1982).

Description of the intervention

Hair makes the scalp less accessible to topical agents. In addition, the proximity of the sensitive skin of the face increases the risk of local adverse effects of treatment, such as atrophy, iatrogenic rosacea or acne and irritation (Horn 2010). The use of topical agents may be further limited by cosmetically unpleasant effects leading to dissatisfaction and decreased compliance.

People with widespread psoriasis including the scalp may be treated with psoralen combined with ultraviolet A (PUVA) or systemic therapies that may consist of methotrexate, ciclosporin or biologic agents, among others. However, topical treatments remain the first-line therapy for moderate body and scalp psoriasis. There is a wide range of treatment options for scalp psoriasis, including steroids, vitamin D3 analogues, tar preparations, dithranol, salicylic acid and tacrolimus, among others (Ortonne 2009; Papp 2007). These may provide a gamut of therapies for the physician and patient, but it also highlights the lack of an effective, sustainable treatment. All available therapies may partially control signs of psoriasis, but none has been shown to achieve a cure or long-term remission.

Corticosteroids

Topical corticosteroids are one of the mainstay therapies for psoriasis (Ortonne 2009). The molecule binds to specific intracellular (cytosolic) receptors and modulates the inhibition and induction of regulatory proteins. The latter have influence on the transcription of genes coding for pro-inflammatory proteins (such as cytokines, TNF-α). Besides this genomic effect, they further interact with the cellular membrane (Bos 2008). Prolonged use of topical corticosteroids may induce local adverse effects, such as cutaneous atrophy (skin thinning) and telangiectasia (small, dilated blood vessels in the skin), or systemic side effects, such as diabetes, hypertension and hypothalamic-pituitary-adrenal (HPA) axis suppression (Gardinal 2009; Horn 2010). Topical corticosteroids are available in a variety of forms including emollient creams, ointments, gels, sprays, lotions, solutions, nail lacquers, tape and foam (Horn 2010). They are classified according to their potency, but the classification systems are not consistent (seven classes in the USA, four in Germany or the UK). In this review, we categorised topical corticosteroids into four groups (1 to 4) according to the German steroid classification system (Niedner 1996): mild (1), moderate (2), high (3) and very high potency (4). We listed the following agents as corticosteroids of moderate potency: fluocinolone acetonide 0.01%, hydrocortisone 17-butyrate 0.1%, desoximetasone 0.05%, triamcinolone acetonide as 0.1% and 0.2% solution. Corticosteroids of high potency are amcinonide 0.1%, betamethasone dipropionate, betamethasone valerate as 0.1%, 0.12% and 1% solution, halcinonide 0.1%, fluocinonide, desoximetasone 0.25% and mometasone furoate. The only corticosteroid of very high potency within this review is clobetasol propionate 0.05%. None of the included studies analysed corticosteroids of mild potency.

Vitamin D analogues

Topical vitamin D (calcitriol) and its analogues (calcipotriol, tacalcitol) are an important alternative to corticosteroids for the long-term treatment of psoriasis (Papp 2007). After binding to their cytoplasmic receptor (VDR) and translocation into the nucleus, they initiate the transcription of vitamin D responsive genes through interaction with other regulatory proteins. This process regulates cell differentiation and causes inhibition of cell proliferation and inflammation (Bos 2008; Kragballe 1990). Although topical vitamin D analogues are a safe alternative, initially they commonly cause peri-lesional irritation, but the main concern may be the possible but rare increase of serum and urine calcium levels. Therefore, the total concentration should not exceed 100 g/week (Kragballe 1993). However, calcipotriol, the most established vitamin D derivative, has not been shown to affect calcium homeostasis (Kragballe 1993; van de Kerkhof 2001). It can be dispensed as a cream, lotion, solution or shampoo, each at a concentration of 50 µg/gm.

Tar-based preparations

There are a number of different tar preparations including pine tar and coal tar. The latter is the most effective and frequently used (Papp 2007). It is a semisolid by-product obtained through the distillation of bituminous coal, and it was employed in ancient times, both as monotherapy for psoriasis and in combination with other topical agents, systemic medicines and phototherapy (Arnold 1997; Cosmetic Ingredient Review Expert Panel 2008; Frankel 2010; Paghdal 2009). The polycyclic aromatic hydrocarbons in coal tar make the skin more sensitive to UV light (Menter 2010). However, the main mode of action remains unclear (van de Kerkhof 2001; Papp 2007). Tar has anti-inflammatory, antiproliferative and strong pruritus-reducing properties, but due to the unpleasant smell, cosmetic disadvantage and mutagenic potential, it became less popular in the treatment of scalp psoriasis (van de Kerkhof 2001). Therefore, many efforts have been made to increase its acceptability and tar is now available in non-staining and washable formulations including lotions and shampoo or in combination with other active agents (Dogra 2010; van de Kerkhof 2001).

Calcineurin inhibitors

Calcineurin is an intracellular enzyme that regulates the transcription of certain genes. In leucocytes, such as T-helper cells and Langerhans cells, it activates the transcription of pro-inflammatory cytokines such as interleukins (IL-2, IL-4, IL-10) and interferon-gamma. Tacrolimus and pimecrolimus are nonsteroidal immunosuppressing macrolactams that block calcineurin and subsequently the proliferation and activation of these immune cells (Luger 2007;

Panhans-Gross 2001). Some studies, including randomised controlled trials, have shown the potential efficacy and safety of using calcineurin inhibitors for many dermatologic conditions (Day 2008; Menter 2010). In psoriasis, calcineurin inhibitors may be used as an alternative, especially for those body regions, such as the face, which are prone to adverse events during long-term treatment with topical corticosteroids (Dogra 2010). Based on reports of conditions other than psoriasis, a carcinogenic risk has been the subject of ongoing discussion (Niwa 2003; Weischer 2007). Calcineurin inhibitors have not yet been approved as topical treatment for psoriasis.

Anthralin (dithranol)

Anthralin (dithranol) is a synthetic version of chrysarobin, derived from the Araroba tree of South America. It has been shown to induce a release of reactive oxygen species with an inhibiting effect on the proliferation of keratinocytes and the transformation of leucocytes (Hegemann 1992; Mahrle 1994). It is used in increasing concentrations (0.1% to 3%) for application to the scalp. It has been shown that anthralin is more easily applied during hospitalisation, although out-patient short-contact therapies are also in practice. Common adverse events are discolouration of the hair and irritation of the skin (Dogra 2010; van de Kerkhof 2001). A few studies support the use of anthralin combined with other topical treatments or UVB phototherapy to improve the response in psoriasis of the body (Dogra 2010; Yamamoto 2000).

Salicylic acid

Due to its potent keratolytic effect, salicylic acid is often the initial treatment option where excessive scaling is present. It is most frequently used in a 5% to 10% preparation, but other formulations, such as in a solution, gel or petroleum jelly, are available. Salicylic acid appears to increase the penetration of other topical agents, such as corticosteroids, making a combination therapy meaningful (Chan 2009; van de Kerkhof 2005).

Antifungals

As previously mentioned, an overgrowth of *Pityrosporum* (*Malassezia* yeast) may be associated with inflammatory skin disorders such as scalp psoriasis or seborrhoeic dermatitis. Therefore, broad-spectrum antifungals such as azole derivatives (e.g. ketoconazole) or ciclopirox olamine are a therapeutic approach for the treatment of scalp psoriasis (Puig 2010). Ketoconazole blocks the synthesis of the cholesterin-like ergosterol, an essential component of the fungal cell membrane, leading to disruption and fungal cell death (Faergemann 2007). Ciclopirox, on the other hand, has a very complex fungistatic and fungicidal mode of action: it affects cell metabolism, leading to decreased uptake of essential substrates and increases the intracellular concentration of toxic peroxides. In addition, ciclopirox shows antimicrobial properties (Roques 2006).

How the intervention might work

Topical preparations consist of an active agent within a vehicle of emollients or moisturisers. A diverse array of products is used to ensure the penetration of the active ingredient (Ortonne 2009; Staubach 2014; van de Kerkhof 2001; von Stebut 2014). They can be categorised as shampoos, hydrophilic vehicles (alcohol-based lotions, foam, hydro-gel, solution) and lipophilic preparations (cream, ointment, lipo-gel, oil). They help to maintain the integrity of the cells of the scalp when damage occurs due to abnormal cell growth. Additionally, they have anti-inflammatory properties and reduce itching (Fluhr 2008; Staubach 2014). Depending on disease severity and the person's preference, different application methods may be used: short-contacts (shampoo), leave-ons (e.g. lotion, gel, cream) or even occlusive dressings. Particularly in scalp psoriasis, a convenient preparation is crucial for acceptability and hinges on the person's personal preference. The choice of the vehicle is therefore as critical as the active agent itself in order to encourage patient compliance and, thus, treatment efficacy (Chan 2009).

Corticosteroids, vitamin D analogues, calcineurin inhibitors and coal tar preparations use their anti-proliferative, immuno-suppressive and anti-inflammatory properties to act upon the underlying histopathological process of psoriatic lesions. The choice of the most appropriate treatment depends on the severity of the disease and whether acute or maintenance therapy is needed.

Why it is important to do this review

Many different regimens have been studied for the treatment of scalp psoriasis: antifungals, dithranol, retinoids, vitamin D analogues, corticosteroids, phototherapy, pulsed magnetic fields, Grenz rays, keratolytics, emollients, steroids, salicylic acid, calcipotriol, coal tar, dithranol and tacrolimus, among others (Khan 1981; Patel 2008). However, there is still no evidence-based consensus in the literature to support decision-making during clinical practice. Therefore we have systematically assessed the evidence for the efficacy of topical treatments for scalp psoriasis in order to be able to offer guidance to healthcare practitioners in their clinical practice.

The plans for this review were published as a protocol 'Topical treatments for scalp psoriasis' (Jales 2012).

OBJECTIVES

To assess the efficacy and safety of topical treatments for scalp psoriasis.

METHODS

Criteria for considering studies for this review

Types of studies

We only included randomised controlled trials (RCTs) of parallel-group, cross-over or within-patient design.

Types of participants

We included participants of all ages who were diagnosed with scalp psoriasis according to clinical or biopsy findings used by authors of primary studies, for example, the classical history, signs and symptoms, and typical histopathologic features (Rzany 1998).

Types of interventions

We made no restrictions regarding the topical active agent, the agent vehicle or the type of comparison. The following topical medications were included:

- corticosteroids (e.g. betamethasone dipropionate, clobetasol propionate);
- vitamin D (calcipotriol);
- corticosteroid plus vitamin D combination products (e.g. betamethasone dipropionate plus calcipotriol);
- corticosteroid plus salicylic acid combination products;
- tar-based preparations (e.g. coal tar, pine tar);
- other combination products, containing dithranol, coconut oil, urea or salicylic acid;
- ciclopirox olamine (antifungal);
- tacrolimus; and
- cocois.

Types of outcome measures

Primary outcomes

1. Reduction in clinician-assessed severity.
2. Improvement in quality of life.
3. Adverse events requiring withdrawal of treatment, such as serious allergic reactions.

Secondary outcomes

1. Subjective reduction in severity of psoriasis.
2. Minor adverse events not requiring withdrawal of treatment such as rash or itching.
3. Time free of disease or duration of response as measured by the proportion of participants relapsing to baseline scores during continued treatment or following discontinuation of treatment. We analysed outcomes according to short-term (≤ six months) and long-term (> six months) evaluations.

Search methods for identification of studies

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

Electronic searches

We searched the following databases up to 17 August 2015:

- the Cochrane Skin Group Specialised Register using the search terms 'scalp and psoria*';
- the Cochrane Central Register of Controlled Trials (CENTRAL 2015, Issue 7) using the search strategy in Appendix 1;
- MEDLINE via Ovid (from 1946) using the strategy in Appendix 2;
- EMBASE via Ovid (from 1974) using the strategy in Appendix 3; and
- LILACS (Latin American and Caribbean Health Science Information database, from 1982, using the search terms (cuero cabelludo and psoria$) or (scalp and psoria$) and the controlled clinical trials topic-specific query filter.

Trials registers

We searched the following trials registers on 15 September 2015 using the search term "scalp psoriasis" unless otherwise stated:

- the ISRCTN registry (www.controlled-trials.com);
- the US National Institutes of Health Ongoing Trials Register (www.clinicaltrials.gov);
- the Australian New Zealand Clinical Trials Registry (www.anzctr.org.au), using the terms "scalp AND psoriasis";
- the World Health Organization International Clinical Trials Registry Platform (www.who.int/trialsearch/);
- the EU Clinical Trials Register (https://www.clinicaltrialsregister.eu/).

Searching other resources

Reference lists

We scanned the bibliographies of retrieved studies for further references to relevant RCTs.

Handsearching

We handsearched the following six psoriasis-specific conferences of the past 12 years up to September 2015 for relevant RCTs presented as abstracts:

- American Academy of Dermatology (AAD);
- European Academy of Dermatology and Venerology (EADV);
- Deutsche Dermatologische Gesellschaft (DDG);
- Psoriasis - From Gene to Clinic;

- Psoriasis International Network - Paris; and
- International Federation of Psoriasis Associations (IFPA) - Stockholm.

Adverse effects

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

Correspondence

We attempted to obtain unpublished data via correspondence with trial authors and sponsors if contact details were available.

Data collection and analysis

Some parts of the methods section of this review use text that was originally published in the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011).

Selection of studies

Two authors (JGS and SR) independently screened abstracts of all publications obtained from the searches. For those that we considered as possibly relevant, we sought to obtain the full article. We read all available full texts to assess their relevance based on the inclusion criteria.
The same authors screened all conference abstracts of the associations listed above for eligibility.

Data extraction and management

Two authors (JGS and SR) independently extracted data from the included studies. Whenever disputes arose, we achieved resolution by consultation with a third author (AJ). For data extraction, we utilised Microsoft Office Excel 2003.

Assessment of risk of bias in included studies

We assessed the methodological quality of the trials included in the review using the criteria described in the*Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011):

- Was the random allocation sequence adequately generated?
- Was allocation adequately concealed?
- Was knowledge of the allocated interventions after assignment prevented (performance bias or detection bias)?
- Were incomplete outcome data adequately addressed?
- Are reports of the study free of suggestion of selective reporting?
- Was the study apparently free of other bias?

We classified each of the items as low, high or unclear risk of bias (see Characteristics of included studies).

Measures of treatment effect

We expressed the results of the single studies as risk ratios (RR) with 95% confidence intervals (CI) for dichotomous outcomes, and mean differences (MD) and 95% CI for continuous outcomes. Where it was not possible to calculate a point estimate due to missing measures of variance for continuous outcomes, we described the data qualitatively. If included studies were sufficiently homogeneous, we pooled the effect estimates of the single studies in a meta-analysis. Specifically for dichotomous data with statistically significant effect estimates, we expressed the results as number needed to treat to benefit (NNTB) with 95% confidence intervals and the baseline risk to which it applies (Christensen 2006). We planned to calculate the standardised mean difference when the trials assessed the same outcome, but used different instruments or scales. However, the included trials did not use different instruments or scales to make this procedure necessary.

Unit of analysis issues

The unit of analysis was based on the individual participant (unit to be randomised for interventions to be compared). We analysed cross-over study designs by using the first phase of the trials (before crossing over the treatments), as it was difficult to determine whether there was any carry-over effect. In cases where the study design was based on within-participant studies (instead of a cross-over design), or even if insufficient information was available to perform these analyses, we reported the estimate effects separately in additional tables in the same manner as they appeared in the original publications (Higgins 2011).
There were numerous multi-arm studies. However, there was no risk of unit of analysis error, since we did not include any intervention or control group twice in the same meta-analysis.

Dealing with missing data

We analysed data using intention-to-treat (ITT) wherever possible. If outcome data or statistics were missing, we attempted to contact the authors or sponsors of the study to request these data. Where missing data or statistics were not available from authors or sponsors, we conducted available case analysis. Where studies had not already conducted ITT analysis for dichotomous efficacy outcomes, we imputed missing data as treatment failure. We then recalculated the data by following the ITT principle. However, some studies that had missing data only reported the total amount of drop-outs, but not the number of drop-outs per treatment group. In these cases, we conducted available case analysis as well, since treatment failure imputation was not possible.
We planned to impute missing standard deviations for continuous outcomes where appropriate, however the majority of the included studies with continuous outcome data (e.g. TSS) had missing standard deviations, so we were unable to do this.

Assessment of heterogeneity

We quantified inconsistency among the pooled estimates using the I^2 statistic (where I^2 statistic = [(Q - df)/Q] x 100% [Q is the Chi^2 statistic and df its degree of freedom]). This illustrates the percentage of the variability in effect estimates resulting from heterogeneity, rather than sampling error (Higgins 2002; Higgins 2003). We presented data using a random-effects model (DerSimonian 1986). Wherever heterogeneity among the included studies was substantial, we did not pool study results, but presented them individually. We then attempted to explain the heterogeneity using prespecified subgroups and sensitivity analyses.

Thresholds for the interpretation of the I^2 statistic can be misleading, since the importance of inconsistency depends on several factors. A rough guide for the interpretation is as follows (Higgins 2011):

- 0% to 40% = might not be important;
- 30% to 60% = may represent moderate heterogeneity*;
- 50% to 90% = may represent substantial heterogeneity*;

and

- 75% to 100% = considerable heterogeneity*.

*The importance of the observed value of the I^2 statistic depends on the magnitude and direction of effects and the strength of the evidence for heterogeneity (e.g. P value from the Chi^2 statistic, or a confidence interval for the I^2 statistic).

Assessment of reporting biases

We planned to assess publication bias by preparing a funnel plot. However, as none of the comparisons included more than 10 studies, funnel plots would not give any meaningful information.

Data synthesis

We synthesised and presented qualitative information relative to methods, risk of bias, description of participants and outcome measures in a Characteristics of included studies table within the review. For quantitative data, we meta-analysed the data using the random-effects model, since substantial clinical and methodological heterogeneity were expected between the studies, which by themselves can generate substantial statistical heterogeneity. When data from primary studies were not parametric (e.g. effects reported as medians, quartiles, etc), or they were without sufficient statistical information (e.g. standard deviations, standard error, etc), we presented them qualitatively.

Subgroup analysis and investigation of heterogeneity

We planned to perform subgroup analysis according to age range, severity of scalp psoriasis and type of available treatments. Wherever meta-analysis for a class of agents was performed, we additionally analysed subgroups with respect to the individual active agent and its vehicle (e.g. rinse-off or leave-ons). Particularly in the case of steroids, we undertook meta-analysis pooling all agents, regardless of potency, but we analysed effect estimates of subgroups with respect to each individual steroid.

In our investigation for clinical heterogeneity among trials we compared the following characteristics of study populations: age range, the proportion who were female, dosage and disease severity at baseline. We further assessed methodological heterogeneity by comparing study duration, and evaluated whether allocation concealment or blinding of participants and investigator were performed. Possible statistical heterogeneity observed among subgroups was not assumed as a true causal relationship between dependent (estimate effects) and independent variables (the subgroups), but only as hypotheses that could be tested in future trials.

Sensitivity analysis

We carried out sensitivity analyses according to the following methodological aspects: intention-to-treat, available data analysis and concealment of allocation. We further planned to evaluate the estimate effects according to the inclusion and exclusion of studies reported only as abstracts.

'Summary of findings' tables

In 'Summary of findings' tables we present the quality of evidence and the corresponding illustrative risk of important dichotomous outcomes. We focused on three comparisons that we thought to be of major clinical interest:

- Steroids versus vitamin D (Summary of findings for the main comparison).
- Steroid plus vitamin D compared to steroid (Summary of findings 2).
- Steroid plus vitamin D compared to vitamin D (Summary of findings 3).

We graded the level of evidence for dichotomous outcomes using the GRADE approach as described in the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011): we assessed the boundaries of the CI. If the confidence limit crossed the minimal clinically important difference (MID) thresholds we downgraded. The MID represents the smallest difference between treatment groups for an outcome score that clinicians or participants identify as meaningful. GRADE suggests these thresholds to be greater than 25% benefit (1.25) and 25% harm (0.75). If one or both thresholds were crossed we downgraded.

RESULTS

Description of studies

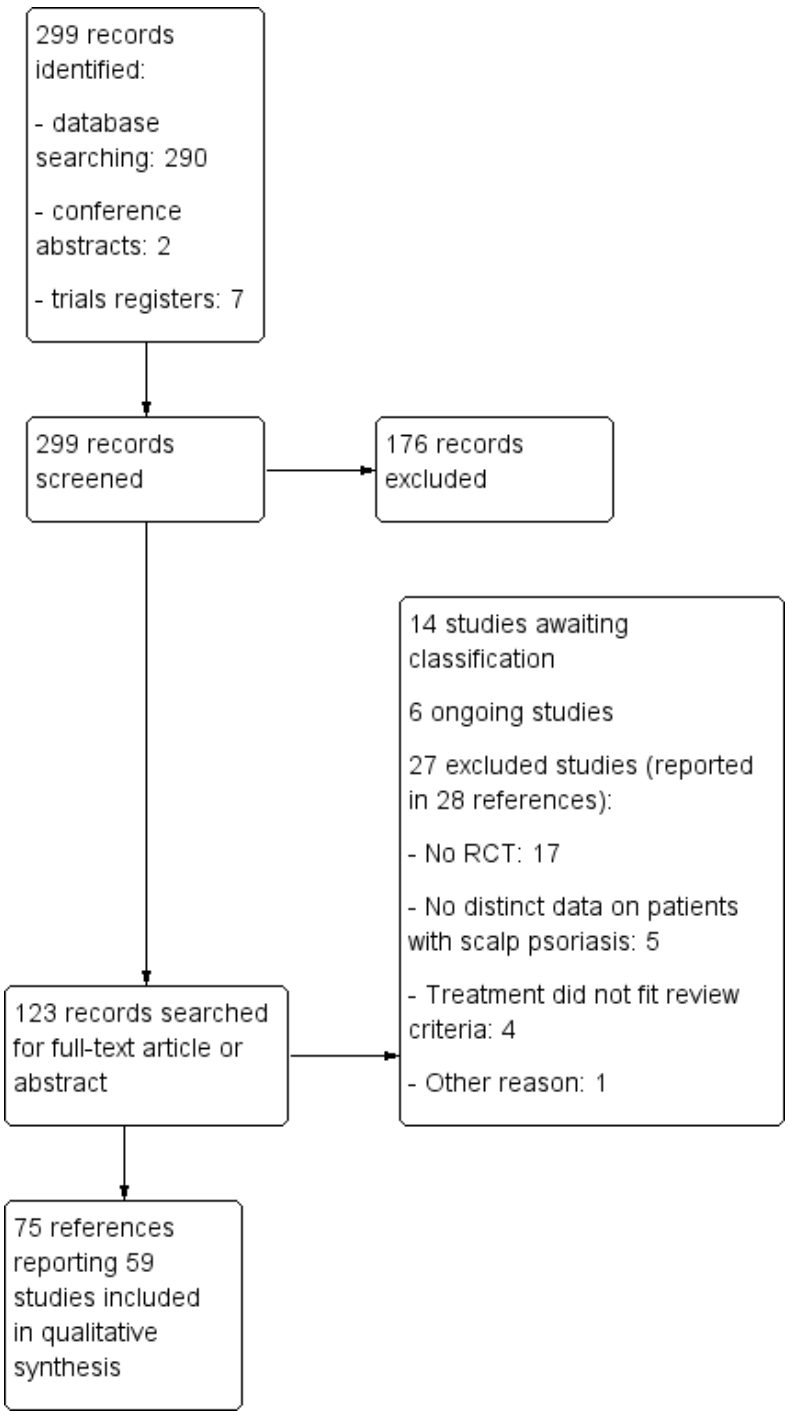
Results of the search

The electronic searches of the six main databases (see Electronic searches) retrieved 290 records. During our handsearch of conference abstracts we detected two additional studies that appeared to meet the inclusion criteria. Our search in the trials registers identified seven further studies. Our screening of the reference lists of the included publications did not reveal any additional RCTs. We therefore had a total of 299 records.

We excluded 176 records based on titles and abstracts. We tried to obtain the full texts or abstracts of the remaining 123 records. We excluded 27 studies (28 references) (see Characteristics of excluded studies). We added 14 records to Characteristics of studies awaiting classification. We classified six studies as Ongoing studies.

We included 59 studies that were reported by the remaining 75 references. For further description of our screening process, see the study flow diagram (Figure 1).

Figure 1. Study flow diagram.



Included studies

This review included 59 studies with a total of 11,561 participants.

Design

Of the RCTs, 40 were head-to-head comparisons, 15 vehicle-controlled and four compared active treatments with each other as well as versus the vehicle. The latter four trials, thus, assessed more than one comparison. Two publications were within-patient (split-face) trials, of which one was active-controlled (Jarratt 1991), and the other vehicle-controlled (Lepaw 1978).

Data on treatment duration were available for all 59 trials. The median duration was four weeks, ranging from five days (Köse 1997), to 52 weeks (Luger 2008). Nine trials (9/59 = 15%) reported data on follow-up visits, with a mean follow-up duration of 2.4 weeks (range: one to eight weeks). We defined follow-up as post-treatment assessments.

The oldest included study was published in 1972 (Harris 1972), the most recent one in 2015 (NCT01195831). Most of the trials (35/59 = 59%) were multicentre studies.

Sample size

Except for one (Barrett 2005), all included trials provided data on the number of randomised participants. The sample size varied from 26 (Andres 2006), to 1505 (Jemec 2008) participants.

Participants

The 59 included trials evaluated a total of 11,561 participants. In 38 studies (38/59 = 64%), data on the age of participants (N = 9051) were available. The mean age of the these participants was 45.2 years. However, this mean score does not include four studies that only provided data on the age range of all included participants. Forty trials (40/59 = 68%) provided information with regard to the gender of the included participants (N = 9061). With a mean of 49% (range: 22% to 68%) the percentage of female was nearly equal to that of the male participants.

In 46 studies (46/59 = 78%; N = 9875 participants) a baseline severity of the study population was reported. In three trials, mean baseline severity data were available only for the whole study population but not for each intervention group. The other 43 studies provided distinct information on baseline severity for each study group. There was a wide spectrum of different severity scores. Most studies (31/46 = 67%) assessed baseline severity by the Total Sign Score (TSS). Others provided different data on baseline severity, e.g. the degree of scaling (Curley 1990), Psoriasis Area and Severity Index (PASI) (Bergstrom 2003; van de Kerkhof 2002), or the percentage of scalp area affected (Feldman 2013). However, we sought to extract any available baseline data for disease severity in order to assess the comparability of the intervention groups.

The definition and the scale of the TSS was not consistent throughout the studies. Some definitions included only the scores of erythema, scaling and thickness, others added the score of pruritus. The scale, therefore, had a range of either 0 to 9, 0 to 12, or 0 to 16, classifying the baseline severity as none, mild, moderate, severe and sometimes very severe. In order to classify the disease severity, we primarily used the definition given by each individual study. In seven studies we calculated the baseline TSS with data reported. In these and other studies, which did not provide a clear definition of the TSS, we adjusted for scale size (0 to 9) and graded the severity as mild (0 to 4.5), moderate (4.6 to 7.5) or severe (7.6 to 9). For 35 trials, a classification of the mean baseline severity was possible: the population of 30 of these trials had a moderate baseline severity. Of the other five trials, two study populations were of mild baseline severity, one of mild to moderate, one of moderate to severe, and one of severe baseline severity.

Interventions

The included studies assessed the following medications:

- corticosteroids (e.g. betamethasone dipropionate, clobetasol propionate);
- vitamin D (calcipotriol);
- corticosteroid plus vitamin D combination products (e.g. betamethasone dipropionate plus calcipotriol);
- corticosteroid plus salicylic acid combination products;
- tar-based preparations (e.g. coal tar, pine tar);
- other combination products, containing dithranol, coconut oil, urea or salicylic acid;
- ciclopirox olamine (antifungal);
- tacrolimus; and
- cocois.

The interventions in the included studies were grouped into 15 main comparisons.

We analysed vehicle-controlled studies and head-to-head trials. The latter also involved comparisons of steroids, which were of varying or similar potency. Furthermore, we included studies that assessed a specific steroid in different application forms or its once- versus twice-daily use.

Applying the active agent in an appropriate vehicle is crucial (Chan 2009). We therefore classified vehicles into two main groups: rinse-offs (including shampoos) and leave-ons. The latter was further divided in two subgroups: hydrophilic (including alcoholic solutions, foams, lotion, hydrogels, oil in water emulsions) and lipophilic leave-ons (ointments, oleo gels, oils, creams, water in oil formulation). In addition, we distinguished occlusive and non-

occlusive dressings. We analysed identical active agents that were not of the same vehicle group as two different topical treatments. We classified topical corticosteroids into four groups (1 to 4) according to the German steroid classification system (Niedner 1996):

1. Mild potency: none of the included trials assessed topical corticosteroids of mild potency.
2. Moderate potency: fluocinolone acetonide 0.01%, hydrocortisone 17-butyrate 0.1%, desoximetasone 0.05%, triamcinolone acetonide as 0.1% and 0.2% solution
3. High potency: amcinonide 0.1%, betamethasone dipropionate, betamethasone valerate as 0.1%, 0.12% and 1% solution, halcinonide 0.1%, fluocinonide, fluocinolone acetonide 0.025%, desoximetasone 0.25% and mometasone furoate.
4. Very high potency: clobetasol propionate.

Outcomes

We further classified our pre-specified outcomes below and recorded the number of studies, which provided data on these outcomes:

Primary outcomes

1) Reduction in clinician-assessed severity:

- number of participants achieving 'clearance' according to the Investigators' Global Assessment of Disease Severity (IGA): 22 studies = 37%;
- number of participants achieving 'response' according to the IGA: 24 studies = 41%;
- mean score of the IGA: six studies = 10%; and
- mean of the Total Severity Score (TSS): 34 studies = 58%.

2) Improvement in quality of life:

- any tool evaluating the improvement in quality of life: four studies = 7%.

3) Adverse events requiring withdrawal of treatment, such as serious allergic reactions. This outcome was reported as 'Number of participants withdrawing due to adverse events': 30 studies = 51%.

Secondary outcomes

1) Subjective reduction in severity of psoriasis:

- number of participants achieving 'clearance' according to the Patients' Global Assessment of Disease Severity (PGA): four studies = 7%;
- number of participants achieving 'response' according to the PGA: 12 studies = 20%; and
- mean score of the PGA: seven studies = 12%.

2) Minor adverse events not requiring withdrawal of treatment such as rash or itching. This outcome was reported as 'Number of participants with at least one adverse event': 39 studies = 66%.

3) Time span free of disease or duration of response as measured by the proportion of participants relapsing to baseline scores during continued treatment or following discontinuation of treatment: no studies.

Most efficacy and safety analyses could only be made for short-term treatments, since 58 studies were carried out for less than six months. The only trial that provided results concerning efficacy and safety for long-term treatment had a study duration of 52 weeks (Luger 2008). However, this study reported the number of participants with satisfactorily controlled disease, which included all those with mild to absent disease status. This outcome did not meet our pre-specified definition of treatment success (number of participants achieving 'response' by IGA) and was therefore not suitable for efficacy analysis. However, we extracted and analysed the long-term safety data.

For eight studies that stated IGA or PGA as continuous outcomes three provided sufficient statistical information in order to determine an effect estimate (Ellis 1988; Feldman 2001; Shuttleworth 1998). The remaining five trials did not report any measure of variance, thus, we described results qualitatively (Ellis 1989; Griffiths 2006; Monk 1995; Regaña 2009; Willis 1986). The studies defined the IGA or PGA score differently. However, for most trials, a higher score meant a better outcome. In one study the IGA was provided as both a dichotomous and continuous outcome (Willis 1986). However, since the authors did not provide any measure of variance, we only extracted the dichotomous data.

Of the 34 trials that reported TSS as an efficacy outcome but no corresponding standard deviation (SD), we either calculated the mean TSS change from baseline or used the mean change provided in the text. Only one study that reported TSS as an efficacy outcome provided the SD (Buckley 2008).

Nine studies reported data on follow-up visits. Neither provided a definition of 'relapse' that was consistent with our protocol, nor did any study measure the time span until relapse occurred.

Excluded studies

Studies that assessed systemic, ultraviolet (UV) or Grenz ray therapy were not eligible for this review. Therefore we excluded studies which allowed any systemic anti-psoriatic treatment or concomitant UV/Grenz ray therapy of the scalp.

Of the 123 identified publications that appeared to meet the inclusion criteria, we excluded 28 (see Characteristics of excluded studies). Seventeen studies did not have a randomised controlled design or did not clearly report any randomisation. Five trials assessed body psoriasis or other scalp dermatoses without providing results for scalp psoriasis separately. In four trials, the treatment did not meet this review's eligibility criteria. One study was of unclear design.

Studies awaiting classification

Fourteen studies are awaiting classification pending further information (Characteristics of studies awaiting classification). We attempted to contact nine authors in order to obtain additional data or information. Only three authors answered our requests. One referred us to the sponsor of his study, who did not respond to our enquiries. One other could not provide any additional data, since the study results were not yet processed. A third author refused to supply any unpublished data. One trial was already completed, but the results are not yet available (Augustin 2014).

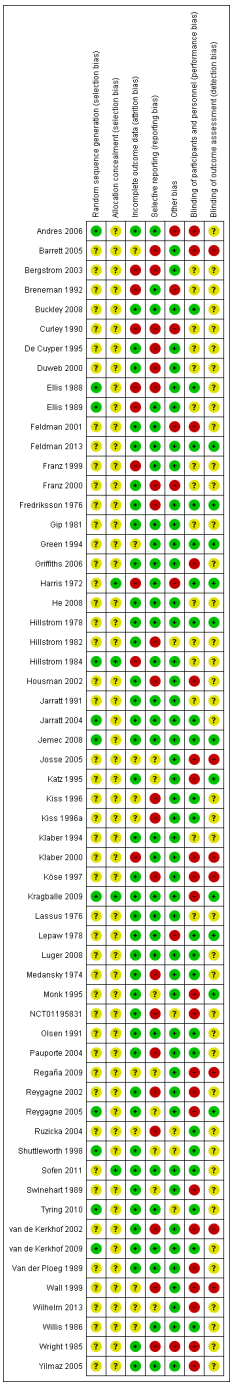
Ongoing studies

After searching the trials registers, we retrieved six records that appeared to meet the inclusion criteria. They are listed in Ongoing studies.

Risk of bias in included studies

An overview of the risk of bias for the included studies, which was considerably heterogenous, is provided in Figure 2. For detailed information concerning the reasons on which our risk evaluation of the individual study is based, please refer to the Characteristics of included studies.

Figure 2. 'Risk of bias' summary: review authors' judgements about each risk of bias item for each included study.Legend: "?" = unclear risk of bias; "+" = low risk of bias; "-" = high risk of bias



Adequate sequence generation

Only 11 trials (19%) reported appropriate randomisation methods and we judged them at low risk of bias. Of this group, nine created a computer-generated randomisation list, one used a table with random digits (Hillstrom 1984), and one reported a randomised block design (Shuttleworth 1998). The other 48 studies did not provide sufficient information to permit judgement as to whether the sequence generation was adequately performed.

Allocation

Only four (7%) of the 59 trials supplied sufficient information to assess whether allocation concealment was ensured throughout the study and we therefore judged them at low risk of bias. The remaining 55 studies did not address this or did not report sufficient information to permit judgement as to whether the allocation concealment was performed appropriately or not.

Blinding

Of the 59 included studies, 33 had a double-blind design, 14 were single-blind studies, two had 'third-party' blinding, six had an open-label design and four did not report any blinding.

Of the 33 studies (56%) with a double-blind design, only seven clearly addressed their method to ensure blinding of participants and outcome assessors (Feldman 2013; Fredriksson 1976; Green 1994; Harris 1972; Hillstrom 1978; Jemec 2008; Lepaw 1978). We judged them to be of low risk of bias for both domains. Eleven double-blind trials did not provide sufficient information on how blinding of participants/personnel and outcome assessment was ensured throughout the study. For this reason, we evaluated the risk of bias as unclear concerning performance and detection bias in these studies (Breneman 1992; Curley 1990; Ellis 1989; Franz 1999; Franz 2000; Gip 1981; Hillstrom 1982; Hillstrom 1984; Jarratt 1991; Klaber 1994; Lassus 1976). We evaluated the other 15 of the 33 studies with a double-blind design to be at low risk of performance bias and unclear risk of detection bias (Buckley 2008; Ellis 1988; Jarratt 2004; Kiss 1996; Kiss 1996a; Luger 2008; Medansky 1974; Olsen 1991; Pauporte 2004; Ruzicka 2004; Shuttleworth 1998; Sofen 2011; Tyring 2010; van de Kerkhof 2009; Willis 1986).

Of the 14 single-blind studies (24%), 12 followed an investigator-only masked design (Andres 2006; Feldman 2001; Griffiths 2006; Housman 2002; Katz 1995; Kragballe 2009; Monk 1995; NCT01195831; Reygagne 2002; Reygagne 2005; Wilhelm 2013; Wright 1985), and we rated them to be at high risk of performance bias. Of these 12 studies, eight did not provide sufficient information on how blinding of outcome assessment was ensured; therefore we rated the risk of detection bias as unclear (Andres 2006; Feldman 2001; Griffiths 2006; Housman 2002; NCT01195831; Reygagne 2002; Wilhelm 2013; Wright 1985). We evaluated the other four studies to be at low risk of detection bias (Katz 1995; Kragballe 2009; Monk 1995; Reygagne 2005).

Two of the 14 studies that were stated to be single-blinded did not clearly state whether investigators or participants were blinded, or whether the outcome assessor was blinded, so we assessed both studies to be at unclear risk concerning performance and detection bias (Bergstrom 2003; De Cuyper 1995).

Two trials (3%) addressed a 'third-party' blinding, but it remained unclear how this was performed (Swinehart 1989; Van der Ploeg 1989). We assessed both studies as being at high risk of performance bias and at unclear risk of detection bias.

We considered six studies (10%) that had an open-label design to be at high risk of performance and detection bias (Barrett 2005; Josse 2005; Klaber 2000; Regaña 2009; van de Kerkhof 2002; Wall 1999).

Another four studies (7%) did not report any blinding. We considered two of them to be at unclear risk of performance and detection bias (Duweb 2000; He 2008). Köse 1997 reported no blinding and due to differences in treatment application and duration between the two intervention groups, it is unlikely that blinding of participants/personnel and outcome assessment was performed, so we rated them to be at high risk of performance and detection bias. For the fourth study, the blinding of participants and personnel was considered not to be possible due to the different application mode in the groups (high risk of performance bias); we rated the risk of detection bias as being unclear (Yilmaz 2005).

Incomplete outcome data

Forty studies (68%) ensured the completeness of the outcome data and we judged them as low risk of bias. Of this group, 14 trials provided data on the intention-to-treat (ITT) population, in 10 studies no drop-outs occurred and in 16 trials the drop-out rate was considered as too small (< 10% per group) to introduce bias.

Of the nine studies (15%) that did not provide complete outcome data and we judged as high risk of bias, two used 'as-treated' analyses, three had questionable reasons to exclude randomised participants from analysis, three did not use appropriate imputation methods while having drop-out rates of more than 10% per group and one did not state the reasons of attrition.

In 10 trials (17%) it remained unclear if the outcome data were sufficiently addressed.

Selective reporting

Thirty studies (51%) reported results for all outcomes that were pre-specified in the methods section. We considered 21 studies

(36%) to be at high risk of selective reporting bias, since they either did not provide results of pre-specified outcomes or additionally reported outcomes that were not mentioned in the methods section.

In eight studies (14%), we rated the risk of bias as unclear for the following reasons: three studies were only available as an abstract, another two studies did not report results for pre-specified outcomes which, however, were not relevant for this review. Three studies did not provide results in sufficient detail.

Other potential sources of bias

We judged eight studies (14%) to be at high risk of an other potential bias:

Due to low baseline disease severity, Breneman 1992 excluded 12 participants from efficacy analysis but included them for safety analysis. This may have led to an overestimation of treatment safety.

Baseline severity was imbalanced between treatment groups in two studies (Andres 2006; Franz 2000). Feldman 2001 did not state IGA or PGA data at baseline. The degree of improvement according to these scores was therefore not evaluable.

During the within-patient study of Lepaw 1978, participants had to apply both drugs three times per day for two weeks. Since no evaluation of compliance was reported, the results might have been biased.

In one study data that were stated in the figures were not consistent with those reported in the text (Curley 1990).

In another trial the application frequency varied among participants, which might have introduced bias (Harris 1972).

One study stopped earlier than scheduled, because too many participants were lost to follow-up (Wright 1985). Thus, it was likely that the effect of the intervention was overestimated.

In five studies (8%) it was unclear whether they had been affected by other potential sources of bias. Hillstrom 1982 assessed blood cortisol levels of some participants, but the criteria for selecting these participants for this specific analysis was unclear. The same accounts for Ruzicka 2004: in some participants, who received calcipotriol, vitamin D metabolites were additionally assessed. The authors did not state why only selected participants underwent this analysis. However, vitamin D metabolites and blood cortisol levels were not relevant for this review. The assessment of NCT01195831 was limited to information that has been published in a trial register. Due to the lack of available data, we could not assess whether disease severity of both treatment groups was similar at baseline. Shuttleworth 1998 reported results of a clinical assessment of overall scalp psoriasis, but this score was not clearly defined. Therefore, the degree of improvement from baseline was not clear. The baseline disease severity of Tyring 2010 was not balanced among the treatment groups. It was unclear if the degree of imbalance could have induced bias.

We could not identify any other potential bias in the remaining 46 studies.

Effects of interventions

See: **Summary of findings for the main comparison** Steroid compared to vitamin D for scalp psoriasis; **Summary of findings 2** Steroid plus vitamin D compared to steroid for scalp psoriasis; **Summary of findings 3** Steroid plus vitamin D compared to vitamin D for scalp psoriasis

In this review, all interventions are grouped into 15 main comparisons, which we have listed below to aid navigation of this section.

1. Steroid: once versus twice daily
2. Steroid versus the vehicle
3. Vitamin D versus the vehicle
4. Steroid plus vitamin D versus the vehicle
5. Steroid versus steroid: very high versus high potency
6. Steroid versus steroid: high versus moderate potency
7. Steroid versus steroid: both of high potency
8. Steroid versus vitamin D
9. Steroid plus salicylic acid versus steroid
10. Steroid plus vitamin D versus steroid
11. Steroid plus vitamin D versus vitamin D
12. Tar and dithranol
13. Steroid: vehicle comparisons
14. Other steroid and salicylic acid containing comparisons
15. Antifungals versus vehicle

We reported where comparisons addressed our pre-specified outcomes. Where outcomes are absent from the text, it is because the included studies did not report the outcome for that particular comparison.

Efficacy outcomes

We extracted data on efficacy outcomes (IGA, PGA, TSS) that were reported for the fourth week after initiation of the trial. Where study duration was shorter or no data were provided for this time point, we reported the next closest evaluation to week four.

Physicians' Global Assessment of disease severity is sometimes used synonymously with IGA (Investigators' Global Assessment of disease severity). However, it should not be confused with Patients' Global Assessment of disease severity (PGA). In this review, we therefore used the term IGA if the assessor evaluated treatment response, and PGA if the participants rated their treatment response.

In accordance with the European Medicines Agency (EMA 2004), we believe the IGA or PGA to be the most practicable outcome for clinicians or participants in order to assess the improvement in scalp psoriasis. We therefore primarily extracted IGA and PGA as dichotomous outcomes ('clearance', 'response') for meta-analysis. If a study only stated mean scores (continuous outcomes), we extracted and analysed these data with the corresponding measure of variance. If there was insufficient statistical information (e.g. standard deviation, SD, standard error, SE), we described the findings qualitatively.

There were a vast variety of IGA or PGA scales grading the psoriatic lesions on the scalp as clear, almost clear or very mild or minimal, mild, moderate, severe or worse. In some cases, the latter indicated the highest, in others the lowest number of the scale. We therefore defined two steps of treatment efficacy: 'clearance' and 'response'. We matched all outcomes that stated clearance, whether assessed by the investigator or participant, with IGA and PGA 'clearance', respectively. IGA and PGA 'response' were defined as participants showing 75% to 100% improvement of disease severity. This also included a treatment response that ranged from almost clear through minimal or very mild or marked improvement to clear based on a five-point scale. All objective and subjective outcomes that corresponded to this definition were matched with IGA and PGA, respectively.

We additionally extracted and calculated the mean difference of the Total Severity Score (TSS) if sufficient statistical information (e.g. standard deviation (SD) or standard error (SE)) was provided. In the absence of the measure of variance, we described TSS data qualitatively as the mean percentage change from baseline.

As the majority of the included studies with continuous outcome data (e.g. TSS) had missing standard deviations, we decided not to use any statistical techniques in order to impute the missing SD. In our opinion, the imputation of SDs would have led to results in our analyses that remain linked to a high uncertainty.

Safety outcomes

To assess tolerability of topical treatments, we evaluated withdrawal rates due to adverse events and the number of participants with at least one adverse event. For these outcomes, we retrieved the total endpoint number reported, whether the outcome assessor rated them as drug-related or not. We found this to be justifiable, since any adverse events that were not drug-related should have been distributed equally among all groups if randomisation was successful. For two reasons, we did not assess the particular risk for certain adverse events. On the one hand, we could not foresee all interventions that our review would include. On the other hand, it was likely that randomised controlled trials (RCTs) used different methods in monitoring or detecting adverse events. Some studies may have searched more accurately for specific adverse events, such as atrophy and, thus, detected a higher incidence than others. However, we aimed to report the sort of adverse event that caused discontinuation of the treatment. We also aimed to report the five most frequent adverse events of each therapy. Yet, for some therapies no or only few adverse events occurred or were reported by the authors.

Sensitivity analysis (Table 2)

To assess the robustness of the effect estimates of meta-analysis, we undertook sensitivity analysis with respect to studies that reported data on an intention-to-treat (ITT) population. In addition, we evaluated effect estimates of trials that performed adequate concealment of allocation. Wherever sensitivity analysis was possible, we stated the findings under the corresponding outcome heading of the comparison.

None of the included abstracts was eligible for meta-analysis. It was therefore not necessary to evaluate estimate effects of meta-analysis according to inclusion and exclusion of abstracts.

1. Steroid: once versus twice daily

One study (N = 79 participants) compared the once versus twice-daily use of betamethasone valerate 0.12% (Feldman 2001).

Primary outcomes

1) Reduction in clinician-assessed severity

- Mean score of the IGA (Investigators' Global Assessment of Disease Severity) (Analysis 1.1)

There was a small difference for this outcome in favour of the twice-daily use, which was statistically significant (mean difference (MD) 0.60; 95% confidence interval (CI) 0.05 to 1.15).

2) Number of participants withdrawing due to adverse events

One participant withdrew because of a burning sensation. The authors did not state if this participant applied the study medication once or twice daily.

Secondary outcomes

1) Subjective reduction in severity of psoriasis

- Mean score of the PGA (Patients' Global Assessment of Disease Severity) (Analysis 1.2).

There was no significant difference between the treatment groups for this outcome (MD 0.40; 95% CI -0.20 to 1.00).

2. Steroid versus the vehicle

Primary outcomes

1) Reduction in clinician-assessed severity

- Number of participants achieving 'clearance' according to the IGA (Analysis 2.1)

Four studies that compared a steroid with its vehicle reported this outcome. Two assessed a steroid of high potency (Ellis 1988; Jemec 2008), and two a very high potency steroid (Olsen 1991; Sofen 2011). Meta-analysis of all four trials, which included 1315 participants, indicated that steroids were significantly more effective than the vehicle (risk ratio (RR) 14.58; 95% CI 7.28 to 29.17; number needed to treat to benefit (NNTB) = 4; 95% CI 4 to 5). Heterogeneity was not important (I^2 = 0%).

Effect estimates were significant for each subgroup: amcinonide 0.1% (RR 16.80; 95% CI 2.29 to 123.30; NNTB = 5; 95% CI 4 to 10), betamethasone dipropionate (RR 10.15; 95% CI 3.83 to 26.88; NNTB = 4; 95% CI 4 to 5), clobetasol propionate as hydrophilic leave-on (RR 22.83; 95% CI 7.31 to 71.30; I^2 = 0%; NNTB = 4; 95% CI 3 to 5).

Sensitivity analysis

Sensitivity analysis with regard to ITT population included two studies (Jemec 2008; Sofen 2011), whereas sensitivity analysis with regard to adequate concealment of allocation only included Sofen 2011. Both supported the effect estimate of the meta-analysis of the four studies (Table 2).

- Number of participants achieving 'response' according to the IGA

Ten studies that compared a steroid with the vehicle addressed this outcome. Nine had a parallel-group and one a within-patient design. Two studies assessed a steroid of moderate potency (Franz 1999; Harris 1972), four investigated steroids of high potency (Jemec 2008; Ellis 1988; Lepaw 1978; Medansky 1974), and four a very high potency steroid (Franz 2000; Jarratt 2004; Olsen 1991; Sofen 2011). Meta-analysis of all nine trials with control groups, including 2114 participants, indicated that steroids were significantly more effective than the vehicle (RR 5.24; 95% CI 3.83 to 7.17; NNTB = 3; 95% CI 3 to 3; Analysis 2.2). Heterogeneity was moderate (I^2 = 44%).

Effect estimates were superior to the vehicle for each subgroup: betamethasone dipropionate (RR 4.06; 95% CI 2.85 to 5.79; NNTB = 3; 95% CI 3 to 3), amcinonide 0.1% (RR 5.19; 95% CI 2.60 to 10.36; NNTB = 3; 95% CI 2 to 4), betamethasone valerate 0.1% (RR 2.96; 95% CI 1.81 to 4.85; NNTB = 3; 95% CI 3 to 5), clobetasol propionate as hydrophilic leave-on (RR 7.93; 95% CI 5.46 to 11.51; NNTB = 2; 95% CI 2 to 2), clobetasol propionate as rinse-off (RR 15.83; 95% CI 2.23 to 112.33; NNTB = 4; 95% CI 3 to 5).

In a split-face comparison, which compared halcinonide 0.1% as a hydrophilic leave-on with the vehicle, 16 out of 27 participants responded on the side treated with the steroid (Lepaw 1978). Only one participant responded on the vehicle side.

Sensitivity analysis

Sensitivity analysis with regard to ITT population included five studies (Franz 2000; Jarratt 2004; Jemec 2008; Medansky 1974; Sofen 2011), and with regard to adequate allocation concealment only included one study (Sofen 2011). Both supported the effect estimate of the meta-analysis of the nine studies (Table 2).

- Mean of the total severity score (TSS) (Analysis 2.3)

Seven studies that compared a steroid with the vehicle reported the reduction of disease severity by measuring the mean change of TSS from baseline (Franz 1999; Franz 2000; Jarratt 2004; Jemec 2008; Olsen 1991; Pauporte 2004; Sofen 2011). Throughout all studies, all steroids led to a higher percentage reduction of TSS, regardless of steroid potency. The mean difference of percentage change from baseline compared to the vehicle ranged from 27% for fluocinolone acetonide 0.01% (Pauporte 2004), to 54% for clobetasol propionate as a hydrophilic leave-on (Sofen 2011). None of the studies reported the measure of variance.

2) Improvement in quality of life

One study (N = 81 participants), which compared clobetasol propionate with its vehicle, assessed quality of life (Sofen 2011). The scalpdex score at the end of treatment indicated that very highly potent clobetasol propionate led to a significantly higher improvement in quality of life than the vehicle (MD -20.70; 95% CI -30.46 to -10.94; Analysis 2.4).

3) Number of participants withdrawing due to adverse events

Six studies that compared a steroid with its vehicle addressed this outcome. Three trials evaluated steroids of high potency (Ellis 1988; Franz 1999; Jemec 2008), and three studies investigated very highly potent steroids (Jarratt 2004; Olsen 1991; Sofen 2011). Meta-analysis of four studies, including 1315 participants, indicated a significantly lower risk of withdrawal in the steroid group (RR 0.27; 95% CI 0.11 to 0.67; Analysis 2.5). The main reasons for withdrawal were burning sensation or irritation at the site of application and other unacceptable adverse events that were not further specified by the authors. The heterogeneity among studies was not important (I^2 = 0%).

The lower risk of withdrawal due to adverse events was only significant for betamethasone dipropionate (N = 692 participants; RR 0.21; 95% CI 0.07 to 0.61). It was not significant for amcinonide 0.1% (N = 165 participants; RR 0.99; 95% CI 0.06 to 15.53) nor for clobetasol propionate in a hydrophilic leave-on (N = 458 participants; RR 0.33; 95% CI 0.03 to 3.13). For betamethasone valerate 0.1% (N = 172 participants) and clobetasol propionate as a rinse-off (N = 142 participants), none of the participants in either group withdrew due to adverse events.

Sensitivity analysis

One study was included in the sensitivity analysis with regard to adequate allocation concealment (Sofen 2011). It did not show any significant difference in the risk of withdrawal due to adverse events between the steroid and the vehicle group. However, sensitivity analysis with regard to the ITT population, which included two studies (Jemec 2008; Sofen 2011), supported the findings of the meta-analysis of the four studies, which was that participants of

the steroid group had a significantly lower risk of withdrawal due to adverse events (Table 2).

Secondary outcomes

1) Subjective reduction in severity of psoriasis

- Number of participants achieving 'response' according to the PGA (Analysis 2.6)

Five studies that compared a steroid with its vehicle reported this outcome. Two studies assessed a steroid of high potency (Franz 1999; Jemec 2008), and three assessed a very highly potent steroid (Franz 2000; Jarratt 2004; Olsen 1991). Data from all five studies with dichotomous data, which included 1571 participants, indicated that steroids were significantly more effective than the vehicle, according to the participants' assessment. The heterogeneity among the studies was substantial (I^2 = 70.4%). This considerable heterogeneity may be explained by the variety of steroids that were assessed. Subgroup analysis indicated that the effect estimates for all steroid subgroups were superior to the vehicle: betamethasone dipropionate (RR 3.04; 95% 2.17 to 4.26; NNTB = 3; 95% CI 2 to 3), betamethasone valerate 0.1% (RR 3.52; 95% CI 1.97 to 6.29; NNTB = 3; 95% CI 2 to 4), clobetasol propionate in a hydrophilic leave-on (RR 6.92; 95% CI 4.42 to 10.83; I^2 = 0%; NNTB = 3; 95% CI 2 to 3), clobetasol propionate as a rinse-off vehicle (RR 14.35; 95% CI 2.02 to 102.12; NNTB = 4; 95% CI 3 to 6).

Sensitivity analysis

Due to clinical heterogeneity of the studies we did not perform meta-analysis and sensitivity analysis was not feasible.

- Mean score of the PGA (Analysis 2.7)

In one study that analysed 131 participants the mean PGA score of the amcinonide 0.1% group was significantly lower compared to the vehicle group (MD -0.87; 95% CI -1.17 to -0.57) (Ellis 1988). This indicated that the steroid led to a greater improvement.

2) Number of participants with at least one adverse event

Seven parallel-group trials and one within-patient study that compared a steroid with its vehicle addressed this outcome. Meta-analysis of the seven studies of parallel-group design, which included 1307 participants, indicated that steroids and the vehicle do not differ significantly in the risk of adverse events (RR 0.87; 95% CI 0.70 to 1.08; Analysis 2.8). Common local adverse events in both treatment groups were a burning or stinging sensation, pruritus and other local irritation. Folliculitis or acne appeared most notably in participants that were treated with steroids. Heterogeneity was not important (I^2 = 0%).

Effect estimates for each steroid subgroup were as follows: betamethasone valerate 0.1% (RR 0.25; 95% CI 0.01 to 5.86; Harris 1972), amcinonide 0.1% (RR 1.39; 95% CI 0.32 to 5.99; Ellis 1988), betamethasone dipropionate (RR 0.87; 95% CI 0.69 to 1.10; Jemec 2008), fluocinolone acetonide 0.01% (RR 3.00; 95% CI 0.13 to 71.61; Pauporte 2004), clobetasol propionate in a hydrophilic leave-on (RR 1.56; 95% CI 0.56 to 4.37; Sofen 2011), clobetasol propionate as a rinse-off (RR 0.59; 95% CI 0.29 to 1.18; Jarratt 2004; Reygagne 2002).

In the split-face study, one out of 27 participants experienced an adverse event on the side treated with the vehicle (Lepaw 1978).

Sensitivity analysis

Sensitivity analysis with regard to ITT population included three studies (Jarratt 2004; Jemec 2008; Sofen 2011), whereas sensitivity analysis with regard to adequate allocation concealment included only Sofen 2011. Both supported the findings of the meta-analysis of seven studies (Table 2).

3. Vitamin D versus the vehicle

Primary outcomes

1) Reduction in clinician-assessed severity

- Number of participants achieving 'clearance' according to the IGA (Analysis 3.1)

Two studies that compared vitamin D with its vehicle reported this outcome (Green 1994; Jemec 2008). Meta-analysis, including 457 participants, indicated that vitamin D was significantly more effective than the vehicle (RR 3.88; 95% CI 1.49 to 10.11; NNTB = 9; 95% CI 6 to 15). Heterogeneity among both studies was not important (I^2 = 16%).

- Number of participants achieving 'response' according to the IGA (Analysis 3.2)

Two studies (Feldman 2013, N = 363 participants; Jemec 2008, N = 408 participants), which compared calcipotriene with its vehicle, reported IGA response rates. The studies were substantially heterogenous (I^2 = 63%). Effect estimates for each individual study indicated that calcipotriene was significantly superior to the vehicle: Jemec 2008 (RR 1.60; 95% CI 1.01 to 2.53; NNTB = 12; 95% CI 7 to 98); Feldman 2013 (RR 2.84; 95% CI 1.70 to 4.74; NNTB = 6; 95% 5 to 11). Both studies addressed data for an ITT population and blinded investigators and participants adequately. Differences in both study populations may explain the clinical heterogeneity. The study population of Jemec 2008 consisted of 55% women. In contrast, the study population of Feldman 2013 consisted of 40% women. The duration of the studies (eight weeks) and dosage (5

µg/ml) were identical. Jemec 2008 used a hydrophilic gel whereas Feldman 2013 used a foam vehicle.

- Mean of the TSS (Analysis 3.3)

Three studies that compared vitamin D with its vehicle addressed the reduction of disease severity by measuring the mean change of TSS from baseline (Green 1994; Jemec 2008; Ruzicka 2004). Vitamin D showed a higher reduction in disease severity than the vehicle. No study reported the measure of variance.

2) Number of participants withdrawing due to adverse events

Three studies that compared vitamin D with its vehicle addressed the number of withdrawals due to adverse events for each group (Green 1994; Feldman 2013; Jemec 2008). Meta-analysis, including 820 participants, indicated no significant difference in the number of withdrawals due to adverse events between the vitamin D and the vehicle group (RR 1.43; 95% CI 0.72 to 2.83; Analysis 3.4). Reasons for withdrawal were pruritus, candidiasis, dermatitis and erythema at site of application or other unacceptable adverse events, which were not further specified by the study authors. Heterogeneity was not important (I^2 = 0%).

Secondary outcomes

1) Subjective reduction in severity of psoriasis

- Number of participants achieving 'clearance' according to the PGA (Analysis 3.5)

One study (N = 49 participants), which compared calcipotriol with its vehicle, reported this outcome (Green 1994). According to the participants' assessment, there was no difference between the treatment groups (RR 1.92; 95% CI 0.19 to 19.82). However, this finding was based on only three outcome events.

- Number of participants achieving 'response' according to the PGA (Analysis 3.6)

One study (N = 408 participants), which compared calcipotriene with its vehicle, addressed this outcome (Jemec 2008). The results indicated that calcipotriene was superior to the vehicle (RR 1.86; 95% CI 1.29 to 2.67; NNTB = 6; 95% CI 4 to 12).

2) Number of participants with at least one adverse event

Three studies, which compared vitamin D with the vehicle, measured the number of participants with at least one adverse event (Green 1994; Feldman 2013; Jemec 2008). Meta-analysis, which included 813 participants, showed no difference between participants treated with vitamin D or the vehicle (RR 1.12; 95% CI 0.92 to 1.36; Analysis 3.7). Heterogeneity was not important (I^2 = 0%). The most common local adverse events in both groups were irritation, burning sensation, pruritus or pain.

Additional studies

The study Ruzicka 2004, which included 273 participants, compared the efficacy and safety of a tacalcitol emulsion with its vehicle. The findings could not be sufficiently analysed since the sample size of each treatment group was not stated. According to the investigators' and participants' assessments, 21.1% and 25.0% of the tacalcitol group, respectively, achieved complete clearance. In contrast, 4.5% of the participants in the vehicle group achieved complete clearance, according to the evaluation of investigators and participants. There were no withdrawals due to adverse events. In both groups, 12 participants experienced adverse events, most frequently local irritation.

The conference poster abstract of Kiss 1996 reported two studies that investigated calcipotriene in different concentrations with the vehicle. One trial (N = 235 participants) assessed calcipotriene 0.005% solution, the other (N = 239 participants) assessed calcipotriene 0.0025% solution. For both studies the sample size of each treatment group was not stated and outcome data were not sufficiently addressed. The findings of both studies could therefore not be analysed. However, the authors reported that both calcipotriene solutions were superior to the vehicle and that safety profiles were similar. Common adverse events were burning, stinging and tingling.

4. Steroid plus vitamin D versus the vehicle

Two studies compared the two-compound combination of betamethasone dipropionate plus calcipotriene with the vehicle (Jemec 2008; Tyring 2010). Both study populations were ethnically different: Jemec mainly assessed Caucasians, while Tyring 2010 focused on participants of Hispanic and Afro-American origin.

Primary outcomes

1) Reduction in clinician-assessed severity

- Number of participants achieving 'clearance' according to the IGA (Analysis 4.1)

The results of Jemec 2008 showed that the two-compound combination was significantly superior to the vehicle for this outcome (N = 677 participants; RR 11.31; 95% CI 4.28 to 29.93; NNTB = 4; 95% CI 3 to 4).

- Number of participants achieving 'response' according to the IGA (Analysis 4.2)

Both studies reported this outcome and showed that the two-compound combination was superior to the vehicle. Heterogeneity between the trials was considerable (I^2 = 92%). This may be explained by the ethnically heterogenous study populations. In addition, the proportion of women in the study population was 35%

(Tyring 2010) versus 55% (Jemec 2008). However, the results of each individual study confirmed the superiority of the two-compound combination: Jemec 2008 (N = 677 participants; RR 4.55; 95% CI 3.02 to 6.85; NNTB = 2; 95% CI 2 to 3), Tyring 2010 (N = 177 participants; RR 1.78; 95% CI 1.21 to 2.60; NNTB = 4; 95% CI 3 to 7).

- Mean of the TSS (Analysis 4.3)

Jemec 2008 (N = 677 participants) addressed the reduction of disease severity by measuring the mean change of TSS from baseline. The two-compound combination showed a higher reduction in disease severity compared to the vehicle (70% versus 36%). This study did not report the measure of variance.

2) Number of participants withdrawing due to adverse events

Both studies addressed this outcome. Meta-analysis indicated that there was no difference between the groups (N = 843 participants; RR 0.48; 95% CI 0.08 to 2.83). Heterogeneity between the trials was moderate (I^2 = 40%). Jemec 2008 did not report the type of adverse events that led to withdrawal. According to Tyring 2010, three participants of the two-compound group withdrew due to adverse events. The reasons were cerebrovascular accident, nausea, depression and tremor. The authors did not believe that the adverse events were drug-related.

Secondary outcomes

1) Subjective reduction in severity of psoriasis

- Number of participants achieving 'response' according to the PGA (Analysis 4.5)

Both studies reported this outcome and showed that the two-compound combination was superior to the vehicle. The percentage of variability in effect estimates represented considerable heterogeneity (I^2 = 83%). This may be explained by the ethnically heterogenous study populations and the different percentage of female participants. Furthermore, more participants in the vehicle group of Tyring 2010 responded to treatment compared to the vehicle group of Jemec 2008 (0.36 versus 0.21). Subgroup analysis confirmed the superiority of the two-compound combination: Jemec 2008 (N = 677 participants; RR 3.33; 95% CI 2.38 to 4.66; NNTB = 3; 95% CI 2 to 3), Tyring 2010 (N = 177 participants; RR 1.74; 95% CI 1.14 to 2.67; NNTB = 4; 95% CI 3 to 11).

2) Number of participants with at least one adverse event

Two studies that compared the two-compound combination product of calcipotriene and betamethasone dipropionate with the vehicle reported the number of participants with at least one adverse event (Jemec 2008; Tyring 2010). Meta-analysis indicated no significant difference (RR 0.86; 95% CI 0.68 to 1.09; Analysis 4.6). Heterogeneity was not important (I^2 = 0%). The most common adverse events in both groups were skin irritation and pruritus. Others, such as a burning sensation, folliculitis and paraesthesia, mainly occurred in participants that applied the two-compound combination.

5. Steroid versus steroid: very high versus high potency

All studies within this comparison compared clobetasol propionate as a steroid of very high potency with betamethasone dipropionate as a steroid of high potency.

Primary outcomes

1) Reduction in clinician-assessed severity

- Number of participants achieving 'clearance' according to the IGA (Analysis 5.1)

Two studies reported this outcome. One had a within-patient design (Jarratt 1991), and the other was a parallel-group trial (Katz 1995). The latter, which assessed 197 participants, found no difference between clobetasol propionate and betamethasone dipropionate (RR 0.68; 95% CI 0.44 to 1.05). The study with a within-patient design confirmed this finding: in a study population of 55 participants, 27 cleared on the side treated with clobetasol propionate, while 28 cleared on the side treated with betamethasone dipropionate.

- Number of participants achieving 'response' according to the IGA (Analysis 5.2)

The results of the parallel-group trial showed no difference between clobetasol propionate and betamethasone dipropionate for this outcome (N = 197 participants; RR 0.95; 95% CI 0.79 to 1.14) (Katz 1995). The within-patient study confirmed this finding: in a study population of 55 participants, 51 responded on the side treated with clobetasol propionate, while 52 responded on the side treated with betamethasone dipropionate (Jarratt 1991).

- Mean of the TSS (Analysis 5.3)

Two studies reported the reduction of disease severity by measuring the mean change of TSS from the baseline. While Katz 1995 reported a higher reduction in TSS by betamethasone dipropionate, Lassus 1976 found clobetasol propionate to be superior. Measure of variance was not reported in either study. These contradictory results may be explained by clinical and methodological heterogeneity among the studies. It was unclear if Lassus 1976 randomised properly, since the authors simply stated that they performed a non-selective sequence generation. In addition, the sample size of Katz 1995 (N = 197 participants) was higher than that of Lassus 1976 (N = 40 participants).

2) Number of participants withdrawing due to adverse events

During both studies (N = 236 participants) that reported this outcome, none of the participants withdrew due to adverse events (Katz 1995; Lassus 1976).

Secondary outcomes

1) Number of participants with at least one adverse event

Two studies that compared clobetasol propionate with betamethasone dipropionate reported the number of participants with at least one adverse event for each group (Katz 1995; Lassus 1976). Meta-analysis that included 236 participants did not indicate any significant difference in the risk of adverse events between the treatment groups (RR 0.90; 95% CI 0.32 to 2.48; Analysis 5.4). Heterogeneity was not important (I^2 = 18%). However, Katz 1995 had a significantly higher incidence of adverse events, with a total number of 69 out of 196. The study reported different types of adverse effects, such as headache, tingling, stinging, numbness, cooling and dry feeling of the skin. Lassus 1976 only detected pruritus and folliculitis in two participants that applied betamethasone dipropionate.

6. Steroid versus steroid: high versus moderate potency

Primary outcomes

1) Reduction in clinician-assessed severity

- Number of participants achieving 'clearance' according to the IGA (Analysis 6.1)

Two studies, which included 190 participants, compared a steroid of high potency with the moderately potent hydrocortisone 17-butyrate 0.1% (De Cuyper 1995; Gip 1981). With regard to clearance, there was no significant difference between the treatment groups (RR 1.16; 95% CI 0.56 to 2.39). Heterogeneity between the trials was not important (I^2 = 35%).

- Number of participants achieving 'response' according to the IGA (Analysis 6.2)

One study assessed treatment response in 123 participants that either received fluocinonide (high potency) or desoximetasone 0.05% (moderate potency) (Willis 1986). There was no significant difference between the treatment groups (RR 0.94; 95% CI 0.61 to 1.44).

- Mean of the TSS (Analysis 6.3)

One study, which compared the highly potent steroid mometasone furoate with moderately potent triamcinolone acetonide 0.1% in 202 participants, addressed reduction of disease severity by measuring the mean change of TSS from baseline (Swinehart 1989). The mean reduction for mometasone furoate and triamcinolone acetonide 0.1% was 79% and 70%, respectively. The measure of variance was not reported.

Secondary outcomes

1) Number of participants with at least one adverse event

One study, which compared highly potent mometasone furoate with moderately potent triamcinolone acetonide 0.1%, reported this outcome for 202 participants (Swinehart 1989). There was no significant difference in the incidence of adverse events between participants treated with mometasone furoate and those receiving triamcinolone acetonide 0.01% (RR 1.12; 95% CI 0.39 to 3.22; Analysis 6.4). Another study (N = 40 participants) compared fluocinolone acetonide 0.025% with hydrocortisone 17-butyrate 0.1% (Gip 1981). No adverse event occurred.

Three studies reported the nature of adverse events that participants in both groups experienced (De Cuyper 1995; Swinehart 1989; Willis 1986). The most frequent were a local burning or stinging sensation, acne, folliculitis or pruritus.

Additional studies

The cross-over study of Housman 2002 (N = 25 participants) compared the efficacy and improvement in quality of life of betamethasone valerate 0.12% foam with fluocinolone acetonide 0.01% oil. Insufficient outcome data were provided and were therefore not eligible for analysis. However, the authors stated that the TSS between the groups was not significantly different before cross-over was performed.

7. Steroid versus steroid: both of high potency

Primary outcomes

1) Reduction in clinician-assessed severity

- Number of participants achieving 'clearance' according to the IGA (Analysis 7.1)

One study that included 203 participants compared mometasone furoate with betamethasone valerate 0.1% (Van der Ploeg 1989). Significantly more participants that were treated with mometasone furoate showed clearing of psoriatic scalp lesions (RR 1.84; 95% CI 1.09 to 3.11; NNTB = 8; 95% CI 4 to 41).

- Number of participants achieving 'response' according to the IGA (Analysis 7.2)

According to Van der Ploeg 1989, significantly more participants responded with mometasone furoate than with betamethasone valerate 0.1% (N = 203; RR 1.28; 95% CI 1.03 to 1.58; NNTB= 7; 95% CI 4 to 43).

- Mean score of the IGA

One study that assessed 59 participants reported IGA as a continuous outcome (Ellis 1989). The mean score according to a scale from 1 ('clear') to 4 ('fair improvement') for amcinonide 0.1% and fluocinonide was 2.25 and 2.2, respectively. Measure of variance was not reported.

- Mean of the TSS (Analysis 7.3)

Two studies addressed reduction of disease severity by measuring the mean change of TSS from baseline. Breneman 1992, which assessed 169 participants, found that TSS reduction between participants treated with fluocinonide was 84% and those treated with betamethasone dipropionate 85%. Van der Ploeg 1989, which included 203 participants, found a mean reduction of 85% and 70% for mometasone furoate and betamethasone dipropionate, respectively. Neither study reported any measure of variance.

2) Number of participants withdrawing due to adverse events

Two studies reported this outcome. Ellis 1989 compared fluocinonide with amcinonide 0.1% and Breneman 1992 assessed fluocinonide and betamethasone dipropionate. According to both trials, there was no significant difference between the treatment groups: Ellis 1989 (N = 59 participants; RR 0.34; 95% CI 0.01 to 8.13), Breneman 1992 (N = 167 participants; RR 1.01; 95% CI 0.06 to 15.91) (Analysis 7.4). However, there were only few withdrawals in both studies: in the study by Ellis 1989, one participant that applied fluocinonide withdrew because of eczematous dermatitis. In the other trial one participant in each group stopped the study medication (Breneman 1992). The one that received betamethasone dipropionate withdrew due to mild cutaneous burning, dryness and tightness. The other that applied fluocinonide experienced severe pruritus and generalised urticaria.

Secondary outcomes

1) Subjective reduction in severity of psoriasis

- Mean score of the PGA.

One study that included 59 participants addressed PGA as a continuous outcome (Ellis 1989). Mean scores for amcinonide 0.1% and fluocinonide, according to a scale from 1 ('clear') to 4 ('fair improvement') were 2.6 and 2.25, respectively. The measure of variance was not reported in the studies.

2) Number of participants with at least one adverse event

Ellis 1989 (N = 59 participants) and Breneman 1992 (N = 167 participants) also addressed the secondary safety outcome. In both trials fluocinonide caused a higher rate of adverse events compared to amcinonide 0.1% or betamethasone dipropionate. However, both findings were not significant: Ellis 1989 (RR 0.09; 95% CI 0.01 to 1.63); Breneman 1992 (RR 0.38; 95% CI 0.10 to 1.38) (Analysis 7.5).

All three studies that assessed steroids of high potency reported the nature of adverse events that occurred during the trial period (Breneman 1992; Ellis 1989; Van der Ploeg 1989). Common adverse events were a burning sensation, itching, acne and folliculitis at the site of application.

8. Steroid versus vitamin D

Primary outcomes

1) Reduction in clinician-assessed severity

- Number of participants achieving 'clearance' according to the IGA (Analysis 8.1)

Four studies, which compared a steroid with vitamin D, addressed this outcome for a total of 2180 participants (Jemec 2008; Klaber 1994; van de Kerkhof 2009; Yilmaz 2005). Meta-analysis showed that the steroid was significantly superior to vitamin D in clearing scalp psoriasis (RR 1.82; 95% CI 1.52 to 2.18; NNTB = 8; 95% CI 7 to 11). Heterogeneity was not important (I^2 = 0%). The quality of the evidence was moderate (Summary of findings for the main comparison).

Subgroup analysis with regard to the individual steroid agents emphasised the superiority of betamethasone valerate 1 mg/ml (RR 1.85; 95% CI 1.31 to 2.60; NNTB = 8; 95% CI 5 to 16; N = 474 participants; Klaber 1994), and betamethasone dipropionate (RR 1.81; 95% CI 1.46 to 2.24; NNTB = 8; 95% CI 6 to 12; N = 1676 participants; Jemec 2008; van de Kerkhof 2009) over vitamin D, but not of mometasone furoate (RR 2.00; 95% CI 0.43 to 9.32; N = 30 participants; Yilmaz 2005).

Sensitivity analysis

Sensitivity analysis with regard to ITT population, which included three studies (Jemec 2008; van de Kerkhof 2009; Yilmaz 2005), supported the findings of the meta-analysis (Table 2).

- Number of participants achieving 'response' according to the IGA (Analysis 8.2)

Three studies that compared a steroid with vitamin D addressed this outcome for a total of 1827 participants. Meta-analysis indicated that the steroid was superior to vitamin D (RR 2.09; 95% CI

1.80, 2.41; NNTB = 4; 95% CI 4 to 5). Heterogeneity among all three studies was not important (I^2 = 0%). The quality of the evidence was high (Summary of findings for the main comparison). Subgroup analysis in respect of the individual steroid reflected this finding: clobetasol propionate (N = 151 participants; RR 1.79; 95% CI 1.17, 2.74; NNTB = 5; 95% CI 3 to 15; Reygagne 2005), betamethasone dipropionate (N = 1676 participants; RR 2.13; 95% CI 1.82 to 2.50, NNTB = 4; 95% CI 4 to 5; Jemec 2008; van de Kerkhof 2009).

- Mean of the TSS (Analysis 8.3)

Five studies that compared steroids with vitamin D addressed the reduction of disease severity by measuring the mean change of TSS from baseline (Jemec 2008; Klaber 1994; Reygagne 2005; van de Kerkhof 2009; Yilmaz 2005). All studies reported a greater reduction in disease severity in participants treated with steroids compared to those receiving vitamin D. The measure of variance was not reported.

2) Number of participants withdrawing due to adverse events

Six studies that compared a steroid with vitamin D addressed the incidence of withdrawals due to adverse events. Meta-analysis of four studies (Klaber 1994; Jemec 2008; van de Kerkhof 2009; Reygagne 2005), which included a total of 2291 participants, indicated that participants in the steroid groups had a significantly lower risk of withdrawal due to adverse events compared to those in the vitamin D groups (RR 0.22; 95% CI 0.11 to 0.42; Analysis 8.4). There was no important heterogeneity among the studies (I^2 = 14%). There were no withdrawals due to adverse events in two studies (Köse 1997; Yilmaz 2005). In one trial (N = 43 participants) participants received either very potent clobetasol propionate in a hydrophilic leave-on or vitamin D as an occlusive lipophilic dressing (Köse 1997). The other study (N = 30 participants) compared mometasone furoate with vitamin D, both agents within a hydrophilic leave-on (Yilmaz 2005). The quality of the evidence was moderate (Summary of findings for the main comparison). No study reported the sort of adverse event that caused discontinuation of the study treatment.

Subgroup analysis with regard to the individual steroid agent reflected this finding for betamethasone valerate 1 mg/ml (N = 474 participants; RR 0.19; 95% CI 0.04 to 0.83; Klaber 1994), and betamethasone dipropionate (N = 1666 participants; RR 0.25; 95% CI 0.08 to 0.74; Jemec 2008; van de Kerkhof 2009). For the latter subgroup, the heterogeneity was substantial (I^2 = 62%). Our investigation for clinical and methodological heterogeneity did not reveal any reasonable explanation: disease severity at baseline, mean age, female proportion and study duration were similar in both studies. The two trials also monitored similar adverse events. However, neither reported the sort of adverse effect that actually caused withdrawal. In one trial (Reygagne 2005), which compared clobetasol propionate with vitamin D, the results indicated a tendency towards a higher incidence of withdrawals due to adverse events in the vitamin D group (RR 0.07; 95% CI 0.00 to 1.13).

Sensitivity analysis

Sensitivity analysis with regard to ITT population, which included three studies (Jemec 2008; Reygagne 2005; van de Kerkhof 2009), supported the finding of the meta-analysis (Table 2).

Secondary outcomes

1) Subjective reduction in severity of psoriasis

- Number of participants achieving 'clearance' according to the PGA (Analysis 8.5)

Two studies that compared a steroid with calcipotriol addressed this outcome for 504 participants (Klaber 1994; Yilmaz 2005). Meta-analysis of this patient-assessed outcome indicated a significantly higher efficacy of steroids in clearing scalp psoriasis compared to calcipotriol (RR 2.22; 95% CI 1.47 to 3.35; NNTB = 8; 95% CI 5 to 15). Heterogeneity was not important (I^2 = 0%).

Sensitivity analysis

Sensitivity analysis with regard to ITT population, which included one study (Yilmaz 2005), supported the finding of the meta-analysis (Table 2).

Both individual steroids were superior to the vitamin D analogue: betamethasone valerate 1 mg/ml (Klaber 1994) (N = 474 participants; RR 2.09; 95% CI 1.36 to 3.22; NNTB = 9; 95% CI 6 to 20) and mometasone furoate (Yilmaz 2005) (N = 30 participants; RR 4.00; 95% CI 1.01 to 15.81; NNTB = 3; 95% CI 2 to 11).

- Number of participants achieving 'response' according to the PGA (Analysis 8.6)

Three studies that compared a steroid with vitamin D addressed this outcome for a total of 1827 participants. Meta-analysis of this patient-assessed outcome indicated a significantly higher efficacy of steroids compared to vitamin D (RR 1.48; 95% CI 1.28 to 1.72; NNTB = 5; 95% CI 5 to 7). There was moderate heterogeneity among the studies (I^2 = 39%). The quality of evidence was moderate (Summary of findings for the main comparison).

The superiority of clobetasol propionate was significant (N = 151 participants; RR 1.54; 95% CI 1.02 to 2.34; NNTB = 6; 95% CI 4 to 73; Reygagne 2005). Two other studies that compared betamethasone dipropionate with vitamin D appeared to be substantially heterogenous (I^2 = 69%). Our investigation for clinical and methodological heterogeneity did not reveal any likely explanation: disease severity at baseline, mean age, female proportion and study duration were similar in both studies. However, in both

the steroid was significantly more effective than vitamin D: van de Kerkhof 2009 (RR 1.34; 95% CI 1.16 to 1.55; NNTB = 7; 95% CI 5 to 13); Jemec 2008 (RR 1.64; 95% CI 1.39 to 1.93; NNTB = 5; 95% CI 4 to 6).

2) Number of participants with at least one adverse event

Five studies that compared a steroid with vitamin D addressed the risk of adverse events for a total of 2320 participants. Data indicated no difference in the risk of adverse events between the treatment groups. There was considerable heterogeneity among the studies (I^2 = 84.6%). See Analysis 8.7.

Subgroup analysis showed that betamethasone valerate 1 mg/ml had a significantly lower risk of causing adverse events compared to calcipotriol (N = 474 participants; RR 0.37; 95% CI 0.25 to 0.53; Klaber 1994). Highly potent betamethasone dipropionate was also shown to have a significantly lower incidence of adverse events than vitamin D (N = 1652 participants; RR 0.82; 95 CI 0.70 to 0.97; Jemec 2008; van de Kerkhof 2009). There was moderate heterogeneity in this subgroup (I^2 = 47%). Köse 1997 did not find a significant difference in the risk of adverse events between participants treated with very high potency clobetasol propionate in a hydrophilic leave-on compared to those receiving calcipotriol as an occlusive lipophilic dressing (N = 43 participants; RR 0.48; 95% CI 0.10 to 2.34). Reygagne 2005 reported a significant lower risk of adverse events in participants treated with the very high potency clobetasol propionate as a shampoo compared to those treated with calcipotriol in a lipophilic vehicle (N = 151 participants; RR 0.34; 95% CI 0.16 to 0.72).

The most common adverse events that occurred with both therapies were local burning sensation and pruritus. Folliculitis and acne especially appeared in participants that applied steroids, whereas irritation and erythema were common local adverse events of vitamin D.

The studies that performed ITT analysis were substantially heterogeneous (I^2 = 77%) (Jemec 2008; Köse 1997; Reygagne 2005; van de Kerkhof 2009). It was therefore not feasible to undertake sensitivity analysis.

Additional studies

The study Duweb 2000 (N = 42 participants) compared betamethasone valerate 1% lotion and calcipotriol solution but was not eligible for analysis, because the outcome data within the publication were not consistent.

9. Steroid plus salicylic acid versus steroid

One study with 59 participants (Fredriksson 1976), which compared a combination product of betamethasone dipropionate and salicylic acid (2.0%) with betamethasone dipropionate alone, addressed the following outcomes:

Primary outcomes

1) Reduction in clinician-assessed severity

- Number of participants achieving 'clearance' according to the IGA (Analysis 9.1)

This outcome with the two-compound combination was not different to the corticosteroid as single preparation (N = 59 participants; RR 1.17; 95% CI 0.84 to 1.63).

- Number of participants achieving 'response' according to the IGA (Analysis 9.2)

This outcome with the two-compound combination was not different to the corticosteroid as single preparation (N = 59 participants; RR 1.08; 95% CI 0.91 to 1.29).

2) Number of participants withdrawing due to adverse events

None of the 59 participants withdrew because of adverse effects.

Secondary outcomes

1) Number of participants with at least one adverse event

None of the 59 participants experienced an adverse effect.

10. Steroid plus vitamin D versus steroid

Primary outcomes

1) Reduction in clinician-assessed severity

- Number of participants achieving 'clearance' according to the IGA (Analysis 10.1)

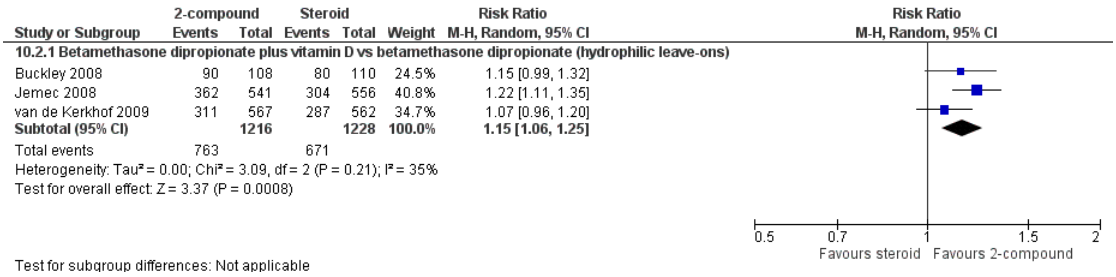
Four studies addressed this outcome for a total of 2474 participants (Buckley 2008; Jemec 2008; van de Kerkhof 2009; Yilmaz 2005). Meta-analysis showed that the two-compound combination is significantly more effective in clearing scalp psoriasis than the steroid alone. The superiority may not be clinically relevant (RR 1.22; 95% CI 1.08 to 1.36; NNTB = 17; 95% CI 11 to 41), which is reflected by a risk difference of 0.06 (95% CI 0.02 to 0.10). There was no important heterogeneity among the trials (I^2 = 0%). The quality of the evidence was moderate (Summary of findings 2).

Subgroup analysis, with respect to the individual steroid agent, showed a significantly higher efficacy of betamethasone dipropionate in combination with calcipotriol than alone (N = 2444 participants; RR 1.21; 95% CI 1.07 to 1.36; NNTB = 18; 95% CI 11 to 46; Buckley 2008; Jemec 2008; van de Kerkhof 2009). In

this subgroup, heterogeneity was not important (I^2 = 0%). One study that assessed mometasone furoate showed no significant difference between treatment groups (N = 30 participants; RR 2.00; 95% CI 0.76 to 5.24) (Yilmaz 2005).

- Number of participants achieving 'response' according to the IGA (Analysis 10.2; Figure 3)

Figure 3. Forest plot of comparison: 10 Steroid plus vitamin D vs steroid, outcome: 10.2 IGA: response.



Three studies, which compared the two-compound combination of betamethasone dipropionate and vitamin D with betamethasone dipropionate alone, addressed this outcome for a total of 2444 participants (Buckley 2008; Jemec 2008; van de Kerkhof 2009). Meta-analysis indicated that the two-compound combination was significantly more effective than betamethasone dipropionate alone (RR 1.15; 95% CI 1.06 to 1.25; NNTB = 13; 95% CI 9 to 24). The superiority may not be clinically relevant, as reflected by a risk difference of 0.09 (95% CI 0.03 to 0.15). There was moderate heterogeneity between the studies (I^2 = 35%). The quality of the evidence was moderate (Summary of findings 2).

- Mean of the TSS (Analysis 10.3)

Four studies addressed the reduction of disease severity by measuring the mean change of the TSS from baseline (Buckley 2008; Jemec 2008; van de Kerkhof 2009; Yilmaz 2005). All two-compound formulations showed a greater reduction of disease severity compared to the steroid alone. The measure of variance was not reported.

2) Number of participants withdrawing due to adverse events

Four studies reported this outcome. Meta-analysis of three trials (Buckley 2008; Jemec 2008; van de Kerkhof 2009), which included a total 2433 participants, indicated no significant differences between the treatment groups (RR 0.88; 95% CI 0.42 to 1.88; Analysis 10.4). The heterogeneity was not important among the studies (I^2 = 0%). None of the authors stated the type of adverse event that caused the withdrawal. The quality of the evidence was moderate (Summary of findings 2). In the other study (N = 30 participants) that assessed mometasone furoate as corticosteroid, no withdrawals occurred (Yilmaz 2005).

Secondary outcomes

1) Subjective reduction in severity of psoriasis

- Number of participants achieving 'clearance' according to the PGA (Analysis 10.5)

One study (N = 30 participants) addressed this outcome (Yilmaz 2005). Mometasone furoate tended to be more effective in combination with calcipotriol than as monotherapy. However, the superiority of the combination therapy was not significant (RR 1.50; 95% CI 0.88 to 2.57).

- Number of participants achieving 'response' according to the PGA (Analysis 10.6)

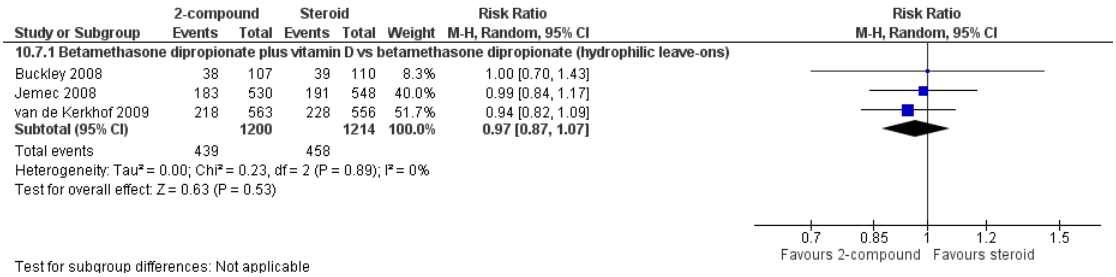
Two studies addressed this outcome for a total of 2226 participants (Jemec 2008; van de Kerkhof 2009). Meta-analysis indicated that betamethasone dipropionate in combination with vitamin D was significantly more effective than betamethasone dipropionate alone (RR 1.13; 95% CI 1.06 to 1.20; NNTB = 13; 95% CI 9 to 26), but the benefit may not be clinically relevant. Heterogeneity

was not important (I^2 = 0%) and the quality of the evidence was high (Summary of findings 2).

2) Number of participants with at least one adverse event

Three studies addressed this outcome for 2414 participants (Buckley 2008; Jemec 2008; van de Kerkhof 2009). Meta-analysis showed no significant differences in the risk of adverse events between participants treated with combination therapy and those treated with betamethasone dipropionate monotherapy (RR 0.97; 95% CI 0.87 to 1.07). There was no important heterogeneity among the three trials (I^2 = 0%). Common adverse events were pruritus, burning sensation, skin pain, folliculitis and alopecia. (See Analysis 10.7; Figure 4).

Figure 4. Forest plot of comparison: 10 Steroid plus vitamin D vs steroid, outcome: 10.7 Number of participants with at least one AE.



11. Steroid plus vitamin D versus vitamin D

Six studies compared the combination of a steroid and vitamin D with vitamin D monotherapy. Four assessed betamethasone dipropionate as the corticosteroid within the combination therapy (Jemec 2008; Kragballe 2009; Luger 2008; NCT01195831; van de Kerkhof 2009), and one used mometasone furoate (Yilmaz 2005).

Primary outcomes

1) Reduction in clinician-assessed severity

- Number of participants achieving 'clearance' according to the IGA (Analysis 11.1)

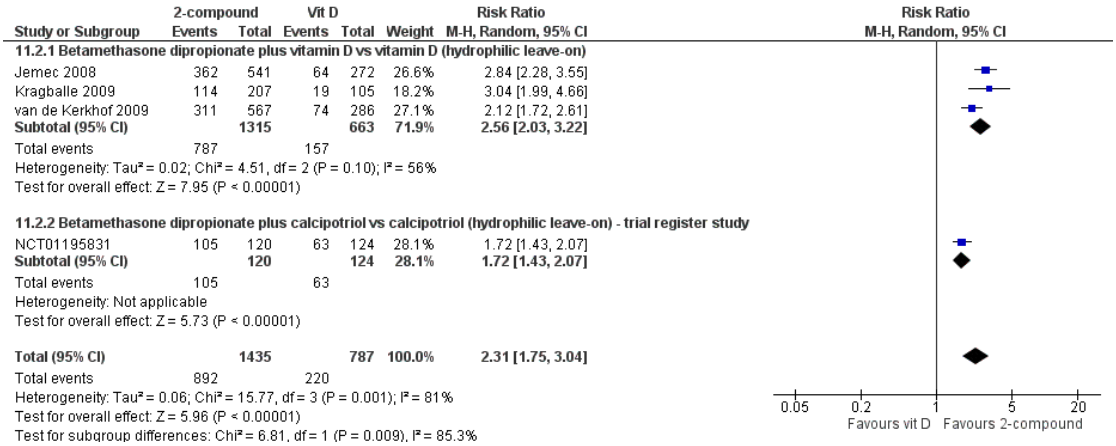
Four studies addressed this outcome for a total of 2008 participants (Jemec 2008; Kragballe 2009; van de Kerkhof 2009; Yilmaz 2005). Meta-analysis showed that the combination therapy was significantly superior to vitamin D monotherapy in clearing scalp psoriasis (RR 2.28; 95% CI 1.87 to 2.78; NNTB = 6; 95% CI 5 to 7). The quality of the evidence was high (Summary of findings 3). Heterogeneity was not important (I^2 = 0%). Subgroup analysis in respect of the type of steroid showed a significantly higher efficacy of both two-compound combinations compared to vitamin D: betamethasone dipropionate plus vitamin D (N = 1978 participants; RR 2.25; 95% CI 1.83 to 2.77; I^2 = 4%; NNTB = 5; 95% CI 5 to 7; three studies: Jemec 2008; Kragballe 2009; van de Kerkhof 2009); mometasone furoate plus calcipotriol (N = 30 participants; RR 4.00; 95% CI 1.01 to 15.81; NNTB = 3; 95% CI 2 to 11; one study: Yilmaz 2005).

Sensitivity analysis

Sensitivity analyses with regard to adequate allocation concealment, which included one study (Kragballe 2009), supported the findings of the meta-analysis of the four studies (Table 2).

- Number of participants achieving 'response' according to the IGA (Analysis 11.2; Figure 5)

Figure 5. Forest plot of comparison: 11 Steroid plus vitamin D vs vitamin D, outcome: 11.2 IGA: response.



Four studies reported this outcome for a total of 2222 participants (Jemec 2008; Kragballe 2009; NCT01195831; van de Kerkhof 2009). There was considerable heterogeneity between the studies (I^2 = 81%). However, all trials found that the two-compound combination was significantly more effective than vitamin D monotherapy (RR 2.31; 95% CI 1.75 to 3.04; NNTB = 3; 95% CI 3 to 4). Thus, heterogeneity may not be clinically important. Several aspects may have contributed to the high level of heterogeneity. We extracted the data from one study, NCT01195831, from the trial register, where not all relevant data (e.g. baseline disease severity) were sufficiently reported. The participants' mean age was more than 10 years younger, and the percentage of female participants was smaller compared to the other three trials (Jemec 2008; Kragballe 2009; van de Kerkhof 2009). The latter three were similar with regard to severity at baseline, mean age, percentage of female participants and study duration. Two studies only masked the investigator, and the application frequency varied between the treatment groups (once versus twice daily) (Kragballe 2009; NCT01195831). The other two trials had a double-blind design and participants applied the study medication once daily (Jemec 2008; van de Kerkhof 2009). The quality of the evidence was moderate (Summary of findings 3).

We created two subgroups that differed in terms of female proportion and mean age of the participants. One subgroup included the trial register study, the other contained the three published trials. The trial register study, which assessed a younger study population and had a lower female proportion, showed a tendency towards a smaller benefit of the two-compound combination over vitamin D. However, effect estimates of both subgroups emphasised the higher efficacy of the two-compound combination product.

Sensitivity analysis

Sensitivity analyses with regard to adequate allocation concealment, which included one study (Kragballe 2009), supported the findings of the meta-analysis of the four studies (Table 2).

- Mean of the TSS (Analysis 11.3)

Four studies addressed the reduction of disease severity by measuring the mean change of TSS from baseline (Jemec 2008; Kragballe 2009; van de Kerkhof 2009; Yilmaz 2005). All studies reported a greater reduction of TSS in participants treated with the two-compound combination. The measure of variance was not reported.

2) Improvement in quality of life

Ortonne 2009 reported quality of life measures for the study population (N = 312 participants) of Kragballe 2009. The investigators used two different tools: the SF-36v2 and the scalp-specific Skindex-16. For the latter, the authors reported a greater improvement from baseline in the two-compound group compared to the calcipotriol group (mean score at week 4: 28.1 (two-compound)

and 13.1 (calcipotriol)). The combination therapy also revealed a greater mean change compared to baseline, according to the SF-36v2: the physical component summary was +0.8 (two-compound) versus -0.8 (calcipotriol) and the mental component summary was +1.6 (two-compound) versus +0.6 (calcipotriol). The measures of variance were not reported.

3) Number of participants withdrawing due to adverse events

- Short-term (Analysis 11.4)

Four studies reported this outcome for short-term therapy (Jemec 2008; Kragballe 2009; NCT01195831; van de Kerkhof 2009). None of the study authors stated which specific adverse events caused withdrawal from the study. There was substantial heterogeneity among the four trials (I^2 = 85.2%). This may be due to the findings of NCT01195831, which did not show a significant difference in tolerability between the treatments (RR 2.07; 95% CI 0.39 to 11.07). Not all data from this trial were available, since we extracted the data from a trial register. Therefore, the baseline severity of the included participants remained unclear. Additionally, the study population differed from the other three trials in terms of mean age and percentage of female participants. We therefore performed a subgroup analysis that included only the three studies Jemec 2008, Kragballe 2009 and van de Kerkhof 2009. According to this subgroup, the two-compound combination led to significantly fewer withdrawals due to adverse events (RR 0.19; 95% CI 0.11 to 0.36). Heterogeneity of the three studies with 1970 participants was not important (I^2 = 0%) and the quality of the evidence was high (Summary of findings 3).
In another study (N = 30 participants) no withdrawals due to adverse events occurred (Yilmaz 2005).

Sensitivity analysis

Sensitivity analyses with regard to adequate allocation concealment, which included one study (Kragballe 2009), supported the findings of the meta-analysis of the three studies (Table 2).

- Long-term (Analysis 11.5)

One study addressed this outcome for the long-term therapy for a total of 869 participants (Luger 2008). After 12 months, significantly fewer participants treated with the combination therapy withdrew due to unacceptable adverse events (RR 0.21; 95% CI 0.10 to 0.42).

Secondary outcomes

1) Subjective reduction in severity of psoriasis

- Number of participants achieving 'clearance' according to the PGA (Analysis 11.6)

One study addressed this outcome (Yilmaz 2005). Mometasone furoate in combination with calcipotriol was significantly more effective in clearing scalp psoriasis than calcipotriol alone (N = 30 participants; RR 6.00; 95% CI 1.61 to 22.34; NNTB = 2; 95% CI 2 to 3).

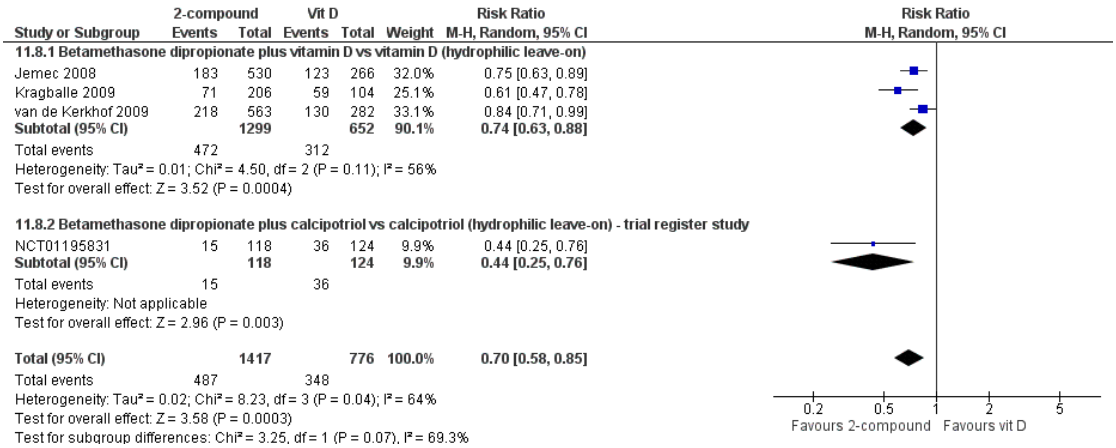
- Number of participants achieving 'response' according to the PGA (Analysis 11.7)

Four studies addressed this outcome for a total of 2222 participants (Jemec 2008; Kragballe 2009; NCT01195831; van de Kerkhof 2009). According to the participants, the two-compound combination was significantly more effective than vitamin D alone (RR 1.76; 95% CI 1.46 to 2.12; NNTB = 4; 95% CI 3 to 6). The quality of the evidence was moderate (Summary of findings 3). Heterogeneity among the trials was substantial (I^2 = 77%), but the direction of effect was consistent throughout the studies. Thus, the high level of heterogeneity may be clinically unimportant. However, there may be different aspects explaining the high degree of heterogeneity. We retrieved data (e.g. baseline severity) from the trial NCT01195831 from the trial register, where information was sparse. In addition, the participants' mean age was more than 10 years younger, and the percentage of female participants was smaller, compared to the other three trials. The latter were similar with regard to severity at baseline, mean age, percentage of female participants and study duration. Two studies only masked the investigator and the application frequency varied between the treatment groups (once versus twice daily) (Kragballe 2009; NCT01195831). The other two trials had a double-blind design and the treatment groups received the topical therapy once a day (Jemec 2008; van de Kerkhof 2009).
We created two subgroups that differed in terms of female proportion and mean age of the participants. One subgroup included the trial register study, the other contained the three published trials. The effect estimates of both subgroups emphasised the higher efficacy of the two-compound combination product compared to vitamin D alone.

2) Number of participants with at least one adverse event

- Short-term (Analysis 11.8; Figure 6)

Figure 6. Forest plot of comparison: 11 Steroid plus vitamin D vs vitamin D, outcome: 11.8 Number of participants with at least one AE (short term).



Four studies reported this outcome for a total of 2193 participants. Heterogeneity was substantial among the four studies (I^2 = 64%). However, all studies showed that significantly fewer adverse events occurred with the two-compound preparation (RR 0.70; 95% CI 0.58 to 0.85). Heterogeneity may therefore be clinically unimportant. The trial register study NCT01195831 was different to the other three trials in terms of mean age and percentage of female participants, and did not report baseline severity. We therefore created two subgroups with respect to mean age. One included the trial register study (NCT01195831; RR 0.44; 95% CI 0.25 to 0.76), the other the three published trials (Jemec 2008; Kragballe 2009; van de Kerkhof 2009). Within the latter, studies were moderately heterogenous (I^2 = 56%; RR 0.74; 95% CI 0.63 to 0.88). The effect estimates of both subgroups emphasised the lower risk of adverse events in the two-compound preparation. Common adverse events in both treatment groups were a burning sensation, pruritus, irritation, folliculitis and pain at the site of application.

Sensitivity analysis

Sensitivity analyses with regard to adequate allocation concealment, which included one study (Kragballe 2009), supported the findings of the meta-analysis of the four studies (Table 2).

- Long-term (Analysis 11.9)

One study reported this outcome for long-term therapy (Luger 2008). After 12 months, significantly fewer participants in the two-compound group experienced adverse events (N = 850 participants; RR 0.58; 95% CI 0.45 to 0.75). The main adverse events were pruritus, burning sensation, irritation, erythema and folliculitis. The authors emphasised that no participant reported skin atrophy. Yet, it was unclear if skin atrophy was actively measured.

12. Tar and dithranol

Primary outcomes

1) Reduction in clinician-assessed severity

- Number of participants achieving 'clearance' according to the IGA (Analysis 12.1)

Three trials that assessed therapies including tar or dithranol addressed this outcome. The study van de Kerkhof 2002 found no significant difference between calcipotriol and a tar/dithranol regimen (N = 88 participants; RR 5.71; 95% CI 0.28 to 115.70). Participants that used the tar/dithranol regimen could either apply the agents separately or in combination. The concentration of the dithranol and tar preparations ranged from 0.125% to 8% and 1% to 25%, respectively. He 2008 showed that significantly more participants achieved clearance of their scalp psoriasis with tacrolimus compared to those treated with pine tar (N = 40 participants; RR 2.75; 95% CI 1.05 to 7.20; NNTB = 3; 95% CI 2 to 15). According to Wright 1985, there was no difference in clearing scalp psoriasis between dithranol/urea or coal tar/salicylic acid (2%), both as lipophilic leave-on combination products (N = 38 participants; RR 1.11; 95% CI 0.90 to 1.38).

- Number of participants achieving 'response' according to the IGA (Analysis 12.2)

Two tar-controlled trials addressed this outcome. One found calcipotriol to be significantly more effective than a dithranol/tar preparation (N = 88 participants; RR 2.58; 95% CI 1.51 to 4.41; NNTB = 3; 95% CI 2 to 5) (van de Kerkhof 2002).

We obtained information on the second study, Barrett 2005, from a correspondence letter. It assessed the once daily use of a combination regimen of calcipotriol as solution together with a tar-based shampoo or a placebo shampoo. The number of participants was unknown. The authors reported that 55.9% of the participants who received the tar-based shampoo and calcipotriol solution, and 51.7% of the group that used placebo shampoo and calcipotriol solution responded within eight weeks of treatment. The difference was not significant, but the letter did not provide more statistical information (e.g. P value or measure of variance).

- Mean score of the IGA

One study that was only available as an abstract compared a shampoo containing urea, salicylic acid, glycolic acid, ichthyol pale and polidocanol to a coal tar shampoo (Regaña 2009). The investigators found that 27 participants treated with the multi-compound shampoo responded better than 10 other participants that applied a coal tar shampoo: mean 2.46 versus 1.80 (on a scale from 0 = poor to 3 = excellent efficacy). The measure of variance was not reported. Another study (N = 162 participants) compared participants treated with clobetasol propionate shampoo with those receiving a tar blend 1% shampoo (Griffiths 2006). On a scale from 0 = none to 5 = very severe scalp psoriasis, the clobetasol propionate group achieved a reduction from 3.4 to 1.9 (-44%) whereas the tar blend group decreased from 3.5 to a mean of 3.0 (-14%). The measure of variance was not reported.

According to Monk 1995, which included 34 participants, the IGA of participants treated with "ung cocois co" improved by 73% compared with 42% improvement in participants treated with coal tar. The study authors did not report any measure of variance.

- Mean of the TSS (Analysis 12.3)

Seven studies addressed the reduction of disease severity by measuring the mean change of TSS from baseline for a vast variety of treatments compared to tar preparations (Griffiths 2006; He 2008; Klaber 2000; Monk 1995; van de Kerkhof 2002; Wall 1999; Wright 1985). Tar, as a single preparation or in combination therapy, was less effective compared to each individual experimental treatment. Only coal tar in combination with calcipotriol showed a greater reduction (48%) than calcipotriol alone (41%) (Wall 1999). In this study, all participants applied calcipotriol twice daily within a hydrophilic leave-on and coal tar shampoo or a non-medicated shampoo twice a week, depending on the study group to which they had been randomised. The measure of variance was not reported.

We obtained data from another study by correspondence (Barrett 2005). It assessed the once-daily use of a combination regimen of calcipotriol as solution together with either a tar-based shampoo or a placebo shampoo. The number of participants was unknown. The authors reported that participants who received the tar-based shampoo with calcipotriol solution had a significantly greater reduction in the mean TSS than those who used placebo shampoo with calcipotriol solution (P value = 0.04). The letter did not report TSS data in more detail.

2) Quality of life

Data from Barrett 2005, which were obtained by letter, assessed the once-daily use of a combination regimen of calcipotriol as solution together with either a tar-based shampoo or a placebo shampoo. The number of participants was unknown. Quality of life improved in both treatment groups according to the Dermatology Life Quality Index (DLQI), but there was no significant difference between regimens. However, the correspondence did not report DLQI data in more detail.

3) Number of participants withdrawing due to adverse events

Four tar-controlled trials addressed this outcome (see Analysis 12.4). One that included 446 participants found a significantly lower risk of withdrawal in participants treated with a shampoo containing tar/coconut oil/salicylic acid (0.5%) compared to those treated with calcipotriol solution (RR 2.05; 95% CI 1.17 to 3.60) (Klaber 2000). Another study that included 88 participants found no significant difference in withdrawal rates between participants treated with calcipotriol and those treated with a tar/dithranol regimen (RR 1.15; 95% CI 0.07 to 17.75) (van de Kerkhof 2002). Also no significant difference was found in participants treated with clobetasol propionate and those who received a tar blend preparation (N = 162 participants; RR 1.03; 95% CI 0.04 to 24.87; Griffiths 2006), as well as in those who applied cocois or coal tar (N = 34 participants; RR 4.47; 95% CI 0.23 to 86.77; Monk 1995). In the latter study, two participants that applied cocois withdrew from the trial: one because of skin tightness, the other because of folliculitis. The other studies did not report which adverse event had led to withdrawal.

Secondary outcomes

1) Subjective reduction in severity of psoriasis

- Number of participants achieving 'clearance' according to the PGA (Analysis 12.5)

One tar-controlled trial that included 88 participants addressed PGA clearance rates (van de Kerkhof 2002). There was no significant difference in the clearance between calcipotriol and a tar/dithranol combination regimen, according to participants' assessment (RR 3.43; 95% CI 0.14 to 81.93).

- Number of participants achieving 'response' according to the PGA (Analysis 12.6)

One tar-controlled trial (N = 88 participants) addressed PGA response rates (van de Kerkhof 2002). There was a significantly higher efficacy seen in calcipotriol compared to a tar/dithranol combination regimen, according to the participants' assessment (RR 1.72; 95% CI 1.07 to 2.76; NNTB = 5; 95% CI 3 to 24).
We obtained information from another study in a letter (Barrett 2005). It assessed the once-daily use of a combination regimen containing calcipotriol as solution together with either a tar-based shampoo or a placebo shampoo. The number of participants was unknown. There was no significant difference between the treatment groups according to the patient-assessed overall response. The letter did not contain more detailed information.

- Mean score of the PGA

Three tar-controlled studies addressed PGA as a continuous outcome without providing any measure of variance. Griffiths 2006 reported mean scores at the end of treatment for participants receiving clobetasol propionate and those treated with tar blend (N = 162 participants). On a scale from 0 = no change to 5 = clear, the mean score of the clobetasol propionate group was 2.6 and the mean score of participants treated with tar blend was 0.9. In the study Monk 1995, which included 34 participants, PGA showed a mean improvement of 73% in participants treated with ung cocois co compared with 33% improvement in participants treated with coal tar. Another study compared a shampoo containing urea, salicylic acid, glycolic acid, ichthyol pale and polidocanol to a coal tar shampoo (Regaña 2009). The investigators found that 27 participants treated with the multi-compound shampoo responded better than 10 other participants who were applying a coal tar shampoo: mean 2.63 versus 1.70 (on a scale from 0 = poor to 3 = excellent efficacy).

2) Number of participants with at least one adverse event

Please see Analysis 12.7

Calcipotriol versus tar/dithranol combination regimen (hydro/lipophilic leave-on combination)

One study found no significant difference in the incidence of adverse events between the treatments (N = 87 participants; RR 1.54; 95% CI 0.95 to 2.51) (van de Kerkhof 2002). Both treatment groups experienced disorders of the skin and appendages, the central and peripheric nervous system and the respiratory system, among others.

Calcipotriol in a hydrophilic leave-on versus coal tar/coconut oil/salicylic acid (0.5%) in a rinse-off preparation

One study that included 445 participants found a significantly higher risk of adverse events for participants treated with calcipotriol solution compared to those treated with a shampoo containing tar/coconut oil/salicylic acid (0.5%) (RR 1.66; 95% CI 1.35 to 2.05) (Klaber 2000). Participants mainly experienced lesional and peri-lesional irritation.
In the study by Griffiths 2006, which included 162 participants, 11 participants in the clobetasol propionate group experienced burning, pruritus, tingling or unacceptable worsening of psoriasis, and one participant in the tar blend group reported mild tightness and burning on the scalp but the difference was not significant (RR 3.73; 95% CI 0.50 to 27.99).

Tacrolimus versus pine tar (lipophilic leave-ons)

One study found no significant difference in the risk of adverse events between the treatments (N = 40 participants; RR 0.33; 95% CI 0.04 to 2.94) (He 2008).

Dithranol/urea combination versus coal tar plus salicylic acid (2%) combination (lipophilic leave-ons)

One study found a significantly higher risk of adverse events for participants treated with a dithranol/urea combination compared to those treated with a coal tar/salicylic acid (2%) combination therapy (N = 38 participants; RR 16.67; 95% CI 2.44 to 113.85) (Wright 1985). Stinging and burning occurred with both treatments. However, only dithranol caused skin staining.

Cocois versus coal tar (lipophilic leave-on versus rinse-off)

One study that included 34 participants found no significant difference in the risk of adverse events between the treatments (RR 1.78; 95% CI 0.18 to 17.80) (Monk 1995). The participants experienced tightness of the skin, folliculitis or irritation.
Calcipotriol/tar versus calcipotriol/placebo (hydrophilic leave-on/shampoo versus hydrophilic leave-on/shampoo)
We obtained information from another study by letter (Barrett 2005). The authors assessed the once-daily use of a combination regimen containing calcipotriol in solution together with either tar-based shampoo or placebo shampoo. The number of participants was unknown. The authors stated that adverse events were similar and acceptable among the treatment groups, but did not provide more detailed information.

13. Steroid: vehicle comparisons

Primary outcomes

1) Reduction in clinician-assessed severity

- Number of participants achieving 'clearance' according to the IGA (Analysis 13.1)

Rinse-off versus rinse-off

In the study Josse 2005, the experimental group applied betamethasone dipropionate lotion plus RV3423A shampoo alternated with extra gentle shampoo every day. The control group received the combination of betamethasone dipropionate lotion plus extra gentle shampoo alone. There was no significant difference between the treatment regimens in clearing scalp psoriasis (N = 79 participants; RR 1.63; 95% CI 0.65 to 4.04).

- Number of participants achieving 'response' according to the IGA (Analysis 13.2)

Foam versus lotion

The study Franz 1999 found betamethasone valerate 0.1% to be significantly more effective within a foam preparation than within a lotion (N = 115 participants; RR 1.55; 95% CI 1.12 to 2.13; NNTB = 4; 95% CI 3 to 13).

Foam versus solution

The study Franz 2000 found the efficacy of clobetasol propionate to be no different whether in a foam preparation or a solution (N = 125 participants; RR 1.17; 95% CI 0.92 to 1.48).

- Mean of the TSS (Analysis 13.3)

Six studies addressed the reduction of disease severity by measuring the mean change of TSS from baseline. Clobetasol propionate as a hydrophilic leave-on vehicle led to a greater decrease in TSS than as a rinse-off shampoo (Andres 2006; Reygagne 2002). Foam was superior to a lotion or a solution, whether with clobetasol propionate or betamethasone valerate 0.1% as active agent (Franz 1999; Franz 2000). Betamethasone dipropionate with RV3423A shampoo and extra gentle shampoo in daily alternation led to a 10% higher reduction in TSS than with extra gentle shampoo alone (Josse 2005). The measurement of variance was not reported in any study.

One study that assessed 70 participants compared mometasone furoate within an emulsion (LAS41002) with the same steroid within a solution (Wilhelm 2013). The study could not be sufficiently analysed, because it was only available as an abstract and a power-point presentation. For instance, the number of participants per treatment group remained unclear. The authors stated that there was no significant difference between regimens (mean ratio 0.97; 95% CI 0.85 to 1.10).

2) Quality of life

Foam versus solution

Bergstrom 2003 compared the treatment efficacy and improvement in quality of life of 32 participants receiving either clobetasol propionate within foam or within a combination regimen of cream and solution. The findings could not be sufficiently analysed, because the sample size of each treatment group was not provided. The quality of life was measured by two scores, the EQ-5D and the DLQI. In the former score, clobetasol propionate in a foam preparation showed a stronger improvement in quality of life than when applied within a solution. However, the improvement according to the DLQI was not significantly different between the vehicles.

3) Number of participants withdrawing due to adverse events

Foam versus lotion

In the study Franz 1999, which assessed 115 participants, none of the participants, whether treated with betamethasone valerate 0.1% within a foam preparation or a lotion, withdrew due to adverse events.

Secondary outcomes

1) Subjective reduction in severity of psoriasis

- Number of participants achieving 'response' according to the PGA (Analysis 13.4)

Foam versus lotion

According to Franz 1999, betamethasone valerate 0.1% was significantly more effective as a foam preparation than as a lotion, according to the participants' assessment (N = 115 participants; RR 1.66; 95% CI 1.22 to 2.26; NNTB = 4; 95% CI 3 to 8).

Foam versus solution

Franz 2000 found the efficacy of clobetasol propionate to be no different whether in a foam preparation or a solution, according to the participants' assessment (N = 125 participants; RR 1.16; 95% CI 0.88 to 1.53).

2) Number of participants with at least one adverse event

Rinse-off versus hydrophilic leave-on

According to the study Reygagne 2002, the risk of adverse events did not significantly differ between participants treated with clobetasol propionate as a rinse-off vehicle and a hydrophilic leave-on (N = 124 participants; RR 1.94; 95% CI 95% CI 0.18 to 20.81). Most participants reported mild stinging or burning and one person who used clobetasol propionate shampoo experienced moderate folliculitis. See Analysis 13.5.

One study (N = 172 participants) compared two vehicles, foam and solution, that contained betamethasone valerate 0.1% as active agent (Franz 1999). Adverse events included a stinging and burning sensation, as well as pruritus on the scalp. Another study (N = 32 participants) stated that clobetasol propionate foam caused a minimal burning sensation after application, compared to clobetasol propionate solution (Bergstrom 2003). However, the authors of both studies did not report the number of participants from each group that experienced at least one adverse event.

Emulsion versus solution

One study that assessed 70 participants compared mometasone furoate within an emulsion (LAS41002) with mometasone furoate within a solution (Wilhem 2013). The study could not be sufficiently analysed, because it was only available as an abstract and power-point presentation. The authors stated that in both groups together a total of three serious and eight non-serious adverse events occurred. They were classified as unlikely to be related to the study drug.

14. Other steroid and salicylic acid containing comparisons

Primary outcomes

1) Reduction in clinician-assessed severity

- Number of participants achieving 'clearance' according to the IGA (Analysis 14.1)

Betamethasone dipropionate plus salicylic acid (2%) versus triamcinolone acetonide 0.2% plus salicylic acid (2%) (hydrophilic leave-ons)

One study found salicylic acid (2%) in a combination with betamethasone dipropionate to be significantly more effective than in a combination with triamcinolone acetonide 0.2% in clearing scalp psoriasis (N = 61 participants; RR 2.64; 95% CI 1.47 to 4.74; NNTB = 3; 95% CI 2 to 4) (Fredriksson 1976).

Betamethasone dipropionate plus salicylic acid versus betamethasone valerate 0.1% (hydrophilic leave-ons)

Two studies reported this outcome for a total of 115 participants treated either with betamethasone dipropionate in a combination with salicylic acid (2%) or with betamethasone valerate 0.1% as a single preparation (Curley 1990; Hillstrom 1978). Meta-analysis indicated no significant difference between the treatment groups (RR 1.40; 95% CI 0.59 to 3.32). Heterogeneity among the studies was not important (I^2 = 28%).

Betamethasone dipropionate plus salicylic acid versus clobetasol propionate (hydrophilic leave-ons)

One study compared the combination of betamethasone dipropionate and salicylic acid (2%) with clobetasol propionate monotherapy (Hillstrom 1982). Even though there was no statistically significant difference, the two-compound combination tended to lead more often to clearing of psoriatic scalp lesions than clobetasol propionate (N = 50 participants; RR 1.40; 95% CI 0.97 to 2.01).

Betamethasone dipropionate versus triamcinolone acetonide 0.2% plus salicylic acid (2%) (hydrophilic leave-ons)

Betamethasone dipropionate as monotherapy was significantly more effective than the two-compound combination in clearing psoriatic scalp lesions (N = 60 participants; RR 2.26; 955 CI 1.23 to 4.16; NNTB = 3; 95% CI 2 to 8; Fredriksson 1976).

- Number of participants achieving 'response' according to the IGA (Analysis 14.2)

Betamethasone dipropionate plus salicylic acid (2%) versus triamcinolone acetonide 0.2% plus salicylic acid (hydrophilic leave-ons)

The two-compound product including betamethasone dipropionate was significantly more effective (RR 1.61; 95% CI 1.17 to 2.20; N = 61 participants; NNTB = 3; 95% CI 2 to 7; Fredriksson 1976).

Betamethasone dipropionate versus triamcinolone acetonide 0.2% plus salicylic acid (2%) (hydrophilic leave-ons)

The two-compound combination was shown to be significantly less effective than betamethasone dipropionate as monotherapy (N = 60 participants; RR 1.48; 95% CI 1.06 to 2.07; NNTB = 4; 95% CI 3 to 15; Fredriksson 1976).

- Mean of the TSS

One study, which compared the combination of desoximetasone 0.25% and salicylic acid (1%) with betamethasone valerate 0.1%, addressed the reduction of disease severity by measuring the mean change of TSS from baseline (Hillstrom 1984). The two-compound combination showed a higher reduction of disease severity (78%) compared to betamethasone valerate 0.1% (56%). The measurement of variance was not reported.

2) Number of participants withdrawing due to adverse events

Betamethasone dipropionate plus salicylic acid versus clobetasol propionate (hydrophilic leave-ons)

There was no significant difference in the risk of withdrawal due to adverse events between the treatment groups (N = 50 participants; RR 0.33; 95% CI 0.01 to 7.81; Hillstrom 1982). The authors did not state the sort of adverse event that caused discontinuation of the therapy. See Analysis 14.3.

Betamethasone dipropionate plus salicylic acid versus triamcinolone acetonide 0.2% plus salicylic acid (hydrophilic leave-ons)

No participant withdrew because of adverse events (Fredriksson 1976).

Betamethasone dipropionate versus triamcinolone acetonide 0.2% plus salicylic acid (hydrophilic leave-ons)

No participant withdrew because of adverse events (Fredriksson 1976).

Secondary outcomes

1) Number of participants with at least one adverse event

Steroid plus salicylic acid versus a different steroid alone

Four studies that compared a steroid and salicylic acid (2%) combination with a steroid alone addressed this outcome for a total of 258 participants.

One study provided data for two different two-compound combinations compared with a steroid (Fredriksson 1976). The steroids assessed in each individual comparison varied from study to study. In two trials in which adverse events occurred, there was no significant difference whether participants were treated with the two-compound combination or with a steroid alone: Hillstrom 1978 (RR 0.50; 95% CI 0.05 to 5.29); Hillstrom 1982 (RR 0.50; 95% CI 0.05 to 5.17). Common adverse events were pruritus, burning and itching. See Analysis 14.4.

In the other two comparisons, no adverse events occurred (Fredriksson 1976; Hillstrom 1984).

15. Antifungals versus vehicle

One study that included 40 participants compared ciclopirox olamine with its vehicle (Shuttleworth 1998).

Primary outcomes

1) Reduction in clinician-assessed severity

- Mean score of the IGA (Analysis 15.1)

There was no significant difference between ciclopirox olamine and its vehicle for this outcome (MD -0.19; 95% CI -2.00 to 1.62).

2) Number of participants withdrawing due to adverse events

There was no significant difference between ciclopirox olamine and the vehicle for this outcome (RR 0.08; 95% CI 0.00 to 1.55). Both participants that discontinued treatment had received the vehicle and experienced severe pruritus and increased scaling. See Analysis 15.2.

Secondary outcomes

1) Subjective reduction in severity of psoriasis

- Mean score of the PGA (Analysis 15.3)

There was no significant difference between ciclopirox olamine and the vehicle for this participant-assessed outcome (MD 0.11; 95% CI -0.52 to 0.74).

2) Number of participants with at least one adverse event

There was no significant difference between ciclopirox olamine and the vehicle for this outcome (RR 1.33; 95% CI 0.32 to 5.44). The authors believed that most adverse events were not treatment-related. However, one participant that applied ciclopirox suffered from psoriasis spreading to his forehead and cheeks, while another that received the vehicle reported severe pruritus. See Analysis 15.4.

ADDITIONAL SUMMARY OF FINDINGS *[Explanation]*

Steroid plus vitamin D compared to steroid for scalp psoriasis

Patient or population: scalp psoriasis
Intervention: steroid plus vitamin D
Comparison: steroid

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Quality of the evidence (GRADE)	Comments
	Risk with steroid	Risk with steroid plus vitamin D				
Number of participants achieving 'clearance' by IGA	Study population 287 per 1000	350 per 1000 (310 to 391)	RR 1.22 (1.08 to 1.36)	2474 (4 RCTs)	⊕⊕⊕◯ MODERATE [1]	-
Number of participants achieving 'response' by IGA	Study population 546 per 1000	628 per 1000 (579 to 683)	RR 1.15 (1.06 to 1.25)	2444 (3 RCTs)	⊕⊕⊕◯ MODERATE [2]	-
Quality of life	Study population 0 per 1000	0 per 1000 (0 to 0)	Not estimable	(0 studies)	-	No study addressed this outcome
Number of participants withdrawing due to adverse events (AE)	Study population		RR 0.88 (0.42 to 1.88)	2433 (3 RCTs)	⊕⊕⊕◯ MODERATE [3]	No study reported the sort of AE that caused withdrawal. In one small study with high risk of bias (Yilmaz 2005, N = 30 participants) no withdrawals occurred.

	12 per 1000	11 per 1000 (5 to 23)				
Number of participants achieving 'response' by PGA	Study population 613 per 1000	692 per 1000 (649 to 735)	RR 1.13 (1.06 to 1.20)	2226 (2 RCTs)	⊕⊕⊕⊕ HIGH	-

*The risk in the intervention group (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).

AE: adverse event; **CI:** confidence interval; **IGA:** investigator's global assessment; **OR:** odds ratio; **PGA:** patient global assessment; **RCT:** randomised controlled trial; **RR:** risk ratio

GRADE Working Group grades of evidence
High quality: We are very confident that the true effect lies close to that of the estimate of the effect
Moderate quality: 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 quality: Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect
Very low quality: We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect

[1] Downgraded by one level for imprecision because CI crosses line of minimal important difference (MID) threshold: statistically significant difference of uncertain clinical importance.
[2] Downgraded by one level for inconsistency due to moderate heterogeneity (I^2 = 35%).
[3] Downgraded by one level for imprecision because CI crosses line of MID threshold: uncertain whether there is any difference.

Steroid plus vitamin D compared to vitamin D for scalp psoriasis

Patient or population: scalp psoriasis
Intervention: steroid plus vitamin D
Comparison: vitamin D

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Quality of the evidence (GRADE)	Comments
	Risk with vitamin D	Risk with steroid plus vitamin D				
Number of participants achieving 'clearance' by IGA	Study population 145 per 1000	330 per 1000 (270 to 402)	RR 2.28 (1.87 to 2.78)	2008 (4 RCTs)	⊕⊕⊕⊕ HIGH	-
Number of participants achieving 'response' by IGA	Study population 280 per 1000	646 per 1000 (489 to 850)	RR 2.31 (1.75 to 3.04)	2222 (4 RCTs)	⊕⊕⊕◯ MODERATE [1]	-
Quality of life	Study population 0 per 1000	0 per 1000 (0 to 0)	Not estimable	(0 studies)	-	Only one study (Ortonne 2009) addressed this outcome, but did not provide sufficient information to allow assessment of the quality of evidence
Number of participants withdrawing due to adverse events	Study population		RR 0.19 (0.11 to 0.36)	1970 (3 RCTs)	⊕⊕⊕⊕ HIGH	No study reported the sort of AE that caused withdrawal. In one small study with high risk of bias (Yilmaz 2005, N = 30 participants) no withdrawals occurred.

	56 per 1000	11 per 1000 (6 to 20)				
Number of participants achieving 'response' by PGA	Study population 427 per 1000	751 per 1000 (623 to 905)	RR 1.76 (1.46 to 2.12)	2222 (4 RCTs)	⊕⊕⊕◯ MODERATE [2]	-

***The risk in the intervention group** (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).

AE: adverse event; **CI**: confidence interval; **IGA**: investigator's global assessment; **OR**: odds ratio; **PGA**: patient global assessment; **RCT**: randomised controlled trial; **RR**: risk ratio

GRADE Working Group grades of evidence
High quality: We are very confident that the true effect lies close to that of the estimate of the effect
Moderate quality: 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 quality: Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect
Very low quality: We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect

[1] Downgraded by one level for inconsistency due to substantial heterogeneity (I^2 = 81%), may be due to different application frequency in studies (once versus twice daily).
[2] Downgraded by one level for inconsistency due to substantial heterogeneity (I^2 = 77%), may be due to different application frequency in studies (once versus twice daily).

DISCUSSION

Summary of main results

This review summarises the evidence of the efficacy and safety of topical treatments for scalp psoriasis. We grouped all 59 included studies into 15 main comparisons of which four were vehicle-controlled. The other 11 head-to-head comparisons investigated either single preparations (e.g. steroid versus vitamin D) or analysed combination therapies (e.g. calcipotriol versus coal tar or coconut oil or salicylic acid). In particular, we also included comparisons that included corticosteroids of similar or different potency. Furthermore, we included one study that evaluated once versus twice-daily use of corticosteroids and studies that assessed corticosteroids in different vehicles. Thirty studies (51%) were either conducted or sponsored by the manufacturer of the study medication. However, not all studies stated their source of financial support.

Efficacy

The evaluation of efficacy is based on outcomes that compared the number of participants where psoriatic scalp lesions responded or cleared due to the individual therapy. Efficacy was assessed either by the investigator or the participant and sometimes by both. However, investigators and participants rated the efficacy of the individual treatments similarly.

Vehicle-controlled comparisons

Based on the results of the studies, corticosteroids, vitamin D and their combination product were all more effective than their vehicle in clearing and reducing scalp psoriasis. In a small trial, ciclopirox olamine was not different to the vehicle in reducing scalp psoriasis.

Head-to-head comparisons

Corticosteroids of high and very high potency were more effective than vitamin D in clearing and reducing scalp psoriasis (Summary of findings for the main comparison). The combination of a corticosteroid with vitamin D was significantly more effective than corticosteroids as monotherapy, but the additional benefit might not be clinically relevant (Summary of findings 2). This is based on a total risk difference of 0.06 (95% confidence interval (CI) 0.02 to 0.10; 'Number of participants achieving clearance by IGA'). Indirect comparison of both treatments also indicated that topical corticosteroids were more successful in the number of participants achieving 'clearance' when compared to the vehicle than the two-compound combination compared to the vehicle (risk ratio (RR) 14.58; 95% CI 7.28 to 29.17 versus RR 11.31; 95% CI 4.28 to 29.93). The two-compound combination was superior to vitamin D alone (Summary of findings 3). We graded the quality of evidence for the direct comparisons as moderate to high, depending on the efficacy outcome.

In a single study, there was no difference in participants achieving 'clearance' between the high potency steroid betamethasone dipropionate and the very highly potent clobetasol propionate. A within-patient study had a similar finding. Within the class of steroids of high potency, mometasone furoate was more effective than betamethasone valerate 0.1%. The twice-daily use of betamethasone valerate 0.12% was better than once-daily by the mean Investigator Global Assessment (IGA) but not the mean Participant Global Assessment (PGA) score, however this was not a clinically important benefit. All corticosteroid head-to-head comparisons were based on the results of single studies and should be interpreted with caution. Moreover, there were poor data on vehicle comparisons. Based on single studies, foam was shown to be superior to lotion, but not to solution.

The addition of salicylic acid to betamethasone dipropionate did not show significant benefit compared to betamethasone valerate alone or clobetasol propionate alone. This finding should be interpreted carefully, since the role of salicylic acid in reducing the scaling may not be sufficiently captured by the IGA.

In one study, whether betamethasone dipropionate was combined with salicylic acid or not participants achieved 'clearance' better than with triamcinolone acetonide when that was combined with salicylic acid.

Among tar-controlled comparisons, more participants achieved a 'response' as determined by the IGA with calcipotriol than with a tar/dithranol regimen and tacrolimus showed better clearance than pine tar. These results were based on poor data and are therefore linked to substantial uncertainty. There are further treatments, such as clobetasol propionate, calcipotriol, cocois or a dithranol/urea combination that may be superior to tar as a single agent or in combination therapy. However, due to poor reporting of measures of variance, it was not possible to determine any statistically significant superiority of treatment efficacy.

Safety

We reported all safety evaluations with regard to the number of participants with at least one adverse event and the withdrawal rate due to adverse events. It should be considered that the particular risk of specific adverse events (e.g. skin irritation, skin atrophy) for individual treatments was not evaluated in this review. Most adverse events were limited to the site of application. Systemic adverse events were significantly rare and most likely not drug-related, as judged by the authors of the studies.

Vehicle-controlled comparisons

Corticosteroids, vitamin D and their combination product did not differ from the vehicle in the risk of adverse events, such as burning sensation, skin irritation or folliculitis. Study authors poorly reported the nature of adverse events that caused withdrawal. However, it appeared that most participants stopped treatment because of unacceptable local adverse events, such as a burning sensation.

The risk of withdrawal due to adverse events did not differ between corticosteroids, vitamin D or their combination product and the vehicle. In fact, one study even detected that betamethasone dipropionate was associated with a lower risk of adverse events leading to withdrawal compared to the vehicle (Jemec 2008). This was shown for both betamethasone dipropionate as a single preparation and in combination with vitamin D. The authors distinguished between withdrawals due to unacceptable adverse events and those due to unacceptable treatment efficacy. However, this finding may be explained by the assumption that participants, who applied the vehicle, withdrew because of dissatisfaction with a lack of relief from distressing symptoms (e.g. pruritus or pain). The distressing symptoms may have been misinterpreted as adverse events. In reality they might have been due to the scalp psoriasis itself and were not adequately relieved by the vehicle.

Head-to-head comparisons

There was moderate quality evidence that corticosteroids led to fewer withdrawals due to adverse events than vitamin D (Summary of findings for the main comparison). The number of participants with adverse events was also lower for steroids compared to vitamin D. Moderate quality evidence also indicated that the two-compound combination did not differ from corticosteroid monotherapy in the number of withdrawals due to adverse events (Summary of findings 2); nor was there a difference in the number of participants with adverse events. High quality evidence indicated that significantly fewer withdrawals due to adverse events were caused by the two-compound combination compared to vitamin D alone (Summary of findings 3). Compared to vitamin D the two-compound combination also caused fewer local adverse events such as skin irritation, for short- and long-term therapy. The better safety profile of the two-compound combination compared to vitamin D was also seen in one trial that assessed long-term treatment (Luger 2008).

Betamethasone valerate 0.1% and dipropionate were better tolerated than calcipotriol in the same vehicle. In contrast, calcipotriol as a hydrophilic leave-on showed a lower risk of causing adverse events than clobetasol propionate as shampoo. However, clobetasol propionate in a hydrophilic vehicle did not differ in the risk of unpleasant side effects compared to calcipotriol when used in an occlusive dressing. The latter two findings were based on poor data and should be interpreted with caution.

Due to poor data we could not make a clear statement about whether there was a difference between individual steroids or if specific vehicles influenced their risk of causing adverse events. Steroid-induced skin atrophy or telangiectasia were remarkably rare. Yet, it is unclear if these particular adverse events did not actually occur or if they were simply not monitored by most studies. Comparisons between individual corticosteroids of moderate, high and very high potency revealed that they did not differ significantly in their low risk of causing adverse events, such as a burning sensation, folliculitis or pruritus on the scalp. However, one of two studies that compared clobetasol propionate (very high potency) with betamethasone dipropionate (high potency), detected remarkably more adverse events in both treatment groups (Katz 1995). This study may have recorded different sorts of adverse events and in a more rigorous manner. According to one study, individual vehicle formulations did not have an impact on the safety properties of clobetasol propionate (Reygagne 2002).

It was not possible to assess the safety features of salicylic acid in combination with corticosteroids, since none of the included studies addressed data that matched the safety outcomes of this review. Tar in combination with salicylic acid, however, caused significantly fewer adverse events (e.g. burning sensation) and withdrawal rates due to adverse events, than calcipotriol monotherapy. It was also shown to be safer than a urea/dithranol regimen, which frequently caused skin staining. However, all other tar preparations did not have different safety profiles to cocois, tacrolimus, calcipotriol or clobetasol propionate.

Quality of life

There was a considerable lack of trials that investigated the quality of life. However, there were two recent trials that addressed this outcome. One found that participants that applied clobetasol propionate experienced a better improvement in quality of life than those treated with the vehicle (Sofen 2011). The other trial revealed that the combination of betamethasone dipropionate and vitamin D was associated with a greater improvement in quality of life compared to calcipotriol monotherapy (Kragballe 2009). Both findings seem reliable, however we did not assess the quality of evidence, because the comparison of clobetasol propionate versus vehicle was not of major interest and the Kragballe 2009 study (see Ortonne 2009) did not provide enough data to calculate an estimate of effect. We could not analyse the results of two other trials in an appropriate manner (Barrett 2005; Bergstrom 2003), because they did not report relevant data either; one concluded that clobetasol propionate within foam improved the quality of life better than clobetasol propionate as a combination programme of cream and solution. The other found no difference in quality of life for the vitamin D solution, whether combined with a tar-based shampoo or vehicle shampoo. These findings should be interpreted with caution.

Overall completeness and applicability of evidence

We aimed to include all topical treatment and found a wide variety of different interventions.

We identified multicentre trials that included large study populations for the interventions that are most established such as topical corticosteroids, vitamin D and their combination therapy. The evidence of the efficacy and safety of these therapies supports the

current European, American and Asian consensus recommendations (Chan 2009; Frez 2014; Ortonne 2009).

A great part of the included interventions were evaluated in single studies, such as tar-controlled interventions, vehicle comparisons, steroids of varying application frequency and salicylic acid in combination with corticosteroids. For these comparisons, the assessment of consistency of results across the studies was limited or not feasible. This may be a considerable threat to external validity.

One reason why there were poor data on 'older' treatments, such as tar preparations, may be that randomised controlled trials were not yet established at that time as the gold standard. Studies that assessed those treatments may simply not be of an adequate design to meet our inclusion criteria. Moreover, the objective of recent studies might have been focused on the comparison of those interventions that have already been shown to be effective and safe.

Only one trial with a duration of 12 months was feasible for long-term safety analysis (Luger 2008). All other included trials were carried out for less than six months. Therefore efficacy and safety analyses are mainly restricted to short-term treatments.

None of the identified studies provided data on the time to relapse as it was defined in the protocol for this review. We therefore did not analyse this outcome.

Only four studies reported the outcome 'quality of life' but it was not in a form in which we were able to evaluate the quality of evidence.

Quality of the evidence

Limitations in study design and implementation

Our 'Risk of bias' assessment showed that limitations in study design and implementation varied considerably among the included studies (Risk of bias in included studies). Only 11 studies clearly addressed the randomisation method and only four study authors stated how they concealed the allocation, which represents a potential risk of selection bias. More than half of the studies had a double-blind design. Of the 14 single-blind studies, only the investigator was blinded in 12 as the study medications varied in application frequency or were applied in different vehicles, however in two studies it was not clear who was blinded. Given that most of the 10 non-blinded trials assessed interventions of minor clinical interest, the risk of performance and detection bias for comparisons of major interest may not be unduly affected. We rated one-third of the trials to be at high or unclear risk of attrition bias.

Indirectness of the evidence

The studies included in this review assessed representative populations, though only a few studies included children (less than 18 years). However, psoriasis in children is a rather rare condition. In this review, we included vehicle- and active-controlled trials, which allowed a clear judgement on comparative efficacy for most interventions.

Inconsistency of the results

In only three instances we downgraded the quality of the evidence because of heterogeneity among the trial results. However, in one case heterogeneity was only moderate and thus we did not seek to identify a plausible explanation. Study results from the four trials that assessed 'IGA response' for the comparison 'Steroid plus vitamin D versus vitamin D' were substantially heterogenous (Jemec 2008; Kragballe 2009; NCT01195831; van de Kerkhof 2009). The study populations differed in mean age and percentage of female participants. Two of the studies only masked the outcome assessor (Jemec 2008; Kragballe 2009), and only two had a double-blind design (Jemec 2008; van de Kerkhof 2009). However, we had serious doubts that these aspects alone were responsible for the variability of results.

Imprecision of the results

We lowered the quality of evidence in only two instances because of serious imprecision. In both cases the confidence interval crossed the minimal important difference (MID) thresholds.

Publication bias

The assessment of publication bias was not feasible, as none of the comparisons included more than 10 studies. For this reason we did not create any funnel plots, since this would not give any meaningful information.

Sensitivity analysis

In one case, sensitivity analysis with respect to allocation concealment did not confirm that steroids caused fewer withdrawals due to adverse events than the vehicle. However, the value of this finding may be questionable for several reasons: only one trial was eligible for sensitivity analysis, because it reported an adequate concealment of allocation (Sofen 2011); the fact that the other studies did not report any allocation concealment does not imply that they did not perform it. Moreover, sensitivity analysis with regard to the intention-to-treat (ITT) population supported the finding that steroids cause fewer withdrawals due to adverse events than the vehicle. It is unlikely that adequate allocation concealment in this one study would have had sufficient impact on this outcome. The contradictory finding may be explained by the small sample (N = 81) in the study by Sofen 2011, although the other study that used clobetasol, Olsen 1991, had a similar finding to Sofen 2011.

Potential biases in the review process

We aimed to minimise potential biases during our search for relevant trials and data extraction. Therefore, two authors independently screened abstracts, evaluated full texts for eligibility, extracted data and screened for ongoing trials. Both authors also searched conferences for relevant poster abstracts and checked the reference lists of included studies for further potentially relevant randomised controlled trials (RCTs). Those studies where we were unable to obtain the full text or where our requests to the study authors or sponsors for unpublished data were unsuccessful are listed in 'Characteristics of studies awaiting classification'. The fact that 14 studies have not yet been incorporated may be a source of potential bias.

Since almost none of the publications clearly stated measures of variance, most available continuous outcomes, particularly total severity scores (TSS), were inaccurate and therefore not feasible for meta-analysis. Even though we calculated the mean percentage TSS change from baseline, an interpretation of these findings remains strongly limited. Furthermore, most TSS data were calculated from graphs, which additionally implies a certain degree of inaccuracy.

Agreements and disagreements with other studies or reviews

As part of a Cochrane review on topical treatments for chronic plaque psoriasis, Mason 2013 investigated treatments for scalp psoriasis with the focus on vehicle-controlled trials and active comparisons with vitamin D preparations. With regard to these treatments, our results concerning efficacy and safety correspond closely. Contrary to Mason 2013, we did not make restrictions with regard to other topical treatments. Our findings concerning topical corticosteroids, vitamin D analogues, tar preparations and application frequency are in accordance with the results of another systematic review (Samarasekera 2013). However, these authors did not find the marginal benefit of the combination product of a potent corticosteroid with calcipotriol compared to corticosteroid as monotherapy. This may be for two reasons: in their meta-analysis of IGA response, the authors did not include the trial Buckley 2008, which found a small benefit of the two-compound combination with respect to IGA and PGA; and Samarasekera 2013 did not meta-analyse data from the participants' assessment of treatment efficacy. Both aspects would have emphasised the small but statistically significant benefit of the combination product.

Shokeen 2014 reviewed the efficacy of topical keratolytic agents and their adjunctive benefit in combination with topical corticosteroids. In concordance with our findings, the authors reported that steroids were highly effective in clearing scalp psoriasis. However, in contrast to our results, Shokeen 2014 concluded that salicylic acid in a single combination product with a corticosteroid may be of additional benefit. This conclusion was based on the results of studies of which some were neither randomised nor controlled. Only one RCT was identified by the authors that evaluated the same corticosteroid as part of the combination product (experimental group) and as monotherapy (control group) (Elie 1983). However, this RCT included participants with different erythematous squamous dermatoses and did not provide results for participants with scalp psoriasis separately. For this reason, we excluded this trial. The only RCT that we could identify that assessed the role of salicylic acid combined with corticosteroids did not indicate a significant additional benefit of the keratolytic agent (Fredriksson 1976). However, the keratolytic effect of salicylic acid may not have been sufficiently assessed by our pre-specified outcomes.

AUTHORS' CONCLUSIONS

Implications for practice

Corticosteroids of high or very high potency are more effective than vitamin D. The combination product of a corticosteroid and vitamin D is of small benefit over corticosteroid monotherapy. The combination product is superior to vitamin D alone. Corticosteroids, vitamin D and their combination product are more effective than the vehicle. Corticosteroids of moderate, high and very high potency are similarly effective. There is not enough evidence to allow a final conclusion as to whether salicylic acid is of additional benefit in combination with corticosteroids. Few and mostly unreliable data suggest that the efficacy of tar or dithranol preparations is limited. There might not be a difference whether corticosteroids are used once or twice daily.

Adverse events were mostly limited to the site of application and included burning sensations, pruritus, skin irritation or folliculitis, among others. For short-term treatment, the combination of corticosteroids with vitamin D and the corticosteroid monotherapy do not differ in their risk of causing adverse events and both were better tolerated than vitamin D alone. For long-term therapy, the two-compound combination caused fewer adverse events and withdrawals due to adverse events than vitamin D monotherapy. Limited evidence indicates no difference in the risk of adverse effects between corticosteroids of moderate, high or very high potency. Tar and dithranol preparations appear to be well tolerated, but the evidence is poor. The tolerability of salicylic acid cannot be analysed due to the lack of relevant data.

Besides some trials on corticosteroids, there are no suitable and reliable data to determine the additional benefit of specific vehicles on the efficacy and safety of active ingredients.

Given the similar safety profile and only slim benefit of the two-compound combination over the steroid alone, monotherapy with generic topical corticosteroids may be fully acceptable for short-term therapy.

The 14 studies in 'Characteristics of studies awaiting classification' may alter the conclusions of the review once assessed.

Implications for research

The evaluation of the efficacy and safety of almost all included treatments is restricted to their short-term use (less than six months). As for any chronic condition, disease control over a long time span without compromising the participant's safety is crucial. Moreover, it is not known whether the relapse of psoriatic lesions is linked to a worsening of the condition. These aspects should be addressed in future randomised controlled trials (RCTs).

The evaluation of tar preparations and other products, such as ciclopirox olamine, tacrolimus, dithranol and urea combination or steroids in combination with salicylic acid, was limited due to insufficient evidence. Some treatments are no longer part of current practice. However, other preparations, such as topical tacrolimus, may remain or become an alternative treatment option for mild disease severity or as part of a treatment regimen for the maintenance of remission. Moreover, there is a need for further evidence to assess the assumption that corticosteroids of moderate, high and very high potency are similarly effective and safe.

For most treatments there is a lack of evidence on the improvement of quality of life. More evidence would help participants and their physicians to decide which treatment may be best. The scalp is a visible part of the body and difficult to treat due to the hair. Therefore, future trials should evaluate patients' tolerance of the topical preparation, which may involve the assessment of smelliness, stickiness or oiliness, among others. This is an important issue with great influence on the quality of life and patient compliance.

The wide spectrum of different efficacy, safety and quality of life tools makes the comparison of different treatments a great challenge. Poor transparency and inconsistent definition of existing tools made it additionally difficult to summarise the evidence. It would be of great benefit to achieve an agreement on an internationally recognised outcome set.

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* *Indicates the major publication for the study*

CHARACTERISTICS OF STUDIES

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

Andres 2006

Methods	This was a single-centre, parallel-group, active-controlled, randomised trial
Participants	**Inclusion criteria of the trial** • Scalp psoriasis involving at least 25% of the scalp • Dermatologic sum score (DSS) of at least 3 **Exclusion criteria of the trial** • Pregnant or breastfeeding women • Women at risk of pregnancy • Subject with ophthalmologic disorders or wearing contact lenses **Washout period** • Specific washout period if concomitant treatment that interferes with psoriasis status or hypothalamic-pituitary-adrenal axis function **Baseline characteristics** • Age (years, mean ± SD): A: 38 ± 9; B: 30 ± 10 • Females N (%): A: 3 (21); B: 8 (67) • DSS (mean ± SD): A: 5.8 ± 1.5; B: 4.7 ± 0.9 matched with Total Sign Score (TSS) • Percent of scalp area affected (mean ± SD): A: 73 ± 28; B: 53 ± 21
Interventions	A: clobetasol propionate 0.05% shampoo, once daily for 4 weeks on dry scalp (N = 14 participants) B: clobetasol propionate 0.05% gel, once daily for 4 weeks on dry scalp and rinsed off after 15 minutes (N = 12 participants)
Outcomes	1. HPA axis suppression (week 1, 2, 3, and 4) 2. Atrophogenicity (week 4) 3. Ocular tolerability (week 4) 4. Overall safety (week 4) 5. DSS (week 1, 2, 3 and 4) matched with total sign score (TSS) Definition: *HPA axis suppression:* pre-stimulation values of serum-cortisol below 7 µg/dl, and/or post-stimulation values lower than 20 µg/dl after 60 minutes of intravenous injection of 0.25 mg cosyntropin *Ocular tolerability:* intraocular pressure, results of slit lamp examination, visual acuity assessment, patient rating of burning or sting sensation on a scale from 0 (absent) to 3 (severe) *Overall safety:* adverse events probably related to treatment *DSS (0-9):* sum of erythema, adherent desquamation and plaque thickening on score from 0 (none) to 3 (severe) Visits: baseline, week 1, 2, 3 and 4
Notes	Galderma Laboratories supported the study and employed all authors
Risk of bias	

Andres 2006 (*Continued*)

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote (page 328): "computer generated randomization list" Comment: probably sufficient
Allocation concealment (selection bias)	Unclear risk	This was not stated
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote (page 330): "Twenty-five of the 26 enrolled subjects completed the study." Comment: insufficient reporting of attrition or exclusion, no imputation method reported, but one drop-out not considered enough to introduce bias
Selective reporting (reporting bias)	Low risk	All reported results were pre-specified outcomes in the methods section
Other bias	High risk	Quote (page 330): "more females in the clobetasol propionate shampoo group [...] symptom severity and extend of involvement at baseline were worse in the clobetasol propionate shampoo group [...]" Comment: imbalance of baseline characteristics likely to bias outcome
Blinding of participants and personnel (performance bias) All outcomes	High risk	Quote (page 328): "due to the different formulations and ways of administration, it was not possible to mask the identity of the treatment from the subjects" Comment: no blinding of participants performed
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote (page 328): "Investigators did not know the treatment provided to the subjects." Comment: insufficient information about method used to blind investigators

Barrett 2005

Methods	This was a multicentre, open-label, parallel-group, randomised trial
Participants	**Inclusion criteria of the trial** • Diagnosis of mild to moderate scalp psoriasis **Exclusion criteria of the trial** This was not stated **Washout period**

	This was not stated **Baseline characteristics** This was not stated
Interventions	A: calcipotriol solution + tar-based shampoo, for 8 weeks B: calcipotriol + non-medicated shampoo, for 8 weeks
Outcomes	1. 'Marked improvement' (week 8) 2. 'Clearance' (week 8) 3. Mean total sign score (TSS) 4. Investigator assessments of time to achieve treatment success or extent of scalp psoriasis 5. Patient assessments of severity, skin flaking, overall response or acceptability 6. Patient assessment of itching 7. Dermatology Life Quality Index 8. Adverse events 9. Laboratory test parameters Definition: *TSS:* composite score for redness, thickness and scaliness Visits: baseline, week 8
Notes	This study was published as a letter Number of participants not stated

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote (page 175): "randomised" Comment: insufficient detail was reported about the method used to generate the allocation sequence
Allocation concealment (selection bias)	Unclear risk	This was not stated
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	This was not stated
Selective reporting (reporting bias)	High risk	Quote: "A greater reduction in the 'mean total sign score' (...) was found for calcipotriol + tar-based shampoo than calcipotriol + non-medicated shampoo (p=0.040)." Quote: "A significant difference in patient assessment of itching in favour of calcipotriol + tar-based shampoo was found (p=0.032)." Comment: not all results were reported in sufficient detail. No baseline data for each

Barrett 2005 (*Continued*)

		specific group reported. Study published as letter only
Other bias	Low risk	No other source of bias identified
Blinding of participants and personnel (performance bias) All outcomes	High risk	Quote (page 175): "open-label" Comment: no blinding performed
Blinding of outcome assessment (detection bias) All outcomes	High risk	Quote (page 175): "open-label" Comment: no blinding performed

Bergstrom 2003

Methods	This was a randomised, single-blind, parallel-group trial
Participants	**Inclusion criteria of the trial** • Older than 18 years • Stable or worsening psoriasis covering at least 3% of the body surface area (BSA) including skin and scalp **Exclusion criteria of the trial** This was not stated **Washout period** • 2 weeks for topical treatment • 4 weeks for oral treatment **Baseline characteristics** • Age, mean (years): 49 • Females N (%): 7 (22) • Psoriasis Area and Severity Index (PASI), mean (SD): A: 12.3 (8.0), B: 9.6 (4.8)
Interventions	A: clobetasol foam, for 2 weeks (N of participants unknown) B: clobetasol cream (0.05%) plus clobetasol solution (0.05%) regimen, for 2 weeks (N of participants unknown) Application frequency varied individually according to patients' decision The study size was 32 participants
Outcomes	1. PASI (week 2) 2. Self administered PASI (SAPASI) (week 2) 3. Quality of life (QOL) (week 2) 4. Patients' compliance (week 2) 5. Patients' satisfaction (week 2) 6. Patients' assessment of ease of medication use (week 2) 7. Cost of treatment (week 2) Definition: *SAPASI:* Assessment according to the PASI performed by the patient *QOL:* assessment according to 2 established tools: DLQI and EQ-5D *Cost of treatment:* to find the cost of treating 1% BSA: amount of medication used (in

	grams) divided by the total percentage BSA treated Visits: baseline and week 2	
Notes	-	
Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Quote (page 408): "patients were randomized into 2 treatment groups" Comment: insufficient detail was reported about the method used to generate the allocation sequence
Allocation concealment (selection bias)	Unclear risk	This was not stated
Incomplete outcome data (attrition bias) All outcomes	High risk	Quote (page 408): "3 were excluded because of noncompliance: 1 did not return for a second visit, 1 misapplied the foam, and 1 applied the medication intermittently over a 3-week period." Comment: per-protocol analysis performed. Unclear if all drop-outs belonged to one group. In this case drop-out rate may be > 10% per group and would introduce relevant bias
Selective reporting (reporting bias)	High risk	Quote (page 409): "The cost per change of one unit in PASI score was $21.60 for patients using foam and $16.42 for those using cream/solution; the difference was not statistically significant" Comment: this outcome was not pre-specified in the method section
Other bias	Low risk	No other potential source of bias identified
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote (page 408): "single-blind design" Comment: unclear which side was blinded
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote (page 408): "single-blind design" Comment: unclear which side was blinded

Breneman 1992

Methods	This was a multicentre, randomised, double-blind, parallel-group trial
Participants	**Inclusion criteria of the trial** • Age was at least 12 years • At least 20% psoriatic scalp involvement • Scalp target area rating of 3 for scaling according to the following scale: 0 (absent) , 1 (slight or mild, minimal), 2 (moderate or average, easily discernible), 3 (severe or extensive, markedly evident) **Exclusion criteria of the trial** This was not stated **Washout period** This was not stated **Baseline characteristics** • Total sign score (TSS): A: 8.8, B: 9.5
Interventions	A: augmented betamethasone dipropionate 0.05% propylene glycol lotion twice daily for 3 weeks (N = 84 participants) B: fluocinonide 0.05% solution twice daily for 3 weeks (N = 85 participants)
Outcomes	1. Total sign score (day 4, 8, 15 and 22) 2. Induration score (day 4, 8, 15 and 22) 3. Scaling score (day 4, 8, 15 and 22) 4. Pruritus score (day 4, 8, 15and 22) 5. Erythema score (day 4, 8, 15 and 22) 6. Global improvement score (day 4, 8, 15 and 22) 7. Clearance of scaling (day 22) 8. Adverse events (drug-related) (day 22) 9. Withdrawals due to adverse events (day 22) Definition: *TSS (0 to 12):* sum of the scores of the 4 disease parameters *Disease parameter:* induration (0 to 3), scaling (0 to 3), pruritus (0 to 3), erythema (0 to 3) *Global Improvement Score:* 1 (cleared), 2 (marked improvement), 3 (moderate improvement), 4 (slight improvement), 5 (no change), 6 (exacerbation) Visits: baseline, day 4, 8, 15 and 22
Notes	-

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote (page 19): "randomized" Comment: insufficient detail was reported about the method used to generate the allocation sequence
Allocation concealment (selection bias)	Unclear risk	This was not stated

Breneman 1992 (*Continued*)

Incomplete outcome data (attrition bias) All outcomes	High risk	Quote (page 19-20): "12 patients [...] were excluded from efficacy analysis because baseline entrance criteria for disease severity were not met" Comment: no intention-to-treat analysis performed. Reason for exclusion considered to introduce bias
Selective reporting (reporting bias)	Low risk	All reported results were pre-specified outcomes in the methods section
Other bias	High risk	Quote (page 19-20): "An additional 12 patients [...] were excluded from efficacy analysis because baseline entrance criteria for disease severity were not met." Comment: these 12 patients with low disease severity were excluded for efficacy evaluations, but included in safety evaluations
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote (page 19): "double-blind" Comment: insufficient detail was reported about the method used to blind study participants or personnel from the intervention a participant received
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote (page 19): "double-blind" Comment: insufficient detail was reported about the method used to blind the outcome assessor from the intervention a participant received

Buckley 2008

Methods	This was a multicentre, prospective, randomised, active-controlled, double-blind, parallel-group trial
Participants	**Inclusion criteria of the trial** • Age at least 18 years • At least 10% psoriatic scalp involvement • Amenable to topical treatment with a maximum of 100 g of medication per week • Total sign score (TSS) at least 4 (each subscore at least 1) • Investigator global assessment (IGA) of at least 3 **Exclusion criteria of the trial** • Patients with erythrodermic or pustular psoriasis • Patients with known or suspected severe renal insufficiency or severe hepatic disorder **Washout period** • 4 weeks for systemic treatment with a potential effect on psoriasis vulgaris (e.g.

	corticosteroids or immunosuppressants) or PUVA therapy on the scalp • 2 weeks for UVB or grenz-ray therapy on the scalp or topical treatment of scalp psoriasis **Baseline characteristics** • Age (years, mean ± SD): A: 48.4 ± 16.5, B: 48.4 ± 14.4 • Females N (%): A: 61 (56.5), B: 59 (53.6) • TSS (mean ± SD): A: 6.79 ± 1.53, B: 6.81 ± 1.63
Interventions	A: calcipotriol 50 µg/g plus betamethasone dipropionate 0.5 mg/g scalp formulation, once daily for 8 weeks (N = 108 participants) B: betamethasone dipropionate 0.5 mg/g (same vehicle), once daily for 8 weeks (N = 110 participants) Patients having 'absence of disease' according to the IGA of disease severity at visits 2 to 5 were allowed to withdraw from the study
Outcomes	**Primary outcomes of the trial** 1. Total sign score (TSS): absolute change from baseline (week 8) **Secondary outcomes of the trial** 1. TSS: percentage change from baseline (week 8) 2. TSS: absolute change from baseline (week 1, 2, 4 and 6) 3. Absolute change in the individual signs of the TSS (week 1, 2, 4, 6 and 8) 4. Absolute change in score for the extent of scalp psoriasis from baseline (week 1, 2, 4, 6 and 8) 5. Investigator's global assessment (IGA) (week 1, 2, 4, 6 and 8) 6. Patient's assessment of treatment success (week 8) 7. Adverse events (AE) (week 8) 8. Serious AE (week 8) 9. Number of patients with at least 1 AE (week 8) 10. Withdrawals due to AE (week 8) 11. Treatment duration (week 8) 12. Treatment compliance (week 8) Definition: *TSS:* sum of the score for each disease parameters ranging from 0 to 12 *Disease parameter (0 (no symptoms) - 4 (very severe symptoms))*: redness, thickness, scaliness *Patient assessment:* 7-category scale: 0 = worse to 6 = cleared, treatment success: patient rated as 'marked improvement', 'almost clear' or 'cleared' *IGA (6-point scale):* 'absence of', 'very mild', 'mild', 'moderate', 'severe', 'very severe' *Extend of scalp psoriasis:* score of 3 = 30% to 49% involvement of the scalp Visits: baseline, week 1, 2, 4, 6 and 8
Notes	The study was sponsored by LEO Pharma A/S, Ballerup, Denmark

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote (page 108): "randomized" Comment: insufficient detail was reported about the method used to generate the al-

Buckley 2008 *(Continued)*

		location sequence
Allocation concealment (selection bias)	Unclear risk	This was not stated
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote (page 109): "All patients who had received any trial medication and from whom the presence or confirmed absence of adverse events was available were included in the safety analysis set.[...] The primary efficacy criterion was analysed for the intention-to-treat (ITT) population [...] a last observation carried forward approach was used." Comment: missing data have been imputed using appropriate methods. Incomplete outcome data sufficiently reported
Selective reporting (reporting bias)	Low risk	All reported results were pre-specified outcomes in the methods section
Other bias	Low risk	No other source of bias identified
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote (page 108): "double blind [...] same vehicle" Comment: blinding probably sufficient
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote (page 108): "double blind [...] same vehicle" Comment: insufficient information about method used to ensure blinding of outcome assessor throughout the study

Curley 1990

Methods	This was a double-blind, randomised, active-controlled trial
Participants	**Inclusion criteria of the trial** • Patient with dry scalp psoriasis **Exclusion criteria of the trial** • Patients with skin infection • Pregnant or breastfeeding women • Patients with moist lesions • Concomitant treatment that could affect the course of the disease (e.g. other anti-inflammatory treatment) **Washout period** • 4 weeks prior to beginning of study for topical corticosteroid treatment **Baseline characteristics** • Scaling: A: 16 (severe), 6 (moderate); B: 13 (severe), 4 (moderate)

Curley 1990 (*Continued*)

Interventions	A: betamethasone dipropionate 0.05% with salicylic acid 2% lotion, twice daily for 3 weeks (N = 22 participants) B: betamethasone valerate 0.1% lotion, twice daily for 3 weeks (N = 17 participants)
Outcomes	1. Induration (day 7, 14 and 21) 2. Lichenification (day 7, 14 and 21) 3. Excoriation (day 7, 14 and 21) 4. Erythema (day 7, 14 and 21) 5. Crusting (day 7, 14 and 21) 6. Scaling (day 7, 14 and 21) 7. Pruritus (day 7, 14 and 21) 8. Pain (day 7, 14 and 21) 9. Exudation (day 7, 14 and 21) 10. Percentage area of involvement of the lesion (day 7, 14 and 21) 11. Overall evaluation (day 21) matched with IGA = "cleared" 12. Number of patients with at least 1 adverse event (AE) (day 21) 13. Withdrawals due to AE (day 21) 14. Withdrawals due to loss to follow-up (day 21) 15. Withdrawals due to treatment failure (day 21) 16. Time point of first notable improvement 17. Cosmetic acceptability (day 21) Definition: *Outcome 1 to 9:* severity graded on a 4-point scale 'none', 'slight', 'moderate', 'severe' *Overall evaluation:* graded on a 5-point scale from 'cured' to 'worse' *Percentage area of involvement:* estimated approximately *Outcome 16 to 17 :* assessed by patient Visits: baseline, day 7, 14 and 21
Notes	This study was supported by a grant from Schering-Plough Ltd 56 participants: 39 psoriasis, 17 eczema

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Quote (page 203): "Patients were allocated at random" Comment: insufficient detail was reported about the method used to generate the allocation sequence
Allocation concealment (selection bias)	Unclear risk	This was not stated
Incomplete outcome data (attrition bias) All outcomes	High risk	Quote (page 203): "Of the 59 patients who entered the trial, 3 were excluded from the analysis because of protocol violations." Quote (page 205): "Of the 56 patients included in the study, 47 completed the 3-

Curley 1990 *(Continued)*

		week treatment regime, and nine were regarded as treatment failures." Comment: no ITT analysis performed. Unclear if 'treatment failures' (N = 9 participants) were included in overall evaluation or if any imputation method was used
Selective reporting (reporting bias)	High risk	Quote (page 203): "The other symptoms of crusting, induration, lichenification and exudation were not widespread enough at baseline to warrant evaluation." Comment: not all pre-specified outcomes reported
Other bias	High risk	Number of participants listed in diagram of overall evaluation (Fig. 3) not consistent with number of participants reported in the text
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote (page 203): "treatments were applied in a double-blind manner" Comment: insufficient detail was reported about the method used to blind study participants or personnel from the intervention a participant received
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote (page 203): "treatments were applied in a double-blind manner" Comment: insufficient detail was reported about the method used to blind the outcome assessor from the intervention a participant received

De Cuyper 1995

Methods	This was a randomised, single-blind, active-controlled trial
Participants	**Inclusion criteria of the trial** This was not stated **Exclusion criteria of the trial** This was not stated **Washout period** This was not stated **Baseline characteristics** This was not stated
Interventions	A: hydrocortisone 17-butyrate 0.1% emulsion, twice daily for 4 weeks (N = 74 participants)

De Cuyper 1995 (*Continued*)

	B: betamethasone 17,21 dipropionate 0.05% lotion, twice daily for 4 weeks (N = 76 participants) Patients could withdraw if healing occurred prior to week 4
Outcomes	1. Erythema (week 2 and 4) 2. Induration (week 2 and 4) 3. Scaling (week 2 and 4) 4. Pruritus (week 2 and 4) 5. Overall severity (week 2 and 4) 6. Clearance (week 4) matched with IGA = 'cleared' 7. Adverse events (week 4) Visits: baseline, week 2 and 4
Notes	This study was published as a conference abstract

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Quote (page S104): "randomized" Comment: insufficient detail was reported about the method used to generate the allocation sequence
Allocation concealment (selection bias)	Unclear risk	This was not stated
Incomplete outcome data (attrition bias) All outcomes	Low risk	No ITT analyses for safety data used: 71 out of 76 (betamethasone group) and 70 out 74 (hydrocortisone group) reported. However, number of missing data not considered as likely to introduce bias significantly
Selective reporting (reporting bias)	High risk	Only data about clearance reported Data available for only 1 adverse event Insufficient reporting about other outcomes assessed
Other bias	Low risk	No other source of bias identified
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote (page S104): "single-blind study" Comment: insufficient information about which side was blinded
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote (page S104): "single-blind study" Comment: insufficient information about which side was blinded

Duweb 2000

Methods	This was a randomised, active-controlled, parallel-group trial
Participants	**Inclusion criteria of the trial** • Scalp psoriasis **Exclusion criteria of the trial** This was not stated **Washout period** • 2 weeks (no detailed information respecting systemic or topical treatment) **Baseline characteristics** • Age (years, mean (range)): 33.5 (6 to 61) • Females N (%): 15 (36) • Total sign score (TSS), mean: A: 5.1, B: 5.4
Interventions	A: calcipotriol 50 µg/ml solution, twice daily for 6 weeks (N = 24 participants) B: betamethasone valerate 1% lotion, twice daily for 6 weeks (N = 18 participants)
Outcomes	1. TSS (week 2, 4 and 6) 2. Erythema (week 2, 4 and 6) 3. Thickness (week 2, 4 and 6) 4. Scaling (week 2, 4 and 6) 5. Percentage of response to treatment (week 6) matched with IGA 6. Recurrences 7. Number of patients with at least 1 adverse event (AE) (week 6) Definition: *TSS (0 to 12):* sum of erythema, thickness and scaling score *Erythema/scaling/thickness score (0 to 4):* 0 = absent to 4 = severe *Percentage of response to treatment:* percentage of patients categorised into 'worse', 'no change', 'mild', 'marked' (IGA = 'very mild'), 'cleared' (IGA = 'clear') Visits: baseline, week 2, 4 and 6
Notes	TSS was calculated with sign scores reported in figures 2 to 4 by review author

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote (page 65): "randomized" Comment: insufficient detail was reported about the method used to generate the allocation sequence
Allocation concealment (selection bias)	Unclear risk	This was not stated
Incomplete outcome data (attrition bias) All outcomes	Low risk	Data for all randomised patients reported
Selective reporting (reporting bias)	High risk	The pre-specified outcome of recurrences was not reported in the results section

Duweb 2000 (*Continued*)

Other bias	Low risk	No other potential source of bias identified
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	This was not stated
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	This was not stated

Ellis 1988

Methods	This was a randomised, double-blind, placebo-controlled, parallel-group, multicentre trial
Participants	**Inclusion criteria of the trial** • Age of at least 18 years • Psoriasis of the scalp and/or other hairy areas • Psoriasis lesions on other areas of the body • Baseline score (sum of erythema, excoriation, scaling, induration) of at least 6 **Exclusion criteria of the trial** • Intolerance of or hypersensitivity to topical corticosteroids • Pregnant or breastfeeding women • Acute systemic illness • Infection of the skin • Concomitant topical, systemic treatment or PUVA therapy • Patients with pustular (recalcitrant) psoriasis **Washout period** • 2 weeks for topical corticosteroids • 4 weeks for systemic, intralesional or inhaled corticosteroids and for PUVA therapy **Baseline characteristics** • Age (years, mean ± SD): A: 49.7 ± 16.9, B: 48.5 ± 16.5 • Females N (%): A: 39 (51), B: 37 (46) • Disease status: stable N (%): A: 46 (60), B: 46 (58)
Interventions	A: amcinonide lotion 0.1%, twice daily for 3 weeks (N = 83 participants) B: placebo (vehicle), twice daily for 3 weeks (N = 82 participants) Patients were allowed to withdraw, if complete clearance occurred prior to week 3
Outcomes	1. Investigator overall evaluation (week 1, 2 and 3) matched with IGA 2. Erythema (week 1, 2 and 3) 3. Induration (week 1, 2 and 3) 4. Scaling (week 1, 2 and 3) 5. Excoriation (week 1, 2 and 3) 6. Pruritus (week 1, 2 and 3) 7. Patient's overall evaluation (week 1, 2 and 3) matched with PGA 8. Patient acceptability evaluation (week 1, 2 and 3)

	9. Adverse events (AE) (week 1, 2 and 3) 10. Number of patients with at least 1 AE (week 3) 11. Compliance (week 1, 2 and 3) 12. Withdrawal due to AE (week 3) 13. Investigator overall evaluation: clearance (week 3) matched with IGA = 'cleared' 14. Investigator overall evaluation: excellent (week 3) matched with IGA = 'very mild' Definition: *Overall therapeutic efficacy assessed by investigator (1 to 7):* 1 = cleared (complete clearing) , 2 = excellent (> 75% improvement), 3 = good (> 50% improvement), 4 = fair (> 25% improvement), 5 = poor (< 25% improvement), 6 = no effect, 7 = exacerbation (clinical signs and symptoms worse) *Outcomes 2 to 6.:* rated by investigator on a scale from 0 to 3, 0 = absent, 0.5 to 1.0 = mild, 1.5 to 2.0 = moderate, 2.5 to 3.0 = severe *Patient's overall evaluation (0 to 3):* 0 = poor, 1 = fair, 2 = good and 3 = excellent *Patient acceptability evaluation:* form with 11 questions *Compliance:* count of the returned medication bottles Visits: baseline, week 1, 2 and 3
Notes	-

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote (page 316): "computer-generated randomization list designed to produce approximately equal numbers of patients in each study arm" Comment: probably sufficient
Allocation concealment (selection bias)	Unclear risk	This was not stated
Incomplete outcome data (attrition bias) All outcomes	High risk	Quote (page 317): "Those patients who met the protocol requirements and had at least one follow-up visit were included in the analyses of efficacy." Quote (page 323): "For the evaluable patients, the endpoint evaluation was defined as the patient's last valid evaluation." Comment: no ITT analysis, but per protocol analysis performed
Selective reporting (reporting bias)	High risk	Quote (page 323): "Both test formulations were cosmetically acceptable to patients." Quote (page 317): "no formal analysis was performed because there were few adverse events" Comment: insufficient data about prespecified outcome (patient acceptability, com-

Ellis 1988 (*Continued*)

		pliance) reported
Other bias	Low risk	No other source of bias identified
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote (page 314): "double-blind" Comment: vehicle-controlled trial. Blinding probably sufficient
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote (page 314): "double-blind" Comment: insufficient information about how blinding of assessor was ensured throughout the study

Ellis 1989

Methods	This was a randomised, blinded, active-controlled trial
Participants	**Inclusion criteria of the trial** • Adult patients • Psoriasis of the scalp and/or other hairy areas • Pre-therapy (symptom) score of at least 6 **Exclusion criteria of the trial** • Intolerance or hypersensitivity to topical corticosteroids • Pregnant or breastfeeding women • Acute/active systemic illness • Tuberculosis of the skin • Systemic fungal or viral diseases of the skin • Underlying disease that would contraindicate the use of steroids • Skin disease that was refractory to previous corticosteroid therapy • Concomitant topical, systemic treatment or PUVA therapy • Recalcitrant psoriasis not suitable for topical corticosteroid therapy (e.g. acute pustular psoriasis) **Washout period** • 2 weeks for topical corticosteroids • 4 weeks for systemic, intralesional or repository corticosteroids, antimetabolites and for PUVA therapy **Baseline characteristics** • Age (years, mean (range)): A: 42 (19 to 74), B: 47 (19 to 78) • Females N (%): A: 14 (48), B: 9 (33) • Weight (kg, mean (range)): A: 71.7 (39 to 143), B: 85.9 (52 to 143) • Stable disease status N (%): A: 14 (48.3), B: 16 (59.3)
Interventions	A: amcinonide lotion 0.1%, twice daily for 3 weeks (N = 29 participants) B: fluocinonide solution 0.05%, twice daily for 3 weeks (N = 30 participants)
Outcomes	1. Investigator overall evaluation (week 1, 2 and 3) matched with IGA 2. Erythema (week 1, 2 and 3) 3. Induration (week 1, 2 and 3) 4. Scaling (week 1, 2 and 3)

	5. Excoriation (week 1, 2 and 3) 6. Pruritus (week 1, 2 and 3) 7. Patient's overall evaluation (week 1, 2 and 3) matched with PGA 8. Patient cosmetic acceptability evaluation (week 3) 9. Adverse events (AE) (week 1, 2 and 3) 10. Number of patients with at least 1 AE (week 3) 11. Withdrawals due to AE (week 3) Definition: *Overall therapeutic efficacy (1 to 7):* 1 = cleared (complete clearing), 2 = excellent (> 75% improvement), 3 = good (> 50% improvement), 4 = fair (> 25% improvement), 5 = poor (25% improvement), 6 = no effect, 7 = exacerbation (clinical signs and symptoms worse) *Outcomes 2 to 6:* rated by investigator on a scale from 0 to 3, 0 = absent, 0.5 to 1.0 = mild, 1.5 to 2.0 = moderate, 2.5 to 3.0 = severe *Disease symptoms score (0 to 12):* sum of erythema, induration, excoriation, scaling *Patient's overall evaluation (0 to 3):* 0 = poor, 1 = fair, 2 = good and 3 = excellent *Patient cosmetic acceptability evaluation:* form with 11 questions completed by patient Visits: baseline, week 1, 2 and 3
Notes	-

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote (page 472): "patients were sequentially assigned to one of the two treatment groups by means of a computer-generated randomization list" Comment: probably sufficient
Allocation concealment (selection bias)	Unclear risk	This was not stated
Incomplete outcome data (attrition bias) All outcomes	High risk	No intention-to-treat analysis Withdrawal due to adverse events: A: 0, B: 1 Patients excluded from efficacy analysis: A: 0, B: 3
Selective reporting (reporting bias)	Low risk	All reported results were pre-specified outcomes in the methods section
Other bias	Low risk	No other source of bias identified
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote (page 471): "blinded comparison" Comment: insufficient detail was reported about the method used to blind study participants and personnel from the intervention a participant received

Ellis 1989 (*Continued*)

Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote (page 471): "blinded comparison" Comment: insufficient detail was reported about the method used to blind the outcome assessors from the intervention a participant received

Feldman 2001

Methods	This was a multicentre, randomised, single-blind trial
Participants	**Inclusion criteria of the trial** • Older than 18 years of age • History of stable or worsening scalp psoriasis • Psoriasis involving at least 10% of the scalp • Baseline score of at least 6 **Exclusion criteria of the trial** • Intolerance of or hypersensitivity to topical corticosteroids • Pregnant women • Use of topical corticosteroids • PUVA or UVB therapy within 2 weeks prior to the trial • Known allergy to topical corticosteroids • Conditions on the scalp other than psoriasis • Severe and uncontrolled manifestations of any disease (including psoriasis) • Concomitant systemic corticosteroids or retinoids • Known failure to respond to topical corticosteroids within 1 year prior to the study **Washout period** • 2 weeks for PUVA, UVB therapy and topical corticosteroids • 6 weeks for systemic corticosteroids • 8 weeks for systemic and topical retinoids **Baseline characteristics** • Age (years, mean (range)): 50 (17 to 90) • Females N (%): 43 (54) • Global Severity Score (GSS), mean ± SD: A: 8.1 ± 2.2, B: 7.7 ± 2.1 matched with TSS
Interventions	A: betamethasone valerate 0.12%, once daily for 4 weeks (N = 46 participants) B: betamethasone valerate 0.12%, twice daily for 4 weeks (N = 33 participants)
Outcomes	1. GSS (week 4) 2. Investigator's global assessment of response (week 4) matched with IGA 3. Patient's global assessment of response (week 4) matched with PGA 4. Erythema (week 4) 5. Thickness (week 4) 6. Scaling (week 4) Definition: *Investigator's and patients' global assessment of response (0 to 6):* 0 = completely clear, 1= almost clear, 2 = marked improvement, 3 = moderate improvement, 4 = slight improvement, 5 = no change, 6 = worse

	GSS (0 to 12): sum of scores of erythema, thickness and scaling *Erythema (0 to 4):* 0 = no erythema, 1 = faint erythema, pink to very light red, 2 = definite light red erythema, 3 = dark red erythema, 4 = very dark red "beefy" erythema *Thickness (0 to 4):* 0 = no plaque elevation, 1 = slight, barely perceptible elevation, 2 = definite elevation but not thick, 3 = definite elevation, thick plaque with sharp edge, 4 = very thick plaque with sharp edge *Scaling (0 to 4):* 0 = no scaling, 1 = sparse fine scale lesions, 2 = coarser scales, most of lesions covered, 3 = entire lesion covered with coarse scales, 4 = very thick coarse scales, possibly fissured Visits: baseline and week 4
Notes	-

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote (page 387): "Subjects were randomly assigned to either the qd or the bid dosing group by the study coordinator at each site [...]" Comment: insufficient detail was reported about the method used to generate the allocation sequence
Allocation concealment (selection bias)	Unclear risk	This was not stated
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote (page 388): "The results were analysed on the basis of intention-to-treat [...]" Comment: no information about imputation method used (6 drop-outs). No information about the distribution of the drop-outs across groups. However, all randomised patients included for analysis
Selective reporting (reporting bias)	Low risk	All reported results were pre-specified outcomes in the methods section
Other bias	High risk	Slightly different values for erythema and plaque thickness scores reported in text and table 3 (i.e. erythema score: initial mean: 2.7 ± 0.8 (text) versus 2.7 ± 0.7 (table 3)) Inclusion criteria: at least 18 years, but age at baseline ranged from 17 to 90 years Comment: these findings are not considered to have a significant impact on outcomes Quote (page 388): "The subject and the investigator graded the global response at

Feldman 2001 (*Continued*)

		the follow up visit." Comment: no baseline IGA and PGA assessed, thus change in these scores not evaluable
Blinding of participants and personnel (performance bias) All outcomes	High risk	Quote (page 387): "single-blind study" Quote (page 388): "The subjects self-administered the treatment to the entire scalp under the instruction of the study personnel [...]" Comment: insufficient information about which side was blinded
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote (page 387): "single-blind study" Quote (page 387): "The physician-grader performing the evaluations was blinded to the assignment." Comment: insufficient information about method used to ensure blinding of outcome assessor

Feldman 2013

Methods	This was a multicentre, randomised, double-blind, vehicle-controlled, parallel-group trial
Participants	**Inclusion criteria of the trial** • At least 12 years of age • Plaque-type psoriasis involving 3% to 10% of total body surface area (BSA), (excluding the scalp) with Investigator's Static Global Assessment (ISGA) of at least 3 • Target lesion of greater than 2 cm^2 on trunk or extremities with a score of at least 2 on the psoriasis grading scale • Psoriasis involving at least 10% of the scalp and ISGA of at least 3 • Negative urine pregnancy test and adequate contraception for female participants **Exclusion criteria of the trial** • Participation in a previous study regarding calcipotriene foam • Concomitant non-biologic, antipsoriatic treatment • Recent treatment with topicals with beneficial effect on psoriasis (including biologics) • History of immunocompromising disease **Washout period** This was not stated **Baseline characteristics** • Age (years, mean ± SD): A: 45.9 ± 15.3, B: 44.4 ± 15.5 • Females N (%): A: 69 (38), B: 76 (42) • Scalp area affected (%, mean ± SD): A: 34.2 ± 25.6, B: 32.0 ± 25.7
Interventions	A: calcipotriene foam 0.005%, twice daily for 8 weeks (N = 181 participants) B: placebo vehicle foam, twice daily for 8 weeks (N = 182 participants)

Feldman 2013 (*Continued*)

Outcomes	**Primary outcome** 1. Scalp ISGA of 0 to 1 (week 8) matched with IGA **Secondary outcomes** 1. Body ISGA of 0 to 1 (week 2, 4 and 8) 2. Scalp ISGA of 0 to 1 (week 2 and 4) matched with IGA 3. Erythema score of 0 to 1 (week 2, 4 and 8) 4. Scaling score of 0 to 1 (week 2, 4 and 8) 5. Thickness score of 0 to 1 (week 2, 4 and 8) 6. Mean percent reductions in percent BSA of body (week 2, 4 and 8) 7. Mean percent reductions in percent BSA of scalp (week 2, 4 and 8) 8. Adverse events (AE) (week 8) 9. Number of patients with at least 1 AE (week 8) 10. Withdrawal due to AE (week 8) 11. Target lesion score (weeks 2 and 4) Definition: *Scalp ISGA (0 to 5):* 0 = clear, 5 = very severe *Erythema, thickness, scaling score (0 to 5, respectively):* 0 = clear, 5 = very severe *Target lesion score:* sum of erythema, thickness, scaling scores Visits: baseline, week 1, 2, 4 and 8
Notes	This trial was supported by Stiefel, a GSK company, Research Triangle Park, NC NCT01139580

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote (page 301): " Subjects were allocated [...] using a 1:1 randomization schedule generated before the study." Comment: insufficient detail was reported about the method used to generate the allocation sequence
Allocation concealment (selection bias)	Unclear risk	This was not stated
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote (page 301): "All analysis were on the ITT population [...] a last-observation-carried-forward (LOCF) method was used" Comment: missing data sufficiently addressed
Selective reporting (reporting bias)	Low risk	All results were pre-specified outcomes in the methods section
Other bias	Low risk	No other source of bias identified

Feldman 2013 (*Continued*)

Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote (page 301): "Canister were labelled identically", "Study group allocation was unblinded to study personnel after all data were collected and validated [...]" Comment: probably sufficient
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote (page 301): "Canister were labelled identically", "Study group allocation was unblinded to study personnel after all data were collected and validated [...]" Comment: probably sufficient

Franz 1999

Methods	This was a multicentre, randomised, double-blind, active- and vehicle-controlled trial
Participants	**Inclusion criteria of the trial** • Adult patients • At least 10% of scalp surface involved • Psoriasis sign score of at least 6 (at least 2 points for erythema, thickness, scaling, respectively) **Exclusion criteria of the trial** • Systemic antipsoriatic therapy within 4 weeks prior to the trial • Topical therapy on the scalp within 2 weeks prior to the trial **Washout period** This was not stated **Baseline characteristics** • Age (years, mean): A: 46.6, B: 48.6, C: 50.8, D: 48.5 • Females N (%): A: 32 (56), B: 26 (45), C: 14 (50), D: 15 (52) • Total sign score (TSS) (mean): A: 7.87, B: 7.7, C: 8.33, D: 8.08 calculated by review author
Interventions	A: betamethasone valerate foam 0.1%, twice daily for 4 weeks (N = 57 participants) B: betamethasone valerate lotion 0.1%, twice daily for 4 weeks (N = 58 participants) C: placebo foam, twice daily for 4 weeks (N = 28 participants) D: placebo lotion, twice daily for 4 weeks (N = 29 participants)
Outcomes	1. Scaling (week 2 and 4) 2. Erythema (week 2 and 4) 3. Thickness (week 2 and 4) 4. Pruritus (week 2 and 4) 5. TSS (week 2 and 4) calculated by review author 6. Investigator's Global Assessment (IGA) (week 4) 7. Patient's Global Assessment (PGA) (week 4) 8. Adverse events (AE) (week 4) 9. Withdrawal due to AE (week 4) Definition: *IGA /PGA (7-point scale):* lesions rated as completely clear, almost clear (= 'very mild'),

	marked improvement, moderate improvement, slight improvement, no change, worse *Erythema, thickness, pruritus and scaling score (0 to 4, respectively):* 0 = none, 1 = mild, 2 = moderate, 3 = severe, 4 = very severe Visits: baseline, week 2 and 4
Notes	This trial was funded by Connetics Corporation, Palo Alto, California

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Quote (page 629): "[...] randomly assigned to one of four treatment groups in a 2 : 1 : 2 : 1 ratio [...]" Comment: insufficient detail was reported about the method used to generate the allocation sequence
Allocation concealment (selection bias)	Unclear risk	This was not stated
Incomplete outcome data (attrition bias) All outcomes	High risk	Quote (page 631): "One hundred and seventy-two patients (85 men, 87 women), from a total of 190 enrolled, completed the safety and efficacy study." Comment: insufficient reporting of reasons for attrition or exclusions
Selective reporting (reporting bias)	Low risk	All reported results were pre-specified outcomes in the methods section
Other bias	Low risk	No other source of bias identified
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote (page 629): "double-blind study" Comment: insufficient information about how participants and personnel were blinded regarding difference between the 2 vehicles used
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote (page 629): "double-blind study" Comment: insufficient information about how blinding of outcome assessors was ensured throughout the study

Franz 2000

Methods	This was a multicentre, randomised, double-blind, active- and vehicle-controlled trial
Participants	**Inclusion criteria of the trial** • Adult patients • At least 10% of scalp surface involved • Psoriasis sign score of at least 6 (at least 2 points for erythema, thickness, scaling, respectively) **Exclusion criteria of the trial** • Other treatment **Washout period** This was not stated **Baseline characteristics** • Females N (%): 95 (50.5) • Total sign score (TSS): A: 7.28, B: 7.43, C: 9.94, D: 7.00 calculated by review authors
Interventions	A: clobetasol propionate (CP) foam 0.05%, twice daily for 14 days (N = 62 participants) B: CP solution 0.05%, twice daily for 14 days (N = 63 participants) C: placebo foam, twice daily for 14 days (N = 31 participants) D: placebo solution, twice daily for 14 days (N = 32 participants) Assignment in a 2:1:2:1 ratio: CP foam:placebo foam:CP solution:placebo solution
Outcomes	1. Scaling (week 1, 2 and 4) 2. Erythema (week 1, 2 and 4) 3. Plaque thickness (week 1, 2 and 4) 4. Pruritus (week 1, 2 and 4) 5. Investigator's Global Assessment (IGA) (week 2 and 4) 6. Patient's Global Assessment (PGA) (week 2 and 4) 7. Adverse events (AE) (week 4) Definition: *IGA/PGA (7-point scale):* lesions rated as completely clear, almost clear (= 'very mild'), marked improvement, moderate improvement, slight improvement, no change, or worse *Erythema, thickness, pruritus and scaling score (0 to 4, respectively):* 0 = none, 1 = mild, 2 = moderate, 3 = severe, 4 = very severe Visits: baseline, week 1, 2 and 4 (follow-up)
Notes	Funded by Connetics Corporation, Palo Alto, CA, USA

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Insufficient detail was reported about the method used to generate the allocation sequence
Allocation concealment (selection bias)	Unclear risk	This was not stated

Franz 2000 (*Continued*)

Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote (page 536): "All enrolled subjects [...] successfully completed the study." Comment: no missing outcome data
Selective reporting (reporting bias)	High risk	Quote (page 537): "The percentage of patients reporting adverse events and the incidence of adverse events judged as being related to study medication did not differ significantly among the treatment groups." Comment: insufficient data regarding the incidence or characteristics of adverse events reported
Other bias	High risk	Baseline characteristics (TSS, calculated by review authors) not balanced between groups
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote (page 535): "double-blind" Comment: insufficient information about how participants and personnel were blinded regarding difference between the 2 vehicles used
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote (page 535): "double-blind" Comment: insufficient information about how blinding of outcome assessors was ensured throughout the study

Fredriksson 1976

Methods	This was a randomised, double-blind, active-controlled trial
Participants	**Inclusion criteria of the trial** • Patients with psoriasis of the scalp **Exclusion criteria of the trial** • Tuberculosis of the skin • Viral infections with skin lesions • Pregnant or breastfeeding women • No dressings were allowed and no concomitant treatment with topical or systemic corticosteroids, antihistamines or vasoconstrictor **Washout period** This was not stated **Baseline characteristics** • Age (years, range): 18 to 64 • Females N (%): 33 (37)

Fredriksson 1976 (*Continued*)

Interventions	A: betamethasone 17,21-dipropionate 0.05% in alcoholic solution, twice daily for 4 weeks (N = 29 participants) B: betamethasone 17,21-dipropionate 0.05% plus salicylic acid 2.0% in alcoholic solution, twice daily for 4 weeks (N = 30 participants) C: triamcinolone acetonide 0.2% plus salicylic acid 2.0% in alcoholic solution, twice daily for 4 weeks (N = 31 participants)
Outcomes	1. Induration (week 2 and 4) 2. Lichenification (week 2 and 4) 3. Excoriation (week 2 and 4) 4. Inflammation (week 2 and 4) 5. Crusting (week 2 and 4) 6. Scaling (week 2 and 4) 7. Pruritus (week 2 and 4) 8. Pain (week 2 and 4) 9. Physician's overall evaluation (week 2 and 4) 'cured' matched with IGA = 'clear' Definition: *Outcomes 1 to 8:* each rated on a score from 0 to 3: 0 = absence, 1 = mild, 2 = moderate, 3 = severe *Physician's overall evaluation:* clinical cure = complete remission, clinical improvement = marked (> 70% but < 100%), moderate (>30% but < 70%), slight (< 30%), treatment failure = no change or worsening Visits: baseline, week 2 and 4
Notes	-

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote (page 253): "patients were allocated one of the preparations at random" Comment: insufficient detail was reported about the method used to generate the allocation sequence
Allocation concealment (selection bias)	Unclear risk	This was not stated
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote (page 253): "All patients completed the trial period." Comment: data for each outcome completely addressed
Selective reporting (reporting bias)	High risk	Quote (page 253): "There was no statistically significant difference regarding the variables lichenification, excoriation, crusting, scaling, pruritus and pain [...] were present to too small a degree to make an

Fredriksson 1976 (*Continued*)

		analysis meaningful" Comment: some results were not reported. No baseline data for each specific group reported. No baseline severity as inclusion criteria defined
Other bias	Low risk	No other source of bias identified
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote (page 253): "identical plastic bottles bearing only a patient number [...] choice remaining unknown to the investigator and to the patient until the code was broken at the end of the trial" Comment: probably sufficient
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote (page 253): "identical plastic bottles bearing only a patient number [...] choice remaining unknown to the investigator and to the patient until the code was broken at the end of the trial" Comment: probably sufficient

Gip 1981

Methods	This was a randomised, double-blind, active-controlled, parallel-group trial
Participants	**Inclusion criteria of the trial** • Patients with psoriasis of the scalp **Exclusion criteria of the trial** This was not stated **Washout period** This was not stated **Baseline characteristics** • Females N (%): A: 11 (55), B: 16 (80) • Age (years, mean ± SD): A: 41.0 ± 18.1, B: 40.7 ± 16.5 • Desquamation score (mean): A: 4.1, B: 4.1 • Excoriation (mean): A: 2.7, B: 2.8 • Infiltration (mean): A: 4.1, B: 4.0
Interventions	A: hydrocortisone 17-butyrate 0.1% cream, once daily for 4 weeks (N = 20 participants) B: fluocinolone acetonide 0.025% cream, once daily for 4 weeks (N = 20 participants)
Outcomes	1. Desquamation (week 1, 2, 3 and 4) 2. Excoriation (week 1, 2, 3 and 4) 3. Infiltration (week 1, 2, 3 and 4) 4. Clearance (week 1, 2, 3 and 4) matched with IGA: 'clear' 5. Number of patients with at least one adverse event (AE) (week 4) Definition:

Gip 1981 *(Continued)*

	Desquamation, excoriation score (1 to 5, respectively): 1 = none, 5 = very severe *Infiltration score:* 5 = severe, 4 = moderate, 3 = slight, 2 = erythema only, 1 = normal skin alone Visits: baseline, week 1, 2, 3 and 4
Notes	-

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote (page 198): "[...] 40 patients with psoriasis of the scalp were randomly allocated to one of 2 groups." Comment: insufficient detail was reported about the method used to generate the allocation sequence
Allocation concealment (selection bias)	Unclear risk	This was not stated
Incomplete outcome data (attrition bias) All outcomes	Low risk	All outcome data complete
Selective reporting (reporting bias)	Low risk	All reported results were pre-specified outcomes in the methods section
Other bias	Low risk	No other source of bias identified
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote (page 198): "double-blind study" Comment: insufficient detail was reported about the method used to blind study participants or personnel from the intervention a participant received
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote (page 198): "double-blind study" Comment: insufficient detail was reported about the method used to blind assessor from the intervention a participant received

Green 1994

Methods	This was a multicentre, prospective, randomised, double-blind, placebo-controlled, parallel-group trial
Participants	**Inclusion criteria of the trial** • Adults with diagnosis of mild to moderate scalp psoriasis **Exclusion criteria of the trial** • Excessively thick scalp psoriasis • Other dermatological disease of the scalp

	• Marked deterioration of scalp psoriasis at study entry • Concomitant therapy with potent topical corticosteroids, vitamin D or calcium supplements • Other medication (including lithium and beta-blockers) that could interfere with the course of the disease • Conditions such as hypercalcaemia, hepatic or renal disease at entry of study • Women with child-bearing potential with inappropriate contraception **Washout period** • 2 weeks: only non-medicated shampoo was allowed • 2 months: systemic antipsoriatic therapy (including phototherapy) **Baseline characteristics** • Total sign score (TSS), mean: A: 6.75, B: 6.55 (data out of graph)
Interventions	A: calcipotriol solution 50 µg/ml, twice daily for 4 weeks (N = 25 participants) B: placebo vehicle, twice daily for 4 weeks (N = 24 participants)
Outcomes	1. TSS (week 1, 2 and 4) 2. Extent of scalp psoriasis (week 1, 2 and 4) 3. Redness (week 1, 2 and 4) 4. Thickness (week 1, 2 and 4) 5. Scaliness (week 1, 2 and 4) 6. Flaking (weeks 1, 2 and 4) 7. Pruritus (weeks 1, 2 and 4) 8. Patient's overall assessment of treatment response (POA) (weeks 1, 2 and 4) 9. Investigator's overall assessment of treatment response (IOA) (weeks 1, 2 and 4) 10. Patient assessment of flaking and itching (weeks 1, 2 and 4) 11. Number of patients with at least one adverse event (AE) (week 4) 12. Withdrawal due to AE (week 4) 13. Compliance (week 4) 14. Withdrawal due to treatment failure (week 4) 15. Changes in blood work (week 4) Definition: *Redness, scaliness and thickness, pruritus, flaking score (0 to 4):* 0 = absent, 1 = slight, 2 = moderate, 3 = severe, 4 = severest possible *Extent of scalp psoriasis (0 to 5):* 0 = no involvement, 1 = < 20%, 2 = 20% to 39%, 3 = 40% to 59%, 4 = 60% to 79%, 5 = 80% to 100% *IOA/POA (-1 to 3):* -1 = worse, 0 = no change, 1 = slight improvement, 2 = marked improvement, 3 = cleared (matched with IGA/PGA = clear) *Blood work*: haematology and biochemistry (including serum total calcium, hepatic and renal parameters) TSS (0 to 12): sum of the 3 parameters thickness, redness and scaliness Visits: baseline, week 1, 2 and 4
Notes	This study was sponsored by Leo Pharmaceutical Products, Ballerup, Denmark

Risk of bias

Bias	Authors' judgement	Support for judgement

Green 1994 (*Continued*)

Random sequence generation (selection bias)	Unclear risk	Quote (page 483): "[...] patients were randomly allocated to receive either calcipotriol solution (50 /ig/ml) or placebo [...]" Comment: insufficient detail was reported about the method used to generate the allocation sequence
Allocation concealment (selection bias)	Unclear risk	This was not stated
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Quote (page 486): "Forty-six of the 49 patients completed the study-one in the active group withdrew because of local side-effects [...] two in the placebo group withdrew because of an inadequate treatment response." Comment: no ITT analysis used, but all outcomes except for TSS with ITT population reported. No imputation method reported
Selective reporting (reporting bias)	Low risk	All results were pre-specified outcomes in the methods section
Other bias	Low risk	No other source of bias identified
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote (page 483-4): "The active and placebo preparations [...] were similar in appearance, smell, and texture, and supplied in identical packaging." Comment: blinding probably sufficient
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote (page 483-4): "The active and placebo preparations [...] were similar in appearance, smell, and texture, and supplied in identical packaging." Comment: blinding probably sufficient

Griffiths 2006

Methods	This was a 4-week, multicentre, randomised, parallel-group, investigator-masked trial
Participants	**Inclusion criteria of the trial** • Adults (at least 18 years) with diagnosis of mild to moderate scalp psoriasis • At least 15% psoriatic scalp involvement **Exclusion criteria of the trial** • Pregnant or breastfeeding women • Immunocompromised patients

	• Patients with known allergy or contraindications to the studied medications • Concomitant systemic anti-psoriatic medications • Concomitant medication with potential to aggravate the course of the disease **Washout period** • Quote (page 91): "[...] specified washout periods for systemic therapies [...]" **Baseline characteristics** • Total sign score (TSS), mean: A: 6.1, B: 6.2 (data out of graph) • Age (years, mean ± SD): A: 46 ± 14.9, B: 45.4 ± 13.2 • Females N (%): A: 62 (51.2), B: 14 (34.1)
Interventions	A: clobetasol propionate 0.05% shampoo, once daily for 4 weeks (N = 121 participants) B: tar blend 1% shampoo, twice daily for 4 weeks (N = 41 participants) Allocation was done in a 3:1 (A:B) ratio
Outcomes	**Primary outcomes of the trial** 1. Total severity score (TSS) (week 2 and 4) 2. Global severity score (GSS) (week 2 and 4) **Secondary outcomes of the trial** 1. Erythema (week 2 and 4) 2. Thickness (week 2 and 4) 3. Desquamation (week 2 and 4) 4. Pruritus (week 2 and 4) 5. Participants' global assessment of improvement (week 2 and 4) matched with PGA 6. Percentage of scalp involvement (week 2 and 4) 7. Cutaneous safety (week 2 and 4) 8. Number of patients with at least 1 adverse event (AE) (week 4) 9. Withdrawal due to AE (week 4) 10. Ocular safety (week 2 and 4) 11. Cosmetic acceptability (week 4) Definition: *TSS (0 to 9):* sum of scores for erythema, desquamation and plaque thickening *GSS (0 to 5):* 0 = none - 5 = very severe *Erythema, desquamation and thickness, pruritus score (0 to 3):* 0 = absent - 3 = severe *Subject's global assessment of improvement: (-1 to 5):* -1 = worse to 5 = clear *Cutaneous safety:* 0 = none to 3 = severe for telangiectasia, skin atrophy and burning, respectively *Ocular safety:* 0 = none to 3 = severe *Cosmetic acceptability:* questionnaire at the end of the trial with 12 items Visits: baseline, week 2 and 4
Notes	Galderma Medical Affairs assisted in writing the article

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**

Griffiths 2006 (*Continued*)

Random sequence generation (selection bias)	Unclear risk	Quote (page 91): "Subjects were randomized at baseline to either clobetasol propionate 0.05% shampoo or to tar blend 1% shampoo in a ratio of 3:1." Comment: insufficient detail was reported about the method used to generate the allocation sequence
Allocation concealment (selection bias)	Unclear risk	This was not stated
Incomplete outcome data (attrition bias) All outcomes	Low risk	"All efficacy parameters, with the exception of the subject's assessment of global improvement, were analysed at the last visit (ITT analysis) or at the week visit (PP analysis) using an analysis of covariance (ANCOVA), using the baseline variable as a covariate and centre and treatment as factors. " Comment: incomplete outcome data sufficiently addressed
Selective reporting (reporting bias)	Low risk	All reported results were pre-specified outcomes in the methods section
Other bias	Low risk	No other source of bias identified
Blinding of participants and personnel (performance bias) All outcomes	High risk	Quote (91): "[...] investigator-masked [...]" Comment: no blinding of participants or personnel done
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote (page 91): "The investigator was masked to the treatment allocation." Comment: blinding of outcome assessment insufficiently reported

Harris 1972

Methods	This was a multicentre, randomised, parallel-group, double-blind trial
Participants	**Inclusion criteria of the trial** • Patients with diagnosis of scalp psoriasis **Exclusion criteria of the trial** • Concomitant treatment with any other topical or systemic corticosteroid, antibiotic or antihistamine **Washout period** This was not stated **Baseline characteristics**

Harris 1972 *(Continued)*

	• Females N (%): 36 (46) • Number of patients (%) with severe scaling: A: 23 (62), B: 19 (58)
Interventions	A: micronized betamethasone 17-valerate 0.1% in isopropyl alcohol lotion, twice daily for 2 weeks (N = 45 participants) B: vehicle, twice daily for 2 weeks (N = 33 participants)
Outcomes	1. Clinical response (day 5, 8, 14) 2. Lichenification (day 14) 3. Excoriation (day 14) 4. Inflammation (including degree of inflammation) (day 14) 5. Crusting (day 14) 6. Scaling (day 14) 7. Vesiculation (day 14) 8. Exudation (day 14) 9. Fissures (day 14) 10. Maceration (day 14) 11. Pruritus (day 14) 12. Burning (day 14) 13. Pain (day 14) 14. Secondary bacterial infection (day 14) 15. Adverse events (AE) (day 14) 16. Withdrawal due to treatment failure (day 14) Definition: *Patient's clinical response:* rated on a score from 1 to 6: 1 = no evaluation, 2 = exacerbation, 3 = poor or no effect, 4 = fair, partial clinical control of condition (less than 50%), 5 = good, moderate clinical control of condition (50% to 75%), 6 = excellent, complete clinical control of condition (75% or more) (matched with IGA = responder) *Outcomes 2 to 14*: graded on a score from 1 to 4: 1 = none, 2 = slight, 3 = moderate, 4 = severe Visits: baseline, day 5, 8 and 14
Notes	The study investigated 2 groups separately: patients with seborrhoeic dermatitis and patients with psoriasis of the scalp

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote (page 640): "[...] according to a randomized code." Comment: insufficient detail was reported about the method used to generate the allocation sequence
Allocation concealment (selection bias)	Low risk	Quote (page 393): "The test preparations ware supplied to each investigator in identical packages, code labelled for blind randomized assignment to patients. [...] Mas-

Harris 1972 *(Continued)*

		ter codes for each study were maintained separately from the investigators" Comment: probably sufficient
Incomplete outcome data (attrition bias) All outcomes	High risk	Quote (page 642): "Of the 95 psoriasis patients entered into the eleven studies, 5 did not return for further follow-up after the initial visit, and 12 were excluded for the following reasons: 9 used a concomitant medicated shampoo and 3 used a concomitant corticosteroid." Comment: no ITT, but per-protocol analysis performed
Selective reporting (reporting bias)	Low risk	All reported results were pre-specified outcomes in the methods section
Other bias	High risk	Quote (page 340): "The majority of the patients were placed on a bid basis." Comment: insufficient information about how many and why participants were placed on bid or opd basis. Performance bias possible
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote (page 639): "They compared a betamethasone valerate lotion and a placebo (the lotion vehicle) [...]" Quote (page 640): "Neither patient nor physician was aware of which of the two was being used." Comment: probably sufficient blinding performed
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote (page 639-40): "The test preparations ware supplied to each investigator in identical packages, code labelled for blind randomized assignment to patients [...] " Quote (page 639): "They compared a betamethasone valerate lotion and a placebo (the lotion vehicle) [...]" Quote (page 640): "Neither patient nor physician was aware of which of the two was being used." Comment: probably sufficient blinding performed

He 2008

Methods	This was a randomised, parallel-group trial
Participants	**Inclusion criteria of the trial** • Plaque psoriasis of the head and face **Exclusion criteria of the trial** • Need for systematic antipsoriatic treatment • Any other skin disease in the region of psoriasis lesions • Pregnant or breastfeeding women • Severe conditions of the heart, liver or kidney • Weakened immune system **Washout period** • Within 2 weeks to randomisation: glucocorticoids or other topical treatment • Within 4 weeks to randomisation: any therapy for psoriasis or immunosuppressants **Baseline characteristics** • Females N (%): 19 (47.5) • Age (years, mean (range)): 41.5 (18 to 65) • Total sign score (TSS): A: 8.90, B: 9.56 TSS was calculated by the review author
Interventions	A: tacrolimus 0.1% ointment, twice daily for 8 weeks (N = 20 participants) B: pine tar 5% ointment, twice daily for 8 weeks (N = 20 participants)
Outcomes	1. Dander (week 2, 4, 6 and 8) 2. Erythema (week 2, 4, 6 and 8) 3. Pruritus (week 2, 4, 6 and 8) 4. Thickness/infiltration (week 2, 4, 6 and 8) 5. Severity score of sign symptoms matched with TSS 6. Area score (week 2, 4, 6 and 8) 7. Cure rate (week 2, 4, 6 and 8) matched with IGA = 'clear' 8. Response rate (week 2, 4, 6 and 8) 9. Adverse events (AE) (week 8) Definition: *Cure rate:* percent of patients with the change ratio of an area score of 100% *Response rate:* percent of patients with the change ratio of an area score of 75% *Area score:* 5-point score: 0 = psoriasis completely improved, 1 = 75% to 90% improvement, 2 = 50% to 74% improvement, 3 = 25% to 49% improvement, 4 = < 25% improvement *Severity score of sign symptoms (0 to 16):* sum of dander, erythema, pruritus, thickness/infiltration scores *Dander, erythema, pruritus, thickness/infiltration scores:* each rated on a scale from 0 = none to 4 = very severe Visits: baseline, week 2, 4, 6 and 8
Notes	This article was translated by Mrs. Sai Zhao of Systematic Review Solutions Ltd, China

Risk of bias

Bias	Authors' judgement	Support for judgement

He 2008 (*Continued*)

Random sequence generation (selection bias)	Unclear risk	Quote (page 254, abstract): "patients were randomly assigned" Comment: insufficient detail was reported about the method used to generate the allocation sequence. No further information in the article found by the translator
Allocation concealment (selection bias)	Unclear risk	This was not stated
Incomplete outcome data (attrition bias) All outcomes	Low risk	No ITT analysis reported, but data for all randomised participants provided
Selective reporting (reporting bias)	Low risk	All reported results were pre-specified outcomes in the methods section
Other bias	Low risk	No other source of bias identified
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	This was not stated
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	This was not stated

Hillstrom 1978

Methods	This was a randomised, double-blind, parallel-group trial
Participants	**Inclusion criteria of the trial** • Patients with diagnosis of scalp psoriasis **Exclusion criteria of the trial** • Infection (viral or microbial) of the skin • Pregnant or breastfeeding women • Concomitant medication with interfering potential to the course of disease **Washout period** This was not stated **Baseline characteristics** This was not stated
Interventions	A: betamethasone 17,21-dipropionate solution plus salicylic acid in 2% alcoholic solution, twice daily for 3 weeks (N = 39 participants) B: betamethasone valerate solution, twice daily for 3 weeks (N = 39 participants)
Outcomes	1. Overall treatment response (week 1, 2 and 3) matched with IGA: 'clear' 2. Adverse events (AE) (week 3) 3. Number of patients with at least 1 AE (week 3) 4. Cosmetic acceptability (week 3)

	Definition: *Overall treatment response (6-point scale):* graded as 'cure', 'marked improvement' (> 70%) , 'moderate improvement' (30% to 70%), 'slight improvement' (≤ 30%), 'no change' or 'worse' Visits: baseline, week 1, 2 and 3	
Notes	-	
Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Quote (page 48): "The patients were randomly allocated to one of the two groups [...]" Comment: insufficient detail was reported about the method used to generate the allocation sequence
Allocation concealment (selection bias)	Unclear risk	This was not stated
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote (page 49, Table III): "*patient No. 8 not evaluated" (for week 2), "**patient No. 72 not evaluated" (for week 3) No ITT analysis performed, but influence on outcome data not considered as significant
Selective reporting (reporting bias)	Low risk	All results were pre-specified outcomes in the methods section
Other bias	Low risk	No other source of bias identified
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote (page 48): "The bottles looked identical. Neither staff nor patients knew who received which treatment until the trial was finished." Comment: blinding probably sufficient
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote (page 48): "The bottles looked identical. Neither staff nor patients knew who received which treatment until the trial was finished." Comment: blinding probably sufficient

Hillstrom 1982

Methods	This was a randomised, double-blind, parallel-group trial
Participants	**Inclusion criteria of the trial** • Patients with diagnosis of scalp psoriasis **Exclusion criteria of the trial** • Infection of the skin (microbial or viral) • Pregnant women • Concomitant medication with interfering potential **Washout period** This was not stated **Baseline characteristics** • Data only for 51/53 randomised patients reported • Age (years, mean): 36 • Females N (%): 28 (54.9)
Interventions	A: betamethasone 17, 21-dipropionate plus salicylic acid 2% alcoholic solution, twice daily for 3 weeks (N = 25 participants) B: clobetasol propionate lotion, twice daily for 3 weeks (N = 25 participants) Participants could withdraw prior to week 3 if healing occurred
Outcomes	1. Induration (week 1, 2 and 3) 2. Lichenification (week 1, 2 and 3) 3. Crusting (week 1, 2 and 3) 4. Pruritus (week 1, 2 and 3) 5. Scaling (week 1, 2 and 3) 6. Pain (week 1, 2 and 3) 7. Investigator's overall evaluation (week 1, 2 and 3) 'cure' matched with IGA: 'clear' 8. Adverse events (AE) (week 3) 9. Number of patients with at least 1 AE (week 3) 10. Withdrawal due to AE (week 3) 11. Cortisol blood level (day -1, 3, 7, 14 and 21) Definition: *Investigator's overall evaluation:* patient's response from initial state rated as 'cure' = complete remission of signs and symptoms, 'marked improvement' = $\geq$ 70%, 'moderate improvement' = 30% to 70%, 'slight improvement' = $\leq$ 30%, 'failure' = no change or worse Visits: baseline, week 1, 2 and 3
Notes	-

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote (page 419): "patients were randomly allocated." Comment: insufficient detail was reported about the method used to generate the allocation sequence

Hillstrom 1982 (*Continued*)

Allocation concealment (selection bias)	Unclear risk	This was not stated
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote (page 419): "Two of the patients did not return at the follow-up visits. The remaining fifty-one patients [...] did not show any treatment group differences" Quote: (page 420): "One patient [...] has been excluded from the evaluation of efficacy due to concomitant therapy with methotrexate." Quote (page 420): "In the Dermovate group [...] three were treatment failure and two drop-outs" Comment: no ITT analysis and no adequate imputation method performed. Insufficient reporting about reasons for drop-out. However, attrition considered too small (< 10%) to have a relevant impact on outcome
Selective reporting (reporting bias)	High risk	Quote (page 420): "Pruritus [...] was the only symptom showing a statistically significant difference" Comment: insufficient reporting of this outcome. In addition, no data for other prespecified outcomes (induration, lichenification, crusting, pain, scaling) reported
Other bias	Unclear risk	Selection criteria for patients of which the blood cortisol level was assessed unclear. Selection bias possible
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote (page 419): "using a double-blind technique" Comment: insufficient detail was reported about the method used to blind study participants or personnel from the intervention a participant received
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote (page 419): "using a double-blind technique" Comment: insufficient detail was reported about the method used to blind the outcome assessor from the intervention a participant received

Hillstrom 1984

Methods	This was a randomised, double-blind, parallel-group trial
Participants	**Inclusion criteria of the trial** • Patients with diagnosis of scalp psoriasis **Exclusion criteria of the trial** • Patients treated with other corticosteroids 1 week prior to the study • Infection of the skin • Pregnant or breastfeeding women • Concomitant medication with interfering potential **Washout period** This was not stated **Baseline characteristics** • Total sign score (TSS), mean: A: 7.15, B: 7.4 calculated by review author • Females N (%): 24 (60)
Interventions	A: desoximethasone solution 0.25% plus salicylic acid 1%, twice daily for 2 weeks (N = 20 participants) B: betamethasone valerate solution 0.1%, twice daily for 2 weeks (N = 20 participants)
Outcomes	1. Degree of severity (week 1, 2 and 3) matched with TSS 2. Erythema (week 1, 2 and 3) 3. Infiltration (week 1, 2 and 3) 4. Pruritus (week 1, 2 and 3) 5. Scaling (week 1, 2 and 3) 6. Patient's overall evaluation (week 1, 2 and 3) 7. Investigator's overall evaluation (week 1, 2 and 3) 8. Adverse events (week 1, 2 and 3) 9. Cosmetic acceptability (week 1, 2 and 3) 10. Withdrawal due to treatment failure (week 3) Definition: *Outcomes 1 to 4.:* each graded on a score from 0 to 3: 0 = none, 1 = slight, 2 = moderate, 3 = severe *Degree of severity (0 to 12):* sum of erythema, scaling, infiltration and pruritus Patient's and investigator's overall evaluation: results rated as 'much better', 'slightly better', 'no change', 'slightly worse', 'much worse' *Cosmetic acceptability:* results rated by the patient as 'very good', 'good', 'moderate', 'poor', 'no answer' Visits: baseline, week 1, 2 and 3 (follow-up)
Notes	-

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote (page 171): "The randomization was done in advance by the manufacturer with the aid of a table with random digits and kept secret from the doctor during the

Hillstrom 1984 *(Continued)*

		study." Comment: probably sufficient sequent generation
Allocation concealment (selection bias)	Low risk	Quote (page 171): "The randomization was done in advance by the manufacturer with the aid of a table with random digits and kept secret from the doctor during the study." Comment: probably sufficient
Incomplete outcome data (attrition bias) All outcomes	High risk	Quote (page 172, Table 1): "Two patients are not included because they were treatment failures after the first week of treatment." Comment: no ITT analysis and no adequate imputation method performed
Selective reporting (reporting bias)	Low risk	All results were pre-specified outcomes in the methods section
Other bias	Low risk	No other source of bias identified
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote (page 171): "50ml bottle with identical appearance. [...] the two solutions differed in odour [...]" Comment: unclear if odour could affect outcome
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote (page 171): "50ml bottle with identical appearance. [...] The doctor was informed that the two solutions differed in odour and that he was not allowed to sniff them." Comment: blinding probably insufficiently ensured

Housman 2002

Methods	This was a randomised, single-blind, parallel-group trial
Participants	**Inclusion criteria of the trial** • Patients with stable or worsening scalp psoriasis • At least 18 years • At least 10% of the psoriatic scalp involvement • Global score of at least 3 and maximum 6 **Exclusion criteria of the trial** • Known allergy to topical corticosteroids (including betamethasone) • Allergy to nuts or peanuts

	• Additional non-psoriatic scalp condition • Severe or uncontrolled disease (including psoriasis) • Patients with history of treatment failure with topical corticosteroids within the previous year • 4 weeks prior to the study: systemic therapy (including corticosteroids, retinoids) or PUVA therapy • 2 weeks prior to the study: topical therapy (including retinoids, corticosteroids, medicated (e.g. coal tar, zinc, ketoconazole, selenium sulfide) shampoos) • Inadequate contraception • Concomitant medication with interfering potential **Washout period** • 2 weeks: topical therapy (see exclusion criteria) • 4 weeks: systemic therapy (see exclusion criteria) **Baseline characteristics** • Age (years, mean ± SD): 50 ± 14 • Females N (%): 13 (54) • Total severity score (TSS), mean ± SD: 5.2 ± 1.0
Interventions	A: betamethasone valerate 0.12% foam, twice daily for 2 weeks (N = 13 participants) B: fluocinolone acetonide 0.01% oil, once daily for 2 weeks (N = 12 participants) Cross-over took place after 2 weeks
Outcomes	1. TSS (day 14 and 28) 2. Investigator's assessment of global response (day 14 and 28) 3. Patient's assessment of global response (day 14 and 28) 4. Quality of life (QOL) (day 14 and 28) 5. Treatment preference measure (day 14 and 28) 6. Erythema (day 14 and 28) 7. Thickness (day 14 and 28) 8. Scaling (day 14 and 28) 9. Pruritus (day 14 and 28) Definition: *TSS:* sum of erythema, scaling and thickness score *Outcomes 4 to 7.:* each graded on a score from 0 to 4, higher scores indicating worse severity *Patient's and investigator's global response:* results rated on a scale from 0 to 6, higher scores indicating worse disease severity *Treatment preference measure (-21 to +21):* for both intervention each characteristic "ease of application", "application time", "absorption", "how it feels to odour", "how it feels on skin" and "how much it stains" were rated by the patient on a scale from -3 to 3: -3 = extremely unappealing, -2 = moderately unappealing, -1 = slightly unappealing, 0 = neutral, +1 = slightly appealing, +2 = moderately appealing and +3 = extremely appealing *QOL score:* patients graded each intervention on a scale from -3 to 3: -3 = will greatly worsen quality, -2 = will moderately worsen the quality, -1 = slightly worsen the quality, 0 = will have no effect, +1 = will slightly improve the quality, +2 = will moderately improve the quality and +3 = will greatly improve the quality Visits: baseline, day 14 and 28
Notes	This study was supported by Connetics Corporation

Housman 2002 (*Continued*)

Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Quote (page 28): "[...] each patient was randomized [...]" Comment: insufficient detail was reported about the method used to generate the allocation sequence
Allocation concealment (selection bias)	Unclear risk	Quote (page 28): "The physician-grader was blinded to treatment-group assignment." Comment: insufficient information about how allocation concealment was performed
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote (page 29): "Twenty-four of 25 patients completed the trial (1 patient was lost to follow-up)." Comment: no ITT analysis performed, but attrition not considered to have a significant impact on outcome
Selective reporting (reporting bias)	High risk	Quote (page 29): "total severity scores [...] were not significantly different for the medications" Comment: insufficient reporting of relevant outcomes: TSS, erythema, scaling, thickness, pruritus, investigator's/patient's global assessment of response and QOL score Quote (page 29): "As a final indication of preference, 18 patients requested prescriptions for particular medications at the conclusion of the study: 11 requested foam, 4 requested oil, and 1 requested both" Comment: this outcome was not pre-specified in the methods section
Other bias	Low risk	No other source of bias identified
Blinding of participants and personnel (performance bias) All outcomes	High risk	Quote (page 27): "[...] single-blind trial [...]" Comment: blinding of patients not possible due to physical difference of vehicles (foam versus oil). This might have an impact on subjective outcomes (pruritus, quality of life)

Housman 2002 (*Continued*)

Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote (page 27): "[...] single-blind trial [...]" Comment: insufficient reporting about method of blinding

Jarratt 1991

Methods	This was a randomised, double-blind, bilateral-paired comparison (split-face) trial
Participants	**Inclusion criteria of the trial** • Diagnosis of moderate to severe scalp psoriasis • Presentation of erythema and scaling in target lesions **Exclusion criteria of the trial** This was not stated **Washout period** This was not stated **Baseline characteristics** • Age (years, range): 19 to 78 • Females N (%): 32 (58) • Pruritus score: 1.8 (data out of graph)
Interventions	A: augmented betamethasone dipropionate 0.05% lotion, once daily for 3 weeks (N = 55 participants) B: clobetasol propionate 0.05% solution, once daily for 3 weeks (N = 55 participants) This was a split-face comparison
Outcomes	1. Degree of change in total severity/sign score (TSS) (day 4, 8, 15 and 22) 2. Global evaluation score (day 4, 8, 15 and 22) matched with IGA: 'clear', 'responder' 3. Induration (day 4, 8, 15 and 22) 4. Pruritus score (day 4, 8, 15 and 22) 5. Patient's preference of treatment (day 4, 8, 15 and 22) 6. Cosmetic acceptability (day 4, 8, 15 and 22) 7. Adverse events (AE) (day 22) Definition: *Degree of change:* difference between TSS during treatment and pre-treatment divided by the TSS at pre-treatment, multiplied by 100 *TSS (0 to 3):* sum of erythema, thickness, scaling and pruritus scores *Pruritus score (0 to 3):* 0 = none, 1 = mild, 2 = moderate, 3 = severe *Global evaluation score:* comparison of the patients' overall disease status at each return visit to their initial baseline condition Visits: baseline, day 4, 8, 15 and 22
Notes	This was a split-face comparison

Risk of bias

Jarratt 1991 (*Continued*)

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote (page 105): "Treatment assignment to the right or left side was determined by a random code." Comment: insufficient detail was reported about the method used to generate the allocation sequence
Allocation concealment (selection bias)	Unclear risk	This was not stated
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote (page 107, Table 2): "**Endpoint= the last valid visit, independent of the visit day on which it occurred." Comment: only for endpoint (day 22) data for the ITT population for efficacy analysis reported using the last observation carried forward (LOCF) imputation method. Other visits: per-protocol population
Selective reporting (reporting bias)	Low risk	All results were pre-specified outcomes in the methods section
Other bias	Low risk	No other source of bias identified
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote (page 105): "double-blind" Comment: insufficient detail was reported about the method used to blind study participants or personnel
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote (page 105): "double-blind" Comment: insufficient detail was reported about the method used to blind the outcome assessor

Jarratt 2004

Methods	This was a multicentre, randomised, double-blind, placebo-controlled, parallel-group trial
Participants	**Inclusion criteria of the trial** • Global severity score (GSS) of at least 3 • Age of at least 12 years **Exclusion criteria of the trial** • Pregnant, nursing or pregnancy-planning women • Patients with known allergy to components of intervention products • Systemic treatment for scalp psoriasis • Necessity of concomitant psoriasis therapy

	• Excessive UV exposure **Washout period** • Quote (page 368): "[...] specified wash-out periods for systemic anti-psoriatic medications." **Baseline characteristics** • Age (years, mean ± SD): A: 45.1 ± 15.28, B: 45.1 ± 15.71 • Females N (%): A: 57 (60), B: 25 (53.2) • Total severity score (TSS), mean ± SD: A: 6.5 ± 1.06, B: 6.7 ± 1.22
Interventions	A: clobetasol propionate 0.05% shampoo, once daily for 4 weeks (N = 95 participants) B: vehicle shampoo, once daily for 4 weeks (N = 47 participants) Assignment in 2:1 (A:B) ratio
Outcomes	**Primary outcome of the trial** 1. GSS ≤ 1 (week 4) **Secondary outcomes of the trial** 1. TSS (week 2, 4, 6) 2. Pruritus (week 2, 4, 6) 3. Erythema (week 2, 4, 6) 4. Scaling (week 2, 4, 6) 5. Induration/thickness of plaques (week 2, 4, 6) 6. Pruritus (week 2, 4, 6) 7. Percentage scalp surface are of involvement (week 4) 8. Investigator's global assessment of improvement (IAGI) (week 4) 9. Patient's global assessment of improvement (PAGI) (week 4) 10. Adverse events (AE) (week 4) 11. Withdrawal due to AE (week 4) 12. Maintenance of GSS less than or equal 1 (week 6) Definition: *GSS (0 to 5):* 0 = clear, 1 = minimal, 2 = mild, 3 = moderate, 4 = severe, 5 = very severe *TSS (0 to 9):* sum of erythema, thickness, scaling scores *Outcomes 2 to 5.:* each rated on score from 0*to* 3: 0 = none, 3 = severe IAGI/PAGI (0*to* 5): scale from 0 = clear to 5 = very severe (matched with IGA/PGA = responder) Visits: baseline, week 2, 4 and 6 (follow-up)
Notes	This study was supported by Galderma R&D Inc.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote (page 368): "computer-generated randomization list" Comment: probably adequate sequence generation
Allocation concealment (selection bias)	Unclear risk	This was not stated

Jarratt 2004 (*Continued*)

Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote (page 368-369): "The intent-to-treat (ITT) population was primary for the efficacy analysis. [...] with missing data imputed using the last observation carried forward (LOCF) [...]" Comment: incomplete outcome data sufficiently addressed
Selective reporting (reporting bias)	Low risk	All reported results were pre-specified outcomes in the methods section
Other bias	Low risk	No other source of bias identified
Blinding of participants and personnel (performance bias) All outcomes	Low risk	This was a double-blind trial with vehicle used as control
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	This was a double-blind trial with vehicle used as control, but insufficient reporting about how blinding of the investigator was performed and maintained

Jemec 2008

Methods	This was a multicentre, randomised, double-blind, active- and vehicle-controlled, 4-arm, parallel-group trial
Participants	**Inclusion criteria of the trial** • Global severity score (GSS) of at least 3 • Age: older than 18 years • At least 10% of psoriatic scalp involvement • Patients with history of psoriasis of the body • Investigator's assessment of clinical signs: at least 1 sign rated as 'moderate' and the other as at least 'slight' • Investigator's Global Assessment (IGA): 'mild' to 'severe' **Exclusion criteria of the trial** • Within previous 6 months: systemic treatment with biologicals (e.g., alefacept efalizumab, etanercept, infliximab) • Within previous 4 weeks: PUVA- or grenz ray therapy, systemic treatment with possible effect on scalp psoriasis (e.g. corticosteroids, vitamin D analogues, retinoids, immunosuppressants) • Within previous 2 weeks: topical treatment of the scalp (except for medicated shampoos and emollients), topical treatment of the face, trunk or limbs with very potent corticosteroids, UVB therapy • Planned initiation of or changes to concomitant medication that could affect scalp psoriasis (e.g. beta blockers, antimalaria drugs, lithium) • Planned exposure to the sun that may affect course of disease • Current diagnosis of erythrodermic, exfoliative or pustular psoriasis

Jemec 2008 (*Continued*)

	• Skin infection (fungal, bacterial, viral, parasitic) • Atrophic skin on the scalp • Co-morbidity: abnormality of calcium homeostasis associated with clinically significant hypercalcaemia, severe renal insufficiency, severe hepatic disorder **Washout period** • 2 weeks: topical anti-psoriatic treatments and UVB-therapy (according to exclusion criteria) • 4 weeks: systemic anti-psoriatic treatment (according to exclusion criteria) • 6 months: systemic biological treatments (according to exclusion criteria) **Baseline characteristics** • Age (years mean ± SD): A: 47.9 ± 15.4, B: 49.5 ± 15.9, C: 50.1 ± 16.6, D: 49.6 ± 15.8 • Females N (%): A: 282 (52.1), B: 323 (58.1), C: 151 (55.5), D: 75 (55.1) • Total sign score (TSS, mean ± SD): A: 6.7 ± 1.9, B: 6.9 ± 1.8, C: 6.8 ± 1.8, D: 7.0 ± 1.9
Interventions	A: calcipotriene 50 µg/g plus betamethasone dipropionate 0.5 mg/g gel, once daily for 8 weeks (N = 541 participants) B: betamethasone dipropionate 0.5 mg/g gel, once daily for 8 weeks (N = 556 participants) C: calcipotriene 50 µg/g gel, once daily for 8 weeks (N = 272 participants) D: placebo-vehicle, once daily for 8 weeks (N = 136 participants) Assignment in 4:4:2:1 ratio Quote (page 457): "Patients graded to have "absence of disease" [...] could stop treatment with study medication at the investigator's discretion, but after implementation of a protocol amendment were required to remain in the study and attend all clinic visits."
Outcomes	**Primary outcome of the trial** 1. IGA: "absence of disease"/"very mild disease" (week 8) **Secondary outcomes of the trial** 1. IGA (week 2 and 4) 2. TSS (week 1, 2, 4, 6 and 8) 3. Patient's assessment of overall response: "cleared"/"almost clear" (week 8) matched with PGA: responder 4. Redness (week 1, 2, 4, 6 and 8) 5. Thickness (week 1, 2, 4, 6 and 8) 6. Scaliness (week 1, 2, 4, 6 and 8) 7. Compliance (week 1, 2, 4, 6 and 8) 8. Adverse events (AE) (week 8) 9. Number of patients with at least 1 AE 10. Withdrawal due to AE (week 8) 11. Blood samples (week 8) Definition: *IGA (6-point scale):* disease severity rated as 'absence of disease', 'very mild disease', 'mild disease', 'moderate disease', 'severe disease' and 'very severe disease' *Patient's assessment of overall response (7-point scale):* extent and severity of scalp lesions rated as 'worse', 'unchanged', 'slight improvement', 'moderate improvement', 'marked improvement', 'almost clear' and 'cleared' *AE:* including severe AEs

Jemec 2008 (*Continued*)

	Blood samples: serum calcium and serum albumin *Erythema, thickness, scaling score:* 0 = no signs, 1 = slight signs, 2 = moderate signs, 3 = severe signs, 4 = very severe signs *TSS (0-12):* sum of erythema, thickness, scaling scores Visits: baseline, week 1, 2, 4, 6 and 8
Notes	This trial was supported by LEO Pharma A/S, Ballerup, Denmark

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Quote (page 456): "[...] according to a pre-planned computer-generated randomization code list [...]" Comment: probably adequate sequence generation
Allocation concealment (selection bias)	Unclear risk	This was not stated
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote (page 457-8): "All randomized patients were included in the full analysis set and were analysed for efficacy. [...] using last observation carried forward [...]" Comment: ITT analysis and appropriate imputation method performed
Selective reporting (reporting bias)	Low risk	All reported results were pre-specified outcomes in the methods section
Other bias	Low risk	No other source of bias identified
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote (page 457): "Packaging and labelling of the investigational products or placebo contained no evidence of their identity. [...] No effects of the Investigational Products revealed the identity of the individual treatment allocations" Comment: blinding probably sufficient
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote (page 457): "Packaging and labelling of the investigational products or placebo contained no evidence of their identity. [...] No effects of the Investigational Products revealed the identity of the individual treatment allocations" Comment: blinding probably sufficient

Josse 2005

Methods	This was a mono-centre, randomised, open-labelled, parallel-group trial
Participants	**Inclusion criteria of the trial** • Patients with scalp psoriasis with scaly erythematous plaques • At least 10% of psoriatic scalp involvement • Moderate lesion score (LS, 3 < LS < 6) **Exclusion criteria of the trial** This was not stated **Washout period** This was not stated **Baseline characteristics** • Age (years, mean ± SD): A: 49 ± 16, B: 45 ± 16 • Females N (%): A: 19 (47.5), B: 18 (46.2) • LS (mean ± SD): A: 5.28 ± 0.91, B: 5.18 ± 1.00 matched with TSS
Interventions	A: betamethasone dipropionate lotion plus RV3423A shampoo alternated with extra gentle shampoo, every day alternation for 4 weeks (N = 40 participants) B: betamethasone dipropionate lotion plus extra gentle shampoo, once daily for 4 weeks (N = 39 participants)
Outcomes	1. LS (week 2, 4 and 8) 2. Erythema (week 2, 4 and 8) 3. Induration (week 2, 4 and 8) 4. Desquamation (week 2, 4 and 8) 5. Pruritus (week 2, 4 and 8) 6. Investigator global efficacy assessment (IGA) (week 4 and 8) 7. Cosmetic acceptability (week 8) 8. Patients' satisfaction (week 8) Definition: *LS (0 to 9):* sum of desquamation, erythema and induration scores *Outcomes 2 to 4:* rated on scale from 0 to 3: 0 = absence, 3 = very severe *IGA:* not defined in this abstract ('healing' matched with 'clear') Visits: baseline, weeks 2, 4 and 8 (not relevant)
Notes	Total sign score (TSS) in data analysis calculated from LS by the review author After 4 weeks, participants were treated until week 8 in a manner that was not relevant for this review This was a conference abstract

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote (page 391): "randomized" Comment: insufficient detail was reported about the method used to generate the allocation sequence
Allocation concealment (selection bias)	Unclear risk	This was not stated

Josse 2005 (*Continued*)

Incomplete outcome data (attrition bias) All outcomes	Unclear risk	This was not stated
Selective reporting (reporting bias)	Unclear risk	Not all pre-specified outcomes reported (e. g. pruritus). Only abstract available
Other bias	Low risk	No other source of bias identified
Blinding of participants and personnel (performance bias) All outcomes	High risk	Quote (page 391): "open-labeled" Comment: no blinding performed
Blinding of outcome assessment (detection bias) All outcomes	High risk	Quote (page 391): "open-labeled" Comment: no blinding performed

Katz 1995

Methods	This was a 2-week, randomised, multicentre, investigator-blinded, parallel-group trial
Participants	**Inclusion criteria of the trial** • Age of at least 18 years • Patients diagnosed with moderate to severe scalp psoriasis (according to overall disease severity score) and otherwise healthy • At least 20% of scalp surface area involved • Stable or worsening disease course • Disease sign/symptom score of at least 6 (scaling score of at least 2 and scaling-erythema score total of at least 4) **Exclusion criteria of the trial** • Pregnant or breastfeeding women • Concomitant treatment for psoriasis (topical or systemic) • Skin atrophy in treatment area at baseline **Washout period** • 2 weeks: topical corticosteroids • 4 weeks: systemic corticosteroids **Baseline characteristics** • Baseline data only provided for the population of efficacy analysis (N = 193 participants) • Age (years, mean ± SD): A: 47.4 ± 16.3, B: 48.5 ± 16.9 • Females N (%): A: 52 (54), B: 55 (57) • Total severity score (TSS, mean): A: 8.4, B: 8.7
Interventions	A: augmented betamethasone dipropionate 0.05% lotion, twice daily for 2 weeks (N = 98 participants) B: clobetasol propionate 0.05% solution, twice daily for 2 weeks (N = 99 participants)
Outcomes	1. TSS (days 4, 8 and 15) 2. Pruritus (days 4, 8 and 15)

	3. Erythema (days 4, 8 and 15) 4. Scaling (days 4, 8 and 15) 5. Induration/thickness of plaques (days 4, 8 and 15) 6. Investigators' evaluation of global clinical response (days 4, 8 and 15) matched with IGA 7. Adverse events (AE) (days 4, 8 and 15) 8. Number of patients with at least 1 AE (day 15) 9. Number of patients with treatment failure (day 15) 10. Withdrawal due to AE (day 15) 11. Skin atrophy score (days 4, 8 and 15) 12. Patient satisfaction (day 15) 13. Cosmetic acceptability (days 15) Definition: *Investigators' evaluation of global clinical response (0 to 6): 1* = clear, 2 = marked improvement (matched with IGA = responder), 3 = moderate improvement, 4 = slight improvement, 5 = no change, 6 = exacerbation *TSS (0 to 12):* sum of erythema, thickness, pruritus, scaling scores *Outcomes 2 to 5 (0 to 3):* each rated as 0 = none, 1 = mild, 2 = moderate or 3 = severe *Skin atrophy score (0 to 3):* rated as 0 = none, 1 = mild, 2 = moderate or 3 = severe *Treatment failure:* no response to treatment or exacerbation Visits: baseline, days 4, 8 and 15
Notes	This study was supported by the Medical and Scientific Affairs Department of Schering Laboratories, Kenilworth, New Jersey

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Quote (page 391): "Patients were randomised" Comment: insufficient detail was reported about the method used to generate the allocation sequence
Allocation concealment (selection bias)	Unclear risk	This was not stated
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote (page 393): "One hundred ninety-seven patients [...] were enrolled; 196 patients [...] were included in the safety analysis and 193 (96 betamethasone dipropionate, 97 clobetasol propionate) in the efficacy analysis." Comment: number and reason for attrition and exclusion adequately reported for each group. They are balanced between groups and considered as too small to have a significant impact on outcomes

Katz 1995 (*Continued*)

Selective reporting (reporting bias)	Unclear risk	No data for pre-specified outcome of skin atrophy reported. This outcome is not relevant for this review
Other bias	Low risk	No other source of bias identified
Blinding of participants and personnel (performance bias) All outcomes	High risk	Quote (page 390): "investigator-blinded" Comment: no blinding of participants
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote (page 392): "Study medications were supplied in commercially available 50-mL bottles that were wrapped in an occlusive vinyl covering to prevent product identification." Comment: blinding of investigator probably sufficient

Kiss 1996

Methods	This publication reported 2 randomised, double-blind, parallel-group trials
Participants	**Inclusion criteria of the trial** • Age of at least 18 years • Patients with moderate scalp psoriasis = overall disease severity of at least grade 4 **Exclusion criteria of the trial** This was not stated **Washout period** • 1 week (not specifically defined for which kind of treatment) **Baseline characteristics** This was not stated
Interventions	A: calcipotriol 0.005% solution, twice daily for 8 weeks (N per group unclear) B: vehicle solution, twice daily for 8 weeks (N per group unclear) N = 235 participants
Outcomes	1. Erythema 2. Scaling 3. Plaque elevation 4. Pruritus 5. Overall disease severity 6. Physician's global assessment Definition: None of the outcomes was further defined. Visits: baseline, day 1, 4 and week 1, 2, 4, 6 and 8
Notes	This publication was published as a poster abstract and reported data about 2 parallel-group trials

Kiss 1996 (*Continued*)

Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Quote (page 301): "randomized" Comment: insufficient information provided on how sequence allocation was performed
Allocation concealment (selection bias)	Unclear risk	This was not stated
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Quote (page 301): "The total subjects enrolled for the first trial was 235 with 204 subjects completing the study." Comment: no ITT analysis performed. Number of drop-outs per group not reported. Number of drop-outs probably too low to introduce significant bias
Selective reporting (reporting bias)	High risk	Quote (page 301): "the mean score for all the psoriasis characteristics evaluated was statistically lower for the calcipotriene solution 0.005% group than its vehicle (p<0.009)" Comment: results insufficiently reported Quote (page 301): "mean serum calcium levels across treatments remained within the normal range" Comment: this outcome was not pre-specified
Other bias	Low risk	No other potential source of bias identified
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote (page 301): "double-blind" Comment: this study was vehicle-controlled. Blinding of participants therefore considered as probably sufficient
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote (page 301): "double-blind" Comment: insufficient information on how blinding of investigators was performed and maintained

Kiss 1996a

Methods	This publication reported 2 randomised, double-blind, parallel-group trials
Participants	**Inclusion criteria of the trial** • Age of at least 18 years • Patients with moderate scalp psoriasis = overall disease severity of at least grade 4 **Exclusion criteria of the trial** This was not stated **Washout period** • 1 week (not specifically defined for which kind of treatment) **Baseline characteristics** This was not stated
Interventions	A: calcipotriol 0.005% solution, twice daily for 8 weeks (N per group unclear) B: vehicle solution, twice daily for 8 weeks (N per group unclear) N = 239 participants
Outcomes	1. Erythema 2. Scaling 3. Plaque elevation 4. Pruritus 5. Overall disease severity 6. Physician's global assessment Definition: None of the outcomes was further defined Visits: baseline, day 1, 4 and week 1, 2, 4, 6 and 8
Notes	This publication was published as a poster abstract and reported data about 2 parallel-group trials

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote (page 301): "randomized" Comment: insufficient information provided on how sequence allocation was performed
Allocation concealment (selection bias)	Unclear risk	This was not stated
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Quote (page 301): "The second trial enrolled 239 subjects with 210 completing the study" Comment: no ITT analysis performed. Number of drop-outs per group not reported. Number of drop-outs probably too low to introduce significant bias

Kiss 1996a (*Continued*)

Selective reporting (reporting bias)	High risk	Quote (page 301): "the mean score for all the psoriasis characteristics evaluated was statistically lower for the calcipotriene solution 0.005% group than its vehicle (p<0.009)" Comment: results insufficiently reported Quote (page 301): "mean serum calcium levels across treatments remained within the normal range" Comment: this outcome was not pre-specified
Other bias	Low risk	No other potential source of bias identified
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote (page 301): "double-blind" Comment: this study was vehicle-controlled. Blinding of participants therefore considered as probably sufficient
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote (page 301): "double-blind" Comment: insufficient information on how blinding of investigators was performed and maintained

Klaber 1994

Methods	This was a multicentre, randomised, double-blind, prospective, parallel-group trial
Participants	**Inclusion criteria of the trial** • Patients diagnosed with stable, mild to moderate scalp psoriasis • History of psoriasis on the body **Exclusion criteria of the trial** • Severe (thick) scalp psoriasis • Seborrhoeic dermatitis of the face and scalp • Infection of the scalp (bacterial or fungal) • Systemic anti-psoriatic treatment (including UV therapy) within 8 weeks prior to the trial • Extensive psoriasis (> 50% of body surface area treated) • Concomitant therapy with > 400 IU vitamin D daily, calcium tablets or other interfering treatment (including lithium, potent topical or systemic corticosteroids) • Significant hepatic or renal disease • Hypercalcaemia • Pregnant or breastfeeding women • Women with inadequate contraception **Washout period** • 2 weeks (not specifically defined) **Baseline characteristics** • Age (years, mean ± SD): A: 45.2 ± 15.9, B: 42.9 ± 15.5

Klaber 1994 *(Continued)*

	• Females N (%): A: 112 (46.7), B: 118 (50.4) • Total sign score (TSS) (mean ± SD): A: 6.4 ± 1.7, B: 6.6 ± 1.7
Interventions	A: calcipotriol 50 µg/ml solution, twice daily for 4 weeks (N = 240 participants) B: betamethasone 17-valerate 1 mg/ml solution, twice daily for 4 weeks (N = 234 participants)
Outcomes	1. TSS (week 1, 2 and 4) 2. Pruritus (week 4) 3. Erythema (week 1, 2 and 4) 4. Scaling (week 1, 2 and 4) 5. Induration/thickness of plaques (week 1, 2 and 4) 6. Flaking (week 4) 7. Extend of scalp psoriasis (week 1, 2 and 4) 8. Investigator's overall assessment of treatment response (week 4) matched with IGA = 'clear' 9. Patient's overall assessment of treatment response (week 4) matched with PGA = 'clear' 10. Adverse events (AE) 11. Number of patients with at least 1 AE 12. Number of patients with treatment failure 13. Withdrawal due to AE 14. Patient's acceptability 15. Compliance (week 1, 2 and 4) 16. Blood sample analysis (week 1 and 4) 17. Relapse rate Definition: *Investigator's/patient's overall assessment of treatment response (1 to 5): 1* = worse, 2 = no change, 3 = slight improvement, 4 = marked improvement, 5 = cleared *TSS (0 to 12):* sum of erythema, thickness, scaling scores *Extend of scalp psoriasis:* 0 = no involvement, 1 = < 20%, 2 = 20% to 39%, 3 = 40% to 59%, 4 = 60% to 79%, 5 = 80% to 100% *Pruritus/flaking score:* rated on a scale from 0 to 3 by patient *Outcomes 3 to 5 (0 to 4):* each rated as 0 = absent, 1 = slight, 2 = moderate, 3 = severe and 4 = severest possible *Patient's assessment of acceptability:* greasiness, ease of application, whether treatment caused dryness of the scalp and odour were rated on as 1 = very poor, 2 = poor, 3 = acceptable, 4 = good, 5 = excellent *Blood sample analysis:* including haematology and biochemistry (with serum total calcium) *Relapse rate:* percentage of patients with satisfactory results after double-blind period, who experience relapse (increase in TSS to at least 50% of baseline at start of study) within 4 weeks after end of treatment Visits: baseline, week 1, 2, 4 and 8 (optional follow-up)
Notes	This study was sponsored and supported by Leo Pharmaceutical Products, Denmark
Risk of bias	

Klaber 1994 (*Continued*)

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote (page 679): "patients were randomized" Comment: insufficient detail was reported about the method used to generate the allocation sequence
Allocation concealment (selection bias)	Unclear risk	This was not stated
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote (page 680): "474 were randomized [...] Twenty-nine patients [...] withdrew from the study, leaving 445 patients [...]" Comment: no ITT analysis performed: data for 236/240 (calcipotriol group) and data for 232/234 (BTM group) reported in efficacy analysis. Missing outcome data balanced between groups and reasons for drop-outs similar. Proportion of missing outcomes considered as not enough to introduce a clinically relevant impact on the intervention effect estimate
Selective reporting (reporting bias)	Low risk	All reported results were pre-specified outcomes in the methods section
Other bias	Low risk	No other source of bias identified
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote (page 679): "double-blind treatment" Comment: insufficient detail was reported about the method used to blind study participants or personnel from the intervention a participant received
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote (page 679): "double-blind treatment" Comment: blinding method of outcome assessment insufficiently reported

Klaber 2000

Methods	This was a multicentre, prospective, randomised, open-label trial
Participants	**Inclusion criteria of the trial** • Patients diagnosed with mild to moderate scalp psoriasis • History or presence of psoriasis on the body • At least 18 years of age

	Exclusion criteria of the trial • Severe (thick) scalp psoriasis • Acute guttate, pustular or erythrodermic psoriasis • Psoriasis limited only to face, or limbs, or trunk • Topical anti-psoriatic treatment within 2 weeks prior to the trial • Systemic anti-psoriatic treatment (including PUVA/UVB-therapy) within 4 weeks prior to the trial • Extensive psoriasis (> 50% of body surface area treated) • Concomitant therapy with > 400 IU vitamin D or > 5000 IU daily, calcium tablets or other interfering treatment • Significant hepatic or renal disease • Pregnant or breastfeeding women • Women seeking for pregnancy • Known hypersensitivity to study medication • Hypercalcaemia **Washout period** • 2 weeks for topical treatment (as described above) • 4 weeks for systemic treatment (as described above) **Baseline characteristics** • Age (years, mean ± SD): A: 45.8 ± 15.6, B: 44.7 ± 16.1 • Females N (%): A: 115 (48), B: 113 (48) • Total sign score (TSS, mean ± SD): A: 5.1 ± 1.4, B: 5.0 ± 1.6
Interventions	A: calcipotriol 50 µg/ml solution, twice daily for 8 weeks (N = 238 participants) B: coal tar 1% plus coconut oil 1% plus salicylic acid 0.5% shampoo, once daily for 8 weeks (N = 237 participants)
Outcomes	1. TSS (week 4 and 8) 2. Pruritus (week 4 and 8) 3. Erythema (week 4 and 8) 4. Scaling (week 4 and 8) 5. Thickness (week 4 and 8) 6. Flaking (week 4 and 8) 7. Extend of scalp psoriasis (week 4 and 8) 8. Investigators' overall assessment (week 4 and 8) 9. Patient's self assessment (week 8) 10. Adverse events (AE) (week 8) 11. Number of patients with at least 1 AE (week 8) 12. Withdrawal due to AE (week 8) 13. Blood sample analysis (week 4 and 8) 14. Urine sample analysis (week 4 and 8) Definition: *Investigators' overall assessment (0 to 5): 0* = worse, 1 = no change, 2 = slight improvement, 3 = moderate improvement, 4 = marked improvement, 5 = cleared *Patients' self assessment:* severity of scalp psoriasis, flaking, pruritus and effectiveness of treatment measured on 100 mm visual analogue scales with left limit (0 mm) representing worst and right limit (100 mm) representing best assessment *TSS (0 to 12):* sum of erythema, thickness, scaling scores *Extend of scalp psoriasis:* 0 = no involvement, 1 = < 20%, 2 = 20% to 39%, 3 = 40% to

	59%, 4 = 60% to 79%, 5 = 80% to 100% *Outcomes 3 to 5 (0 to 4):* each rated as 0 = absent, 1 = slight, 2 = moderate, 3 = severe, 4 = severest possible *Blood sample analyses:* including haematology and biochemistry (serum total calcium, phosphate, albumin, bilirubin, alkaline, phosphatase, alanine aminotransferase, creatinine) *Urine sample analysis:* including urinary calcium and urinary creatinine Visits: baseline, week 4 and 8
Notes	This trial consisted of a second uncontrolled, non-randomised, open-labelled phase after 8 weeks (until week 24) The study was sponsored by Leo Pharmaceuticals

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Quote (page 22): "Treatment was allocated at random." Comment: insufficient detail was reported about the method used to generate the allocation sequence
Allocation concealment (selection bias)	Unclear risk	This was not stated
Incomplete outcome data (attrition bias) All outcomes	High risk	Quote (page 23): "Fifty-two patients were excluded from analysis because of loss to follow-up [...] or stopping study medication [...] The efficacy population therefore consisted of 423 patients" Comment: no ITT analysis performed. More than 10% drop-outs in each group
Selective reporting (reporting bias)	Low risk	All reported results were pre-specified outcomes in the methods section
Other bias	Low risk	No other source of bias identified
Blinding of participants and personnel (performance bias) All outcomes	High risk	Quote (page 22): "open-label design" Comment: no blinding performed
Blinding of outcome assessment (detection bias) All outcomes	High risk	Quote (page 22): "open-label design" Comment: no blinding performed

Kragballe 2009

Methods	This was an international, multicentre, randomised, investigator-blind, parallel-group trial
Participants	**Inclusion criteria of the trial** • Age of at least 18 years • Diagnosis of moderate to severe scalp psoriasis amenable to topical treatment • At least 10% of the scalp surface involved • Total sign score (TSS) of at least moderate or each individual sign of at least slight • Investigator's global assessment of disease severity (IGA) of at least "moderate" **Exclusion criteria of the trial** • Within 4 weeks prior to study: PUVA or Grenz ray, systemic anti-psoriatic therapy • Within 2 weeks prior to study: UVB therapy, topical anti-psoriatic therapy on the scalp, very potent topical corticosteroids the body • Within 6 months prior to study: systemic biological therapy • Unstable forms of psoriasis • Skin disease confounding psoriasis assessment • Infection of the skin • Infestations or atrophy of the scalp • Abnormalities in calcium homeostasis • Severe renal or hepatic co-morbidity • Concomitant therapy that may affect scalp psoriasis • Pregnant or lactating women **Washout period** • 2 weeks to 6 months (as mentioned in exclusion criteria) **Baseline characteristics** • Age (years, mean ± SD): A: 50.8 ± 15.3, B: 51.4 ± 15.6 • Females N (%): A: 117 (56.5), B: 61 (58.1) • TSS (mean ± SD): A: 7.4 ± 1.7, B: 7.1 ± 1.8 • Skindex-16 (mean ± SD): A: 51.5 ± 23.6, B: 49.6 ± 21.0
Interventions	A: calcipotriol 50 µg/g plus betamethasone dipropionate 0.5 mg/g gel, once daily for 8 weeks (N = 207 participants) B: calcipotriol 50 µg/g solution, twice daily for 8 weeks (N = 105 participants) Randomized in a 2:1 ratio Patients whose scalp psoriasis cleared before the end of the 8-week treatment period stopped treatment, but remained in the study
Outcomes	**Primary outcome of the trial** 1. IGA: minimal/clear (week 8) **Secondary outcome of the trial** 1. Total sign score (TSS) (week 1, 2, 4, 6 and 8) 2. Erythema (week 1, 2, 4, 6 and 8) 3. Scaling (week 1, 2, 4, 6 and 8) 4. Thickness (week 1, 2, 4, 6 and 8) 5. IGA: minimal or clear (week 2 and 4) 6. Patient's global assessment (PGA): "clear"/"very mild" (week 8) 7. Pruritus (week 1, 2, 4, 6 and 8) 8. Relapse 9. Time to relapse

	10. Rebound 11. Compliance (week 1, 2, 4, 6 and 8) 12. Quality of life (QOL) - SF-36v2 (week 2, 4 and 8) 13. QOL - Skindex-16 (week 2, 4 and 8) 14. Product acceptability (week 4) 15. Adverse events (AE) (week 1, 2, 4, 6 and 8) 16. Number of patients with at least 11 AE (week 8) 17. Number of patients with drug-related AE (week 8) 18. Withdrawals due to AE (week 8) Definition: *TSS (0 to 12):* sum of erythema, thickness, scaling scores *Outcomes 2 to 4 (0 to 4):* each rated as 0 = absent, 1 = slight, 2 = moderate, 3 = severe, 4 = very severe *IGA (6-point scale):* 0 = absent, 1 = very mild, 2 = mild, 3 = moderate, 4 = severe, 5 = very severe *PGA (5-point scale):* clear, very mild, mild, moderate, severe *Pruritus:* rated by the patient as "none", "mild", "moderate", "severe" *Relapse:* recurrence of at least "moderate" disease according to IGA *Time to relapse:* number of days from the last application of medication to relapse *Compliance:* self reported use of study medication *Rebound:* increase in one category in IGA from baseline *Blood sample analyses:* including haematology and biochemistry (serum calcium) *QOL (published from* Ortonne 2009*):* • *SF-36v2:* multi-item scale assessing eight general health concepts, each rated on an individual scale: physical functioning, limitations due to physical health problems (role physical), bodily pain, general health, vitality, social functioning, limitations due to emotional problems (role emotional) and mental health • *Skindex-16:* questionnaire that comprises 16 questions related to skin conditions *Product acceptability:* rated on a 7-point scale ranging from "very unacceptable" to "very acceptable" Visits: baseline, week 1, 2, 4, 6, 8 and 12, 16 (both: follow-up)
Notes	The study was sponsored by LEO Pharma A/S, Ballerup, Denmark Statistical analysis was conducted LEO Pharma A/S, Denmark and Caudex Medical, UK (supported by LEO Pharma A/S) assisted with manuscript preparation Additional data about quality of life provided by Ortonne 2009

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote (page 160): "a computer-generated schedule randomized patients 2 : 1 to treatment [...]" Comment: probably done
Allocation concealment (selection bias)	Low risk	Quote (page 160): "Each patient was assigned an exclusive randomization code in ascending order."

Kragballe 2009 *(Continued)*

		Comment: probably sufficient
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote (page 161): "The intent-to-treat (ITT) population [...] was used for analysis of all efficacy endpoints. [...] The safety population comprised all patients who received any treatment with study medication and for whom the presence or confirmed absence of AEs was available. A last observation carried forward (LOCF) approach accounted for missing data." Comment: incomplete outcome data sufficiently addressed
Selective reporting (reporting bias)	Low risk	All reported results were pre-specified outcomes in the methods section
Other bias	Low risk	No other source of bias identified
Blinding of participants and personnel (performance bias) All outcomes	High risk	Quote (page 160): "Due to differences in the dosing frequency and formulation between the investigational products, it was not possible to undertake a double-blind study." Comment: lack of blinding not considered as likely to influence the primary outcomes (TSS, IGA). Subjective outcomes (i.e. PGA and QOL scores) likely to be biased
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote (page 160): "The packaging and labels for the medications were identical [...] dispensed by a designated independent non assessor, to maintain blinding of investigators performing the assessments. Patients were instructed not to reveal the formulation or dosing frequency of their medication to their assessor." Comment: blinding of outcome assessment probably sufficient

Köse 1997

Methods	This was a randomised, parallel-group, active-controlled trial
Participants	**Inclusion criteria of the trial** • Psoriasis of the scalp **Exclusion criteria of the trial** This was not stated **Washout period**

	This was not stated **Baseline characteristics** • Quote (page 287): "The two groups were matched at baseline for age, sex and history of psoriasis."
Interventions	A: calcipotriol 50 µg/g ointment (occlusive bandaging over night), once daily for 5 days (N = 21 participants) B: clobetasol 17-propionate scalp solution, twice daily for 10 days (N = 22 participants)
Outcomes	1. Total sign score (TSS) 2. Erythema 3. Scaling 4. Thickness 5. Adverse events 6. Number of patients with at least 1 AE 7. Blood sample analysis Definition: *TSS (0 to 9):* sum of erythema, thickness, scaling scores *Outcomes 2 to 4 (0 to 3):* each rated as 0 = absent, 1 = slight, 2 = moderate, 3 = severe *Blood sample analyses:* including haematology and biochemistry (serum calcium) Visits: before and after each treatment and additionally on day 10 and 20 (follow-up)
Notes	This trial was presented as a correspondence letter

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Quote (page 287): "43 patients were randomly allocated" Comment: insufficient detail was reported about the method used to generate the allocation sequence
Allocation concealment (selection bias)	Unclear risk	This was not stated
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote (page 287): "All patients completed the study." Comment: no use of ITT analysis reported, but no loss to follow-up. Incomplete outcome data sufficiently addressed
Selective reporting (reporting bias)	High risk	Quote (page 287): "85% of patients in the calcipotriol group and 91% of patients in the clobetasol group showed clearance or marked improvement of their scalp psoriasis" Comment: this outcome was not pre-specified in the methods section. Insufficient re-

Köse 1997 *(Continued)*

		porting of TSS and its subscores
Other bias	Low risk	No other source of bias identified
Blinding of participants and personnel (performance bias) All outcomes	High risk	No blinding reported and highly unlikely due to difference in treatment application and duration between the 2 intervention groups
Blinding of outcome assessment (detection bias) All outcomes	High risk	No blinding reported and highly unlikely due to difference in treatment application and duration between the 2 intervention groups

Lassus 1976

Methods	This was a prospective, double-blind, active-controlled, parallel-group trial
Participants	**Inclusion criteria of the trial** • Patients diagnosed with moderate to severe scalp psoriasis • At least 15 years of age **Exclusion criteria of the trial** • No active treatment of the lesions within 1 month prior to the study **Washout period** • 4 weeks **Baseline characteristics** • Total sign score (TSS, mean): A: 7.55, B: 7.3 calculated by review author
Interventions	A: clobetasol propionate 0.05% solution, twice daily for 2 weeks (N = 20 participants) B: betamethasone-17,21-dipropionate 0.05% solution, twice daily for 2 weeks (N = 20 participants)
Outcomes	1. TSS (week 1 and 2) 2. Pruritus (week 1 and 2) 3. Erythema (week 1 and 2) 4. Scaling (week 1 and 2) 5. Thickness (week 1 and 2) 6. Adverse events (AE) (week 2) 7. Number of patients with at least 1 AE (week 2) 8. Withdrawal due to AE (week 2) Definition: *Outcomes 1 to 4 (0 to 3):* each rated as 3 = severe, 2 = moderate, 1 = mild or 0 = absent *TSS (0 to 9):* calculated with given data: sum of erythema, scaling, thickness Visits: baseline, week 1 and 2
Notes	-
Risk of bias	

Lassus 1976 (*Continued*)

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote (page 366): "patients were non-selectively divided into two groups" Comment: considering the year of publication, this was interpreted as a randomised study, but insufficient detail was reported about the method used to generate the allocation sequence
Allocation concealment (selection bias)	Unclear risk	This was not stated
Incomplete outcome data (attrition bias) All outcomes	Low risk	No loss to follow-up. Data for all participants provided.
Selective reporting (reporting bias)	Low risk	All reported results were pre-specified outcomes in the methods section
Other bias	Low risk	No other source of bias identified
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote (page 365): "double-blind evaluation" Comment: insufficient detail was reported about the method used to blind study participants or personnel from the intervention a participant received
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote (page 365): "double-blind evaluation" Comment: insufficient detail was reported about the method used to blind the outcome assessor

Lepaw 1978

Methods	This was a double-blind, placebo-controlled, within-patient trial
Participants	**Inclusion criteria of the trial** • Bilateral psoriatic lesions of the scalp • Lesions similar in severity and persistence **Exclusion criteria of the trial** • No concomitant anti-psoriatic treatment of the scalp were allowed **Washout period** This was not stated **Baseline characteristics** • Age (years, range): 14 to 75 • Females N (%): 13 (44.8)

Lepaw 1978 (*Continued*)

Interventions	A: halcinonide solution 0.1%, 3 times daily for 2 weeks (N = 29 participants) B: placebo-vehicle, 3 times daily for 2 weeks (N = 29 participants) This was a split-face comparison
Outcomes	1. Overall evaluation of therapeutic response (week 2) 2. Comparative evaluation (week 1 and 2) 3. Adverse events (AE) (week 2) 4. Number of patients with drug-related AE (week 2) Definition: *Overall evaluation of therapeutic response:* rapidity and completeness of the therapeutic response rated as excellent (matched with IGA = responder), good, fair or poor *Comparative evaluation:* comparison of preparation judged as 'markedly superior' if the difference was easily discernible and 'slightly superior' if the difference was only barely discernible Visits: baseline, week 1 and 2
Notes	This was a split-face comparison

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote (page 572): "The designation of right or left treatment site was predetermined for the respective drugs by a randomised assignment schedule." Comment: insufficient detail was reported about the method used to generate the allocation sequence
Allocation concealment (selection bias)	Unclear risk	This was not stated
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote (page 572): "Results in two other patients were excluded from the evaluation because each had received, and responded well to, other topical steroids within a week prior to entering the present study. [...] therapeutic benefits [...] may possibly have biased the results of therapy with halcinonide." Comment: reason for missing outcome not related to true outcome. In addition, the number of excluded participants was considered as too small (< 10%) to have a significant impact on outcomes
Selective reporting (reporting bias)	Low risk	All reported results were pre-specified outcomes in the methods section

Lepaw 1978 (*Continued*)

Other bias	High risk	Quote (page 572): "patients were instructed to apply the formulation [...] on one side of the scalp and then, after thoroughly cleansing the hands, apply the solution designated for the contralateral lesions [...] three times a day" Comment: the treatment procedure appears difficult. The authors did not state how they ensured that the patient applied the medication correctly. This may have introduced bias
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote (page 572): "Treatment was administered in a double-blind fashion, [...] supplied in identical bottles labeled only with the patient number and the side of the body to which the contents were to be applied." Comment: this blinding method was probably sufficient. In addition, this trial was vehicle-controlled
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote (page 572): "Treatment was administered in a double-blind fashion, [...] supplied in identical bottles labeled only with the patient number and the side of the body to which the contents were to be applied." Comment: this blinding method was probably sufficient. In addition, this trial was vehicle-controlled

Luger 2008

Methods	This was a 52-week, international, prospective, randomised, double-blind, active-controlled, parallel-group trial
Participants	**Inclusion criteria of the trial** • Patients diagnosed with mild to moderate scalp psoriasis • Lesions amenable to topical treatment • At least 18 years of age • Outpatients • History of psoriasis of the body • At least 10% of scalp surface involved • Investigator's global assessment (IGA) rated as at least "moderate" **Exclusion criteria of the trial** • Topical scalp treatment • Systemic treatment (including PUVA/UVB therapy, grenz ray or biologicals) affecting course of disease • Disorders of calcium metabolism associated with hypercalcaemia

Luger 2008 (*Continued*)

	Washout period • 28 days **Baseline characteristics** • Age (years, mean ± SD): A: 48.5 ± 15.3, B: 49.0 ± 14.7 • Females N (%): A: 234 (55.8), B: 242 (56.1) • 'moderate' IGA, N (%): A: 233 (55.6), B: 239 (55.5) These are baseline data for the safety analysis set, A: 419, B: 431
Interventions	A: calcipotriol 50 µg/g plus betamethasone dipropionate 0.5 mg/g gel, once daily for 52 weeks (N = 429 participants) B: calcipotriol 50 µg/mg (same vehicle), once daily for 52 weeks (N = 440 participants) If clearance occurred during study, patients were allowed to stop treatment, but remained in the study. If recurrence occurred, they restarted the same treatment
Outcomes	**Primary outcome of the trial** 1. Adverse drug reactions (ADRs) 2. Adverse events (AEs) associated with long-term corticosteroid treatment on the scalp **Secondary outcome of the trial** 1. Number of patients with controlled disease (according to IGA) (every 4 weeks until week 52) 2. Patient rating of treatment efficacy (week 52) 3. Withdrawal due to treatment failure (week 52) 4. Withdrawal due to AE (every 4 weeks until week 52) 5. Total withdrawals (week 52) 6. Compliance (week 52) Definition: *IGA (6-point scale):* severity of disease rated as 'absent', 'very mild', 'mild', 'moderate', 'severe', or 'very severe'; 'absent' to 'mild' = 'satisfactory' *Patient ratings of treatment efficacy:* rated as 'satisfactory' or 'not satisfactory' *Compliance*: non-compliance was defined as failure to use the treatment for any reason other than no treatment being required Visits: baseline, every 4 weeks until week 52 (14 visits)
Notes	The study was sponsored by LEO Pharma, Ballerup, Denmark

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Quote (page 322): "patients were randomized in a 1:1 ratio" Comment: insufficient detail was reported about the method used to generate the allocation sequence
Allocation concealment (selection bias)	Unclear risk	This was not stated

Luger 2008 (*Continued*)

Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote (page 323): "Safety analyses comprised all randomized patients who received any trial medication and for whom information was available. [...] Efficacy analyses were performed on the full analysis set, which included all randomized patients." Comment: incomplete outcome data sufficiently addressed
Selective reporting (reporting bias)	Low risk	All reported results were pre-specified outcomes in the methods section
Other bias	Low risk	No other source of bias identified
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote (page 322): "double-blind" Quote (page 323): "same vehicle" Comment: blinding probably sufficient
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote (page 322): "double-blind" Quote (page 323): "same vehicle" Comment: insufficient detail reported about method used to ensure blinding of outcome assessor

Medansky 1974

Methods	This was a multicentre, randomised, double-blind, vehicle-controlled, parallel-group trial
Participants	**Inclusion criteria of the trial** • Patients diagnosed with scalp psoriasis **Exclusion criteria of the trial** • Topical or systemic treatment with corticosteroids within 1 week prior to the study **Washout period** • 1 week for topical and systemic corticosteroids **Baseline characteristics** This was not stated
Interventions	A: betamethasone valerate 0.1% lotion, for 2 weeks (N = 117 participants) B: placebo vehicle, for 2 weeks (N = 102 participants) Frequency of application per day unknown
Outcomes	1. Physician evaluation of efficacy (day 3, 7 and 14) 2. Patient's evaluation of efficacy (day 3, 7 and 14) 3. Physician evaluation as compared to his standard therapy (day 3, 7 and 14) 4. Excoriation (day 3, 7 and 14) 5. Inflammation (day 3, 7 and 14) 6. Scaling (day 3, 7 and 14)

	7. Crusting (day 3, 7 and 14) 8. Pruritus (day 3, 7 and 14) Definition: *Investigator's evaluation of efficacy:* treatment results rated as 'excellent' = complete clinical control of the condition (75% or more), 'good' = moderate control (50% to 75%), 'fair' = partial control (less than 50%), 'poor' = no effect or 'exacerbation' *Outcomes 4 to 8:* evaluated by investigator for treatment differences Visits: baseline, day 3, 7 and 14
Notes	-

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote (page 503): "Each patient was assigned a sequential admission number corresponding to a treatment unit outlined on the accompanying randomization schedule." Comment: insufficient detail was reported about the method used to generate the allocation sequence
Allocation concealment (selection bias)	Unclear risk	This was not stated
Incomplete outcome data (attrition bias) All outcomes	Low risk	Data for all randomised patients reported
Selective reporting (reporting bias)	High risk	Data for the following pre-specified outcomes insufficiently reported: patient's evaluation of efficacy, physician evaluation as compared to his standard therapy, physician evaluation of efficacy at each visit, physician's evaluation of excoriation, inflammation, scaling, crusting, pruritus
Other bias	Low risk	No other source of bias identified
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote (page 503): "double-blind technique" Comment: this was a vehicle-controlled trial
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote (page 503): "double-blind technique" Comment: insufficient detail reported about method used to ensure blinding of outcome assessor

Monk 1995

Methods	This was a multicentre, randomised, single-blind, active-controlled, parallel-group trial
Participants	**Inclusion criteria of the trial** • Patients diagnosed with mild to moderate scalp psoriasis **Exclusion criteria of the trial** • Less than 10 years of age • Systemic anti-psoriatic treatment • Concomitant treatment with coal tar ointment **Washout period** This was not stated **Baseline characteristics** • Total score (mean): A: 7.5, B: 7.0
Interventions	A: ung cocois ointment (12% coal tar, 4% precipitated sulphur and 2% salicylic acid in a coconut oil base), overnight for 2 weeks (N = 18 participants) B: coal tar shampoo, once daily for 2 weeks (N = 16 participants) Participants whose TSS had fallen by less than 50% by week 2 were crossed over to the alternative treatment and re-assessed at week 4
Outcomes	1. Investigator global assessments (IGA) (week 2) 2. Patient global assessments (PGA) (week 2) 3. "Total score" (week 2) matched with TSS 4. Erythema (week 2) 5. Infiltration/thickness (week 2) 6. Scaling (week 2) 7. Adverse event (AE) (week 2) 8. Withdrawal due to AE (week 2) 9. Number of patients with at least 1 AE (week 2) 10. Treatment failure (week 2) Definition: *"Total score"/TSS (0 to 9):* sum of sign scores (0 to 3) of erythema, scaling and thickness *Outcomes 4 to 6 (0 to 3):* each rated as 0 = none, 1 = mild, 2 = moderate, 3 = severe *Treatment failure:* participants whose TSS had fallen by less than 50% by week 2 Visits: baseline, week 2 and 4
Notes	'Total score' of the trial was interpreted as TSS by the review author This study was sponsored by Bioglan Laboratories Ltd, Hitchin, UK

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote (page 159): "patients were randomly allocated to treatment" Comment: insufficient detail was reported about the method used to generate the allocation sequence
Allocation concealment (selection bias)	Unclear risk	This was not stated

Monk 1995 (*Continued*)

Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote (page 160): "Two patients in the Cocois group stopped treatment" Comment: insufficient information at which time point participants stopped treatment and if the authors included all data in the outcome assessment. However, number of drop-outs considered as too small to have a relevant impact on outcomes
Selective reporting (reporting bias)	Unclear risk	Quote (page 160): "Investigator global assessments at 2 weeks indicated an improvement of 73% in the Cocois group and 42% in the Polytar group. Patient global assessments indicated a 73% improvement in the Cocois group and 33% in the Polytar group." Comment: detailed data for IGA and PGA insufficiently reported
Other bias	Low risk	No other source of bias identified
Blinding of participants and personnel (performance bias) All outcomes	High risk	Quote (page 161): "the highly recognizable physical properties of Cocois made it impossible to 'blind' the patients" Comment: no blinding of participants performed
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote (page 160): "The doctor assessing the patient was 'blind' to the treatment allocated, and detailed instructions were given to the patient by the hospital pharmacist." Comment: blinding probably sufficient

NCT01195831

Methods	This was a multicentre, randomised, active-controlled, investigator-blinded, parallel-group trial
Participants	**Inclusion criteria of the trial** • Age: 18 to 65 years • Investigator's assessment of clinical signs of the scalp at least ≥ 2 in one of the clinical signs, redness, thickness and scaliness, and at least 1 in each of the other 2 clinical signs, and total score ≥ 4 • At least 10% scalp surface involvement • History or current clinical signs of psoriasis on trunk and/or limbs **Exclusion criteria of the trial** • Patients with guttate, erythrodermic, exfoliative or pustular psoriasis.

	• Following conditions present on the scalp area: viral lesions, fungal and bacterial skin infections, parasitic infections, skin manifestations in relation to syphilis or tuberculosis, rosacea, acne vulgaris, acne rosacea, atrophic skin, striae atrophicae, fragility of skin veins, ichthyosis, ulcers and wounds • Any other inflammatory skin diseases that may confound the evaluation of scalp psoriasis • Pregnant and breastfeeding women • Inadequate contraception • Within 2 weeks prior to first visit: topical treatment of psoriasis on non-scalp psoriasis lesions with potent or very potent (WHO group III-IV) corticosteroids, topical treatment of immunomodulator, any topical treatment of the scalp (except for non-steroid medicated shampoos and emollients, other types of psoriasis treatment, e. g. Chinese medicine, processed Chinese medicine, or hot spring, etc. • Within 4 weeks prior to second study visit: systemic anti-psoriatic treatment • Within 4 weeks prior to first study visit: PUVA therapy • Within 2 weeks prior to first visit: UVB therapy • Within 12 weeks prior to first visit or during study: treatment with biological therapies • Planned initiation of, or changes to, concomitant medication that could affect scalp psoriasis during the study • Severe impaired renal or hepatic or cardiovascular function • Abnormality of calcium homeostasis • Cushing's disease or Addison's disease • Hypersensitivity to the study medication **Washout period** • 2 weeks to first visit (as mentioned above) • 4 weeks to second visit (as mentioned above) • 12 weeks to first visit (as mentioned above) **Baseline characteristics** • Age (years, mean ± SD): A: 39.87 ± 13.15, B: 38.73 ± 11.87 • Females N (%): A: 47 (39), B: 55 (44)
Interventions	A: calcipotriol 50 µg/g plus betamethasone dipropionate 0.5 mg/g gel, once daily for 4 weeks (N = 120 participants) B: calcipotriol 50 µg/ml solution, twice daily for 4 weeks (N = 124 participants)
Outcomes	**Primary outcome of the trial** 1. Investigator's Global Assessment of Disease Severity (IGA): 'controlled disease' (week 4) matched with IGA 'responder' **Secondary outcomes of the trial** 1. IGA: 'controlled disease' (week 2) 2. Patient's Global Assessment of Disease Severity (PGA): 'controlled disease' (week 2 and 4) matched with PGA 'responder' 3. Patients with success (week 4) 4. Percentage of patients with success for each clinical sign (redness, thickness, scaliness) (week 4) 5. Patient's without itching (week 4) 6. Quality of life (week 2 and 4) 7. Number of patients with at least 1 adverse event (AE) (week 4)

	8. Withdrawal due to AE (week 4) Definition: *IGA (6-point scale):* disease severity rated as 'clear', 'minimal', 'mild', 'moderate', 'severe' and 'very severe' *IGA 'controlled disease':* patients rated as 'clear' or 'minimal' *PGA:* scalp psoriasis rated on a 5-point scale by the patient as 'clear', 'very mild', 'mild', 'moderate', 'severe'. This assessment was made prior to the investigator's assessments *PGA 'controlled disease':* 'clear' or 'very mild' according to Patient's Global Assessment of Disease Severity *Patients with success: according to total sign score (TSS* $\leq$ 1). TSS: redness, thickness and scaliness, each rated by the investigator on a 5-point scale ranging from 0 to 4 (0 = best; 4 = worst). The sum of the 3 individual scores ranged from 0 to 12 (0 = best; 12 = worst) *Percentage of patients with success for each clinical sign:* TSS $\leq$ 1 for each sign *Patient's itching score:* no score definition provided *Quality of life:* no definition provided Visits: week 2 and 4
Notes	This trial was sponsored by LEO Pharma Data and all information were extracted from clinicaltrials.gov (NCT01195831, http://www.clinicaltrials.gov/ct2/show/NCT01195831)

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote (study results): "Allocation: Randomized" Comment: insufficient detail was reported about the method used to generate the allocation sequence
Allocation concealment (selection bias)	Unclear risk	This was not stated
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote (results, serious and other adverse events): "The number of participants at risk is based on the number of participants included in the safety analysis set, i.e. all randomised patients who had at least one dose of medication, and had at least one post-baseline safety assessment (118 out of 120 patients in Xamiol® gel group and all (124) patients in Calcipotriol scalp solution group)." Comment: safety outcome data sufficiently addressed and efficacy outcomes for all randomised participants provided even though it remained unclear whether LOCF was performed

NCT01195831 (*Continued*)

Selective reporting (reporting bias)	High risk	Results for the prespecified outcomes of quality of life and patient's itching score were not addressed
Other bias	Unclear risk	Comparability between study groups limited, since no data on baseline severity provided
Blinding of participants and personnel (performance bias) All outcomes	High risk	Quote: "investigator-blind" Comment: no blinding of participants. However, this may only affect subjective outcomes (e.g. PGA, itching)
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote: "investigator-blind" Comment: vehicles were not identical (gel versus solution). Method on how blinding was performed remained unclear

Olsen 1991

Methods	This was a double-blind, randomised, vehicle-controlled, parallel-group trial
Participants	**Inclusion criteria of the trial** • Adult patients diagnosed with moderate to severe scalp psoriasis • Otherwise healthy • Total score/total sign score (TSS) of at least 6 **Exclusion criteria of the trial** • No systemic anti-psoriatic treatment within the previous 4 weeks • No topical anti-psoriatic treatment (including UV therapy) within the previous 2 weeks **Washout period** • 2 weeks for topical treatment (as mentioned above) • 4 weeks for systemic treatment (as mentioned above) **Baseline characteristics** • Age (years, mean): A: 47, B: 46 • Females N (%): A: 109 (58), B: 100 (53) • Participants with 'moderate' disease N (%): A: 147 (78), B: 156 (83)
Interventions	A: clobetasol propionate 0.05% solution, twice daily for 2 weeks (N = 188 participants) B: placebo vehicle, twice daily for 2 weeks (N = 189 participants) Participants whose condition cleared after 1 week discontinued treatment at that time
Outcomes	1. Investigator global assessments (IGA) (day 14 and 21) 2. Patients evaluation of treatment response (day 14 and 21) 3. "Total score"/TSS (day 4, 8, 14 and 21) 4. Erythema (day 4, 8, 14 and 21) 5. Infiltration/thickness (day 4, 8, 14 and 21) 6. Scaling (day 4, 8, 14 and 21)

	7. Pruritus (day 4, 8, 14 and 21) 8. Adverse event (AE) (day 4, 8, 14 and 21) 9. Withdrawal due to AE (day 14) 10. Blood sample analysis (baseline and 14) Definition: *IGA:* rated on 6-point scale as "clear" = 100% cleared or residual discolouration only, "excellent" = 75% to 99% improvement, "good" = 50% to 74% improvement, "fair" = 25% to 49% improvement, "poor" = < 25% improvement, or "worse" *"Total score"/TSS (0 to 9):* sum of sign scores (0 to 3) of erythema, scaling and thickness *Outcomes 3 to 6 (0 to 3)* with 0.5 increments: each rated as 0 = none, 1 = mild, 2 = moderate, 3 = severe *Patients evaluation of treatment response:* rated as "excellent" (matched with PGA = responder), "good", "fair" or "poor" Visits: baseline, day 4, 8, 14 and 21 (follow-up)
Notes	"Total score" of the trial was interpreted as TSS by the review author This study was supported in part by a grant from Glaxo, Inc., Research Triangle Park, North Carolina

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Quote (page 444): "Patients were randomly assigned" Comment: insufficient detail was reported about the method used to generate the allocation sequence
Allocation concealment (selection bias)	Unclear risk	This was not stated
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote (page 444): "A full course of therapy was completed by 350 patients [...] all returned for the posttreatment visit." Comment: no ITT analysis performed. According to the graph for efficacy outcome at week 2 all evaluated patients were assessed and data reported. This is not consistent with the cited text. However, attrition considered as too small (< 10%) to have a relevant impact on outcome
Selective reporting (reporting bias)	Low risk	All reported results were pre-specified outcomes in the methods section
Other bias	Low risk	No other source of bias identified

Olsen 1991 (*Continued*)

Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote (page 444): "double-blind, vehicle-controlled" Comment: blinding probably sufficient
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote (page 444): "double-blind, vehicle-controlled" Comment: insufficient reporting about how blinding of assessor was ensured throughout the study

Pauporte 2004

Methods	This was a randomised, double-blind, vehicle-controlled, multicentre trial
Participants	**Inclusion criteria of the trial** • Patients with diagnosis of moderate to severe scalp psoriasis • At least 12 years of age • Good general health • At least 20% of scalp surface involvement • Lesions either stable or slowly exacerbating • At least 2 points for each of the 3 signs: erythema, thickening, scaling • Total sign score (TSS) of at least 6 **Exclusion criteria of the trial** • Pregnant, nursing or breastfeeding women • Inadequate contraception • Patients requiring other topical or systemic medications with effect on course of disease (e.g. antibiotics, antihistamines, tranquillisers or antidepressants) • No systemic corticosteroids within the previous 4 weeks • No topical (e.g. corticosteroid) treatment within the previous 7 days **Washout period** • 1 week for topical treatment (as mentioned above) • 4 weeks for systemic treatment (as mentioned above) **Baseline characteristics** • Age (years, mean ± SD): A: 45.6 ± 15.3, B: 46.2 ± 15.1 • Females N (%): A: 21 (51.2) (2 patients not recorded), B: 27 (58.7) • TSS (mean): A: 7.23, B: 7.07
Interventions	A: fluocinolone acetonide 0.01% oil formulation, once daily for 3 weeks (N = 43 participants) B: placebo-vehicle, once daily for 3 weeks (N = 46 participants) After application, the participants covered their scalp with a shower cap either overnight, or for a minimum of 4 hours
Outcomes	1. Physician global evaluations (day 11, 21 and 28) 2. Physician global assessment (day 11, 21 and 28) 3. "Total score"/TSS (day 11 and 21) 4. Erythema (day 11 and 21) 5. Thickness (day 11 and 21)

	6. Scaling (day 11 and 21) 7. Pruritus (day 11 and 21) 8. Adverse event (AE) (day 11 and 21) 9. Number of patients with at least 1 AE (day 11 and 21) Definition: *Physician global evaluations:* improvement from baseline rated as 1 = cleared, 100% clearance of signs/symptoms monitored, residual discolouration excluded, 2 = excellent, 75% but less than 100% improvement of signs/symptoms, 3 = good, 50% but less than 75% improvement of signs/symptoms, 4 = moderate, 25% but less than 50% improvement of signs/symptoms, 5 = slight, less than 25% improvement of signs/symptoms, 6 = no change, no detectable improvement, 7 = exacerbation, flare-up of study site *Physician global assessment:* rated as 'good or better', 'moderate', 'fair or less' *'Total score'/TSS (0 to 9):* sum of sign scores (0 to 3) of erythema, scaling and thickness *Outcomes 3 to 6 (0 to 3):* each rated as 0 = none, 1 = slight or mild, 2 = moderate or average, easily discernable, 3 = severe or extensive, markedly evident Visits: baseline, day 11, 21 and 28 (follow-up)
Notes	'Total score' of the trial was interpreted as TSS by the review author No sponsorship reported, but one author works for Hill Dermaceuticals, Inc., Sanford, FL 32773, USA Patients could deviate from the treatment plan without being eliminated provided that discontinuation/deviation from the study medication was not on more than 2 consecutive days, nor for more than a total of 4 days out of 10

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote (page 361): "Patients were randomized to treatment" Comment: insufficient detail was reported about the method used to generate the allocation sequence
Allocation concealment (selection bias)	Unclear risk	This was not stated
Incomplete outcome data (attrition bias) All outcomes	Low risk	No ITT analysis performed, but attrition considered as too small (< 10%) to have a relevant impact on outcome
Selective reporting (reporting bias)	High risk	The reported outcome "Patient Global Assessment (PGA)" was not pre-specified in the methods section
Other bias	Low risk	No other source of bias identified
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote (page 360): "double-blind, vehicle-controlled" Comment: blinding probably sufficient

Pauporte 2004 (*Continued*)

Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote (page 360): "double-blind, vehicle-controlled" Comment: insufficient detail was reported about the method used to ensure blinding of outcome assessor

Regaña 2009

Methods	This was an open-labelled, randomised, active-controlled, parallel-group trial
Participants	**Inclusion criteria of the trial** This was not stated **Exclusion criteria of the trial** This was not stated **Washout period** This was not stated **Baseline characteristics** • Quote: "There were no significant differences between the groups in terms of age, sex, months of evolution of the psoriasis episode, or initial symptoms."
Interventions	A: shampoo including urea, salicylic acid, glycolic acid, ichthyol pale and polidocanol, once every second day for 8 weeks (N = 27 participants) B: coal tar shampoo, once every second day for 8 weeks (N = 10 participants)
Outcomes	1. Overall efficacy rated by doctor matched with IGA 2. Overall efficacy rated by patient matched with PGA 3. Clinical signs 4. Tolerability 5. Cosmetic properties (day 11 and 21) Definition: *Overall efficacy rated by doctor/patient:* rated on a 4-point scale (0 = poor, 1 = moderate, 2 = good and 3 = excellent) *Tolerability:* rated on a 4-point scale (0 = poor, 1 = moderate, 2 = good and 3 = excellent) *Cosmetic properties:* smell, ease of combing wet hair, ease of combing dry hair, softness of dry hair, shine of dry hair, static electricity and overall cosmetic effect rated on a 4-point scale (0 = poor, 1 = moderate, 2 = good and 3 = excellent) *Clinical signs:* including erythema, desquamation, infiltration, pruritus and stinging sensation rated on a visual analogue scale from 0 to 10 Visits: baseline, week 4 and 8
Notes	The study was only available as a conference abstract This study was sponsored by Isdin

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**

Regaña 2009 (*Continued*)

Random sequence generation (selection bias)	Unclear risk	Quote: "randomized" Comment: the abstract did not provide sufficient detail about the method used to generate the allocation sequence
Allocation concealment (selection bias)	Unclear risk	This was not stated in this conference abstract
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	The abstract does not provide sufficient information whether the findings are based on the ITT population or if any drop-outs occurred
Selective reporting (reporting bias)	Unclear risk	This was a conference abstract. Evaluation therefore limited
Other bias	Low risk	No other source of bias identified
Blinding of participants and personnel (performance bias) All outcomes	High risk	This was an open-label trial
Blinding of outcome assessment (detection bias) All outcomes	High risk	This was an open-label trial

Reygagne 2002

Methods	This was a multicentre, randomised, investigator-blind, 3-arm, active- and vehicle-controlled trial
Participants	**Inclusion criteria of the trial** • Patients with diagnosis of moderate to severe scalp psoriasis • Global Severity Score (GSS) of at least 3 out of 5 • At least 15% of scalp surface involved **Exclusion criteria of the trial** This was not stated **Washout period** This was not stated **Baseline characteristics** • Total severity score (TSS, mean ± SD): A: 5.5 ± 1.5, B: 5.6 ± 1.6, C: no data
Interventions	A: clobetasol propionate 0.05% shampoo, for 4 weeks (N = 63 participants) B: clobetasol propionate 0.05% gel, for 4 weeks (N = 61 participants) C: placebo vehicle shampoo, for 4 weeks (N = 20 participants) Frequency of application per day not reported

Reygagne 2002 (*Continued*)

Outcomes	1. TSS (week 4) 2. GSS (week 4) 3. Subject's Global Assessment of Improvement (week 4) 4. Change in scalp surface area involved (week 4) 5. Adverse event (AE) (week 4) 6. Number of patients with at least 1 AE (week 4) Definition: *TSS (0 to 9):* sum of sign scores (0 to 3) of erythema, scaling and thickness *GSS (0 to 5):* 0 = none to 5 = severe Visits: baseline and week 4
Notes	This trial was presented as a conference abstract

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Quote (page 283): "144 subjects were randomized" Comment: insufficient detail was reported about the method used to generate the allocation sequence
Allocation concealment (selection bias)	Unclear risk	This was not stated
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote (page 283): "The results in the intent-to-treat population (all randomized subjects) were similar." Comment: data for the ITT population not reported. Insufficient reporting of attrition or exclusions, but attrition considered as too small (< 10%) to have a relevant impact on outcome
Selective reporting (reporting bias)	High risk	Data for the following pre-specified outcomes were not reported: 1. GSS (week 4) 2. Subject's Global Assessment of Improvement (week 4) 3. Change in scalp surface area involved (week 4) 4. TSS: no data reported for the vehicle group
Other bias	Low risk	No other source of bias identified
Blinding of participants and personnel (performance bias) All outcomes	High risk	Quote (page 283): "investigator-blind" Comment: subjective outcomes (subject's global assessment) likely to be biased. These

Reygagne 2002 *(Continued)*

		data are not reported and the outcome provided (TSS) is not considered to be influenced by lack of blinding of the participants
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote (page 283): "investigator-blind" Comment: insufficient detail was reported about the method used to blind the outcome assessor

Reygagne 2005

Methods	This was a multicentre, randomised, investigator-masked, parallel-group trial
Participants	**Inclusion criteria of the trial** • Patients with diagnosis of moderate to severe scalp psoriasis • At least 12 years of age • Global Severity Score (GSS) of at least 3 out of 5 • Affected area of at least 2 cm^2 of the scalp **Exclusion criteria of the trial** • Very severe scalp requiring systemic treatment • Known allergy to any component of the study medications • Immuno-compromised patients • History of adverse response to topical or systemic steroid therapy • Concomitant use of other topical or systemic anti-psoriatic treatment of the scalp • Concomitant treatment with medication with aggravating potential (e.g. beta blockers, lithium, antimalarials or NSAIDs) **Washout period** This was not stated **Baseline characteristics** • Age (years, mean ± SD): A: 44.9 ± 16.8, B: 45.7 ± 17.4 • Females N (%): A: 39 (51), B: 41 (55) • Total sign score (TSS) (mean ± SD): A: 4.86 ± 1.95, B: 4.95 ± 1.49
Interventions	A: clobetasol propionate 0.05% shampoo, once daily for 4 weeks (N = 76 participants) B: calcipotriol 0.005% solution, twice daily for 4 weeks (N = 75 participants)
Outcomes	**Primary outcome of the trial** 1. TSS (week 2 and 4) 2. GSS (week 2 and 4) **Secondary outcome of the trial** 1. Erythema (week 2 and 4) 2. Thickness (week 2 and 4) 3. Scaling/desquamation (week 2 and 4) 4. Pruritus (week 2 and 4) 5. Investigator's Global Assessment of Improvement (IGA) (week 4) 6. Patient's Global Assessment of Improvement (PGA) (week 4) 7. Change in scalp surface area involved (week 4) 8. Adverse event (AE) (week 2 and 4)

	9. Skin atrophy (week 2 and 4) 10. Telangiectasia (week 2 and 4) 11. Burning sensation on the scalp/neck/face (week 2 and 4) 12. Number of patients with at least 1 AE (week 2 and 4) 13. Withdrawal due to AE (week 2 and 4) Definition: *TSS (0 to 9):* sum of sign scores of erythema, scaling/desquamation and thickness *Erythema, scaling/desquamation, pruritus and thickness score (0 to 3):* each rated as 0 = none, 1 = mild, 2 = moderate, 3 = severe *GSS (0 to 5):* 0 = none to 5 = very severe *Scalp surface area:* expressed percentage of total scalp surface area *IGA/PGA:* scale from -1 = worse to 5 = cleared *Skin atrophy and burning sensation on the scalp/neck/face:* rated on scale from 0 = none to 3 = severe Visits: baseline, week 2 and 4
Notes	This study was funded by Galderma R&D, Sophia Antipolis, France

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Quote (page 32): "Subjects were randomized, using a computer-generated randomization list" Comment: method of randomisation probably appropriate
Allocation concealment (selection bias)	Unclear risk	This was not stated
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote (page 33): "The superiority analysis was done, using the ITT population [...] (LOCF)." Comment: incomplete outcome data sufficiently addressed
Selective reporting (reporting bias)	Unclear risk	Quote (page 33): "The joint primary outcome measures of GSS and TSS improved in both groups during the study [...] The percentage of scalp surface area affected also showed a significant difference in favour of clobetasol propionate (P = 0.02)." Data for GSS and change in percentage of scalp area affected insufficiently reported
Other bias	Low risk	No other source of bias identified

Reygagne 2005 (*Continued*)

Blinding of participants and personnel (performance bias) All outcomes	High risk	Quote (page 32): "Because the appearance of the two treatments was very different, masking of the treatments' identity to the subjects was not possible." Comment: no blinding of participants done
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote (page 32): "Blinding to investigators was maintained by using independent study personnel to dispense medication and collect returned medication. Subjects were advised not to discuss the study medication with the investigator." Comment: blinding of outcome assessor probably sufficient

Ruzicka 2004

Methods	This was a multicentre, randomised, double-blind, placebo-controlled, parallel-group trial
Participants	**Inclusion criteria of the trial** • Participants with diagnosis of scalp psoriasis • Age between 18 and 79 years **Exclusion criteria of the trial** • Participants with high calcium and phosphate levels at the initiation of the trial • Topical therapy with retinoids or vitamin D3 analogues 2 weeks prior to randomisation • Systemic anti-psoriatic or phototherapy 6 weeks prior to randomisation • Systemic retinoid therapy 12 months prior to randomisation • Severe co-morbidity • Known hypersensitivity to vitamin D analogues • Any co-morbidity which could have influenced effectiveness, safety and tolerability of the study medication • Concomitant use of other topical or systemic anti-psoriatic treatment **Washout period** • Participants used unmedicated shampoo for 2 weeks prior to the initiation of the therapy **Baseline characteristics** • Age (years, mean (range)): 45 (18 to 79) • Females N (%): 133 (49) • Total sign score (TSS, mean (range)): A: 6.2 (3 to 9), B: 6.1 (3 to 9)
Interventions	A: tacalcitol emulsion (4 μg/g), once daily for 8 weeks (N of participants unclear) B: placebo, once daily for 8 weeks (N of participants unclear) N = 273 participants

Outcomes	**Primary outcome of the trial** 1. TSS **Secondary outcome of the trial** 1. Erythema 2. Thickness 3. Scaling 4. Pruritus 5. Participants assessed degree of scaling and pruritus 6. Adverse events (AEs) 7. Number of participants with at least 1 AE 8. Withdrawals due to AE 9. Blood work and urine samples (baseline and week 8) 10. Clearance according to patient's global assessment (PGA) 11. Clearance according to investigators' global assessment (IGA) Definition: *TSS (0 to 12):* sum of sign scores of erythema, scaling and thickness *Erythema, scaling, pruritus and thickness score (0 to 4):* each rated as 0 = none to 4 = very severe *Participants assessed degree of scaling and pruritus:* according to the sign score *Blood work and urine samples:* to assess calcium homeostasis (serum and urine calcium, parathormone, calcitonin, urine creatinine, urine phosphate, calcium/creatinine ratio) Visits: baseline, week 1, 2, 4, 6 and 8
Notes	This study was sponsored by Hermal/BHI, Reinbek, Germany The product name of the tacalcitol emulsion was Curatoderm®

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote (page 165): "randomised" Comment: insufficient information on how sequence allocation was performed
Allocation concealment (selection bias)	Unclear risk	This was not stated
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Quote (page 166): "237 patients were treated" Comment: unclear how many participants were randomised. According to the legends of figures 2-5: results for ITT population provided
Selective reporting (reporting bias)	High risk	Quote (page 166): "21.1 % of the patients of the tacalcitol group achieved complete clearance compared to 4.5% treated with placebo." Quote (page 168): "At the end of treatment

Ruzicka 2004 *(Continued)*

		patients were asked for an overall evaluation of the study medication. Most participants rated the application of emulsion as very good and good. Furthermore, the ease of use of the emulsion was assessed." Comment: these outcomes were not pre-specified in the methods section. Not clear if 'emulsion' included the placebo as well Quote (page 169): "Withdrawal rate were similar between both groups: 1.5% in the tacalcitol group versus 2.9 in the vehicle group. [...] None of the participants withdrew because of safety concerns of the application" Comment: reasons for withdrawal not provided. It is therefore not evaluable if participants withdrew due to adverse events that the investigators might not have rated as drug-related
Other bias	Unclear risk	Quote (page 166): "In 39 patients vitamin D metabolites were additionally assessed" Comment: unclear according to which criteria this group was selected. Selection bias possible
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote (page 165): "double-blind" Comment: vehicle used as control. Participants probably sufficiently blinded
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote (page 165): "double-blind" Comment: insufficient information on how blinding of investigators was performed and maintained

Shuttleworth 1998

Methods	This was a randomised, double-blind, single-centre, parallel-group, vehicle-controlled trial
Participants	**Inclusion criteria of the trial** • Patients with diagnosis of scalp psoriasis • Age between 18 and 70 years **Exclusion criteria of the trial** • Pregnant or breastfeeding women • Inadequate contraception • Known hypersensitivity to the study medication • Participants with diffuse or "helmet" psoriasis • PUVA or anti-psoriatic topical treatment (including corticosteroids, except for

	1% hydrocortisone formulations) within 2 weeks prior to the trial • Concomitant use systemic anti-psoriatic treatment • Concomitant treatment with medication with interfering potential on course of disease • Participants with history of photosensitivity or any eye disease that could be exacerbated by participation **Washout period** • 2 weeks (only use of unmedicated baby shampoo, 3 times a week) **Baseline characteristics** • Age (years, mean ± SD): 41.4 ± 12.0 • Females N (%): A: 12 (41), B: 4 (36) • Clinical assessment of overall scalp psoriasis (mean ± SD): A: 4.93 ± 2.19, B: 4.64 ± 2.65
Interventions	A: ciclopirox olamine 1.5% shampoo, 3 times per week for 4 weeks (N = 29 participants) B: placebo-vehicle, 3 times per week for 4 weeks (N = 11 participants)
Outcomes	1. Overall extent of scalp psoriasis (days 8, 15 and 29) 2. Overall clinical change (days 8, 15 and 29) 3. Clinical assessment of overall scalp psoriasis (days 8, 15 and 29) 4. Scaling (days 8, 15 and 29) 5. Patient's self assessment (days 8, 15 and 29) 6. Patient's overall opinion (day 28) 7. Assessment of acceptability (days 8, 15 and 29) 8. Adverse event (AE) (day 29) 9. Number of patients with at least 1 AE (day 29) 10. Withdrawal due to AE (day 29) 11. Withdrawal due to treatment failure (day 29) Definition: *Overall extent of scalp psoriasis:* 0 = normal scalp, 1 = residual scaling without plaque, 2 = < 25% scalp covered by plaque without thick scaling, 3 = < 25% scalp covered by thick plaque, 4 = 25% to 50% scalp covered by plaque without thick scaling, 5 = 25% to 50% scalp covered by thick scaly plaque, 6 = 50% to 75% scalp covered by plaque without thick scaling, 7 = 50% to 75% scalp covered by thick scaly plaque, 8 = > 75%, scalp covered by plaque without thick scaling, 9 = > 75% scalp covered by thick scaly plaque *Overall clinical change:* 0 = completely cleared, 1 = very much improved, 2 = much improved, 3 = minimally improved, 4 = no change, 5 = minimally worse, 6 = much worse, 7 = very much worse *Scaling:* rated on a scale from 0 to 0.5 = none, 1 to 1.5 = slight, 2 to 2.5 = moderate, 3 to 3.5 = severe, 4 to 4.5 = very severe *Patient's self assessment:* following questions were rated on a scale from 0 = none, 1 = slight, 2 = moderate, 3 =severe, to 4 = very severe: "Which best describes yours scalp psoriasis today?" and "Which best describes your itching today?" *Patient's overall opinion:* following question was rated on a scale from 1 = poor, 2 = fair, 3 = good, 4 = very good, to 5 = excellent: "Overall, how do you rate the treatment you've been using over the last four weeks with respect to your scalp psoriasis?" *Assessment of acceptability:* following questions were rated on a scale from 0 = very dry, 1 = dry, 2 = normal, 3 = greasy, to 4 = very greasy: "Which best describes the dryness/greasiness of your hair today?

	Visits: baseline, days 8, 15 and 29	
Notes	This study was sponsored by Stiefel Laboratories and conducted by Globecrown International Ltd (Maldon, UK) Quote (page 166): "The lower-than-planned recruitment resulted in a reduction in the analytical power of the study."	
Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Quote (page 164): "according to a predetermined randomization schedule [...] The randomization was prepared in blocks of ten with seven patients per block to receive ciclopirox olamine shampoo and three per block to receive matching placebo." Comment: sequence generation probably adequate
Allocation concealment (selection bias)	Unclear risk	This was not stated
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote (page 165): "Three patients failed to complete the study (one on ciclopirox olamine was withdrawn after using a proscribed medication; two on placebo withdrew owing to severe pruritus in one and scalp irritation and increased scaling in the other)" Comment: data about the ITT population not reported, but attrition (3/40) considered as too small (< 10%) to have a relevant impact on outcome
Selective reporting (reporting bias)	Unclear risk	Data for "patient's overall opinion of treatment" insufficiently reported
Other bias	Unclear risk	Inconsistent wording of definition of "clinical assessment of scalp psoriasis" and "extent of scalp psoriasis"
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote (page 163-4): "double-blind [...] matching placebo shampoo base" Comment: vehicle-controlled, blinding of participants and personnel probably sufficient

Shuttleworth 1998 (*Continued*)

Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote (page 163-4): "double-blind [...] matching placebo shampoo base" Comment: insufficient reporting about how blinding of investigator was ensured throughout the study

Sofen 2011

Methods	This was a multicentre, randomised, double-blind, vehicle-controlled, parallel-group trial
Participants	**Inclusion criteria of the trial** • Global severity score (GSS) of at least 3 to 4 • Age of at least 18 years **Exclusion criteria of the trial** • Pregnant, nursing or pregnancy-planning women • Inadequate contraception or positive urine pregnancy test • Psoriasis affecting more than 20% of the body surface area requiring more than 50 g of study medication • History of adverse response to topical or systemic corticosteroids • Chemical process performed on the hair (e.g. colour application) within 2 weeks prior to the study • Patients with known allergy to components of intervention products • Intensive exposure to ultraviolet light during study • Concomitant systemic treatment for body psoriasis • Within 2 weeks prior to the study: topical treatment for scalp psoriasis, including e.g. steroid-containing medication, UVB-exposure, vitamin D3 analogues, anthralin, coal tar, retinoids, salicylic acid urea • Within 4 weeks prior to the study: PUVA therapy, systemic anti-psoriasis treatment • Within 12 weeks prior to the study: biologic therapy **Washout period** • 2 weeks: topical treatment (as mentioned above) • 4 weeks: systemic treatment (as mentioned above) • 12 weeks: biologic treatment (as mentioned above) **Baseline characteristics** • Age (years, mean ± SD): A: 46.0 ± 15.4, B: 43.0 ± 13.7 • Females N (%): A: 25 (61), B: 24 (60) • Total severity score (mean): A: 6.71, B: 6.58 calculated by the review authors
Interventions	A: clobetasol propionate 0.05% spray, twice daily for 4 weeks (N = 41 participants) B: placebo-vehicle, twice daily for 4 weeks (N = 40 participants) Participants with a GSS = 0 at week 2 completed the study at that time
Outcomes	**Primary outcome of the trial** 1. GSS (week 4) matched with IGA **Secondary outcomes of the trial** 1. GSS (week 2) matched with IGA

	2. Total severity score (TSS) (week 2 and 4) 3. Pruritus (week 2 and 4) 4. Erythema (week 2 and 4) 5. Scaling (week 2, 4, 6) 6. Plaque elevation/thickness (week 2 and 4) 7. Extend of scalp surface are of involvement (week 2 and 4) 8. Local tolerability (week 2 and 4) 9. Adverse events (AE) (week 2 and 4) 10. Withdrawal due to AE (week 4) 11. Quality of life (QOL) (week 2 and 4) 12. Compliance (week 2 and 4) Definition: *GSS (0 to 5):* 0 = clear, 1 = minimal, 2 = mild, 3 = moderate, 4 = severe, 5 = very severe *TSS (0 to 12):* sum of erythema, thickness, scaling scores *Outcomes 4 to 6 (0 to 4):* each point of 5-point scale exact defined for each outcome, that can be translated as: 0 = none, 1 = mild, 2 = moderate, 3 = severe, 4 = very severe *Extend of scalp surface involvement:* 0 = none, 1 = < 20%, 2 = 20% to 39%, 3 = 40% to 59%, 4 = 60% to 79% and 5 = 80% to 100% *Pruritus score (0 to 3):* 0 = no itching, 1 = slight itching, 2 = itching as somewhat bothersome, without loss of sleep, 3 = intense itching, night rest interrupted *Local tolerability:* skin atrophy, teleangiectasia, stinging/burning rated on a scale (0 to 3) , 0 = none and folliculitis, assessed as absent or present *QOL:* 'Scalpdex score' used as dermatitis specific instrument with symptom, function and emotion subscales containing 23 questions with the individual question score ranging between 0 (never) and 100 (all the time) *Subject satisfaction:* questionnaire at the end of treatment *Compliance:* participants considered as compliant if they used at least 80% and not more as 120% of expected applications based on self reporting *AE:* in particular absence or presence of Cushing syndrome based on clinical judgement Visits: baseline, week 2 and 4
Notes	Scalpdex data provided by Cook Bolden 2012, poster abstract This study was supported by Galderma Laboratories, L.P., Fort Worth, Texas

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote (page 886): "subjects were randomly assigned" Comment: insufficient detail was reported about the method used to generate the allocation sequence
Allocation concealment (selection bias)	Low risk	Quote (page 886): "Study product [...] was assembled into treatment kits based on the randomisation scheme and contained two bottles of identical product [...] and were numbered sequentially"

Sofen 2011 *(Continued)*

		Comment: probably sufficient
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote (page 887): "safety population included all subjects randomized with documented use of at least one application of study medication [...] missing data for the intend-to-treat population were handled using the last observation carried forward method" Comment: incomplete outcome data sufficiently addressed
Selective reporting (reporting bias)	Low risk	All reported results were pre-specified outcomes in the methods section
Other bias	Low risk	No other source of bias identified
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote (page 886): "Packaging for the active treatment and vehicle spray was similar in appearance" Comment: this was a vehicle-controlled trial. Blinding probably sufficient
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote (page 886): "Packaging for the active treatment and vehicle spray was similar in appearance" Comment: insufficient reporting about how blinding of investigator was ensured throughout the study

Swinehart 1989

Methods	This was a multicentre, randomised, double-blind, active-controlled, parallel-group trial
Participants	**Inclusion criteria of the trial** • Patients with moderate to severe scalp psoriasis • Erythema and scaling present **Exclusion criteria of the trial** This was not stated **Washout period** This was not stated **Baseline characteristics** This was not stated
Interventions	A: mometasone furoate lotion 0.1%, once daily for 3 weeks (N = 103 participants) B: triamcinolone acetonide lotion 0.1%, twice daily for 3 weeks (N = 99 participants)

Swinehart 1989 (*Continued*)

Outcomes	1. Total sign score (TSS) (day 8, 15 and 22) 2. Pruritus (day 8, 15 and 22) 3. Erythema (day 8, 15 and 22) 4. Scaling (day 8, 15 and 22) 5. Induration (day 8, 15 and 22) 6. Global evaluation (week 3) 7. Patient's evaluation of efficacy and cosmetic acceptability (week 3) 8. Local safety evaluation: skin atrophy (week 3) 9. Adverse events (AE) (week 3) 10. Number of patients with at least 1 drug-related AE (week 3) Definition: *TSS (0 to 12):* sum of erythema, thickness, scaling and pruritus scores *Outcomes 2 to 5 (0 to 3):* rated on a 4-point scale 0 = none, 1 = mild, 2 = moderate, 3 = severe *Global evaluation:* scale including marked improvement and complete clearing *Patient's evaluation of efficacy:* scale including excellent and good Visits: baseline, day 8, 15 and 22
Notes	-

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote (page 680): "randomly assigned" Comment: insufficient detail was reported about the method used to generate the allocation sequence
Allocation concealment (selection bias)	Unclear risk	This was not stated
Incomplete outcome data (attrition bias) All outcomes	Low risk	Efficacy analysis (marked improvement or clearing) only reported for 99/103 (mometasone group) and 93/99 (triamcinolone group). Insufficient reporting of attrition or exclusions. No ITT analysis performed Comment: attrition (< 10%) not considered as sufficient to have significant impact on outcomes
Selective reporting (reporting bias)	Unclear risk	Pre-specified outcome of local safety evaluation (skin atrophy) not reported, but this outcome is not considered as relevant for this review
Other bias	Low risk	No other source of bias identified

Swinehart 1989 (*Continued*)

Blinding of participants and personnel (performance bias) All outcomes	High risk	Quote page 680): "third-party blind" Comment: this was a opd versus bid comparison. Thus, blinding of participants and personnel probably not done
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote page 680): "third-party blind" Comment: unclear if outcome assessors were adequately blinded throughout the study

Tyring 2010

Methods	This was a multicentre, randomised, double-blind, vehicle-controlled, parallel-group trial
Participants	**Inclusion criteria of the trial** • Age: at least 18 years • At least 10% of psoriatic scalp involvement • Ethnicity: Hispanic/Latino or Black/African American • Diagnosis of psoriasis of the scalp and limbs/trunk • At least moderate to severe severity **Exclusion criteria of the trial** • Erythrodermic, exfoliative and pustular psoriasis • Skin infection • Skin diseases confounding evaluation of psoriasis • Disorders of calcium metabolism/hypercalcaemia • Pregnant or breastfeeding women • Concomitant anti-psoriatic therapy • Chemical treatment of the hair **Washout period** • 2 weeks: topical treatments and ultraviolet therapy • 4 weeks: systemic treatments • 12 weeks: systemic biological treatments **Baseline characteristics** • Age (years, mean [range]): A: 44.4 (18 to 75), B: 45.8 (22 to 76) • Females N (%): A: 51 (37.8), B: 14 (33.3) • Total sign score (TSS, mean (range)): A: 6.3 (4 to 11), B: 6.2 (4 to 11)
Interventions	A: calcipotriene 50 µg/g plus betamethasone dipropionate 0.5 mg/g, once daily for 8 weeks (N = 135 participants) B: placebo vehicle, once daily for 8 weeks (N = 42 participants) Assignment in a 3:1 ratio Treatment was stopped if clearance occurred and restarted when scalp psoriasis relapsed
Outcomes	**Primary outcome of the trial** 1. Proportion of participants with Investigator's Global Assessment (IGA): clear/minimal (week 8) **Secondary outcome of the trial**

	1. TSS ≤ 1 (week 8) 2. Redness: absent (week 8) 3. Thickness: absent (week 8) 4. Scaliness: absent (week 8) 5. Adverse events (AE) (week 8) 6. Patient's global assessment (PGA) of severity: cleared/very mild (week 8) 7. Blood pressure (mmHg) (week 2, 4, 6 and 8) 8. Serum albumin (week 2 and 4) 9. Serum calcium (week 2 and 4) 10. Blood urea nitrogen (BUN) (week 2 and 4) 11. Creatinine (week 2 and 4) 12. Compliance (week 8) 13. Withdrawal due to AE (week 8) 14. Number of patients with at least 1 drug-related AE (week 8) Definition: *IGA:* disease severity rated as 'clear', 'minimal', 'mild', 'moderate', 'severe' and 'very severe disease' *Patient's global assessment of severity:* rated as 'clear', 'very mild', 'mild', 'moderate', 'severe' *Erythema, thickness, scaling score:* rated from 0 = none to 4 = very severe *TSS (0-12):* sum of erythema, thickness, scaling scores *Compliance:* returned medication was weighted Visits: baseline, weeks 2, 4, 6 and 8
Notes	This study was sponsored by LEO Pharma A/S

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Quote (page 1329): "Randomization was pre-planned according to a computer-generated randomization schedule, and was stratified by ethnicity" Comment: probably appropriate sequence generation
Allocation concealment (selection bias)	Unclear risk	This was not stated
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote (page 1330): "All randomized patients were included in the full analysis set on which all efficacy analyses were performed, unless indicated otherwise [...] A total of 27 (15.3%) randomized patients withdrew during the double-blind phase, 19 (14.1%) in the two-compound group and 8 (19.0%) in the vehicle group." Comment: for efficacy analysis, data for the ITT population was reported, but not the imputation method

Tyring 2010 (*Continued*)

		Quote (page 1330): "Of the randomized patients, seven in the two-compound group and four in the vehicle group provided no data on the presence or absence of adverse events, and so were excluded from the safety analysis set." Comment: reason to exclude these patients from safety set appears reasonable
Selective reporting (reporting bias)	Low risk	All reported results are pre-specified outcomes in the methods section
Other bias	Unclear risk	Baseline IGA (Table 3) of both groups not well matched. IGA = moderate: 81.5% (2-compound) versus 76.2% (vehicle): IGA = severe: 18.5% versus 23.8% Comment: unclear if baseline imbalance may have introduced bias
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote (page 1329): "The packaging and labelling of the two-compound scalp formulation and its vehicle were identical, so it was not possible to distinguish between them by examination." Comment: blinding probably sufficient
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote (page 1329): "The packaging and labelling of the two-compound scalp formulation and its vehicle were identical, so it was not possible to distinguish between them by examination." Comment: unclear if outcome assessors were adequately blinded throughout the study

van de Kerkhof 2002

Methods	This was a multicentre, randomised, open-labelled, active-controlled, parallel-group trial
Participants	**Inclusion criteria of the trial** • Age: at least 18 years • Diagnosis of chronic plaque psoriasis of the body and scalp • Requiring 30 to 50 ml calcipotriol solution per week to the scalp **Exclusion criteria of the trial** • Acute guttate, pustular or severely inflamed psoriasis • Within 6 weeks prior to the trial: systemic anti-psoriatic treatment, PUVA or UVB therapy • Use of treatment (topical or systemic) or concurrent disease known to affect

	calcium metabolism • Impaired renal or hepatic function • History of urolithiasis or hypercalciuria • Active arthritis or immobilisation • Hypo- or hyperthyroidism • Extensive exposure to sunlight • Pregnant or breastfeeding women, or those wishing to be pregnant • Concomitant anti-psoriatic therapy • Chemical treatment of the hair **Washout period** • 2 weeks (not specified) **Baseline characteristics** • PASI (mean (range)): A: 17.1 (4.3 to 48.0), B: 16.7 (5.1 to 44.0)
Interventions	A: calcipotriol (50 µg/g 30 to 50 ml/week) solution, for 4 weeks (N = 41 participants) B: dithranol/tar regimen, for 4 weeks (N = 47 participants) • In this trial psoriasis of the whole body was assessed, including the scalp • In group A: body areas were treated with calcipotriol ointment, the scalp was treated with calcipotriol solution • In group B: dithranol and/or tar could be used either separately or in combination
Outcomes	**Primary outcome of the trial** 1. Change in 24-hour urinary excretion **Secondary outcome of the trial** 1. Total severity score (TSS) (week 1, 2 and 4) 2. Redness (week 1, 2 and 4) 3. Thickness (week 1, 2 and 4) 4. Scaliness (week 1, 2 and 4) 5. Extend of scalp involvement (week 4) 6. Psoriasis Area and Severity Index (PASI) (week 1, 2 and 4) 7. Investigator's assessment of overall response (week 1, 2 and 4) matched with IGA 8. Patient's assessment of overall response (week 1, 2 and 4) matched with PGA 9. Adverse events (AE) (week 4) 10. Number of patients with at least 1 AE (week 4) 11. Withdrawal due to AE (week 4) 12. Blood/urine analysis (week 4) Definition: *Investigator's/patient's assessment of overall response:* rated as 1 = worse, 2 = unchanged, 3 = slight improvement, 4 = moderate improvement, 5 = marked improvement and 6 = clearance *Erythema, thickness, scaling score:* rated as 0 = complete lack of cutaneous involvement, 1 = slight, 2 = moderate, 3 = severe and 4 = severest possible involvement *TSS (0-12):* sum of erythema, thickness, scaling scores *Extend:* assessed by investigator 0 = no involvement, 1 = < 10%, 2 = 10% to 29%, 3 = 30% to 49%, 4 = 50% to 69%, 5 = 70% to 89% and 6 = 90% to 100% involvement *24-hour urinary excretion:* expressed as calcium/creatinine ratio *Blood/urine analysis:* assessment of calcium metabolic parameters (e.g. serum calcium), indices of bone turnover (osteocalcin, alkaline phosphatase and 1-collagen telopeptide (1-CTP))

	Visits: baseline, weeks 1, 2, 4 and 1 week post-treatment (follow-up)
Notes	This study was sponsored by Leo Pharmaceutical Products Quote (page 216): "At most centres, a short-contact dithranol regimen (concentrations varying from 0.125 to 8%) was applied in combination with or without a tar preparation (concentrations varying from 1 to 25%)."

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Quote (page 216): "randomized" Comment: insufficient detail was reported about the method used to generate the allocation sequence
Allocation concealment (selection bias)	Unclear risk	This was not stated
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote (page 217): "Except for 1 patient (randomised to dithranol/tar) who left the study after randomisation but before treatment was initiated, all randomised patients were included in the analyses of efficacy and safety" Comment: no ITT analysis performed, but drop-out not considered to introduce bias
Selective reporting (reporting bias)	High risk	Outcome data at 1 week of follow-up not reported
Other bias	Low risk	No other source of bias identified
Blinding of participants and personnel (performance bias) All outcomes	High risk	Quote (page 216): "Blinding of the study was not considered possible due to the staining properties of tar and dithranol." Comment: no blinding of participants or personnel was done
Blinding of outcome assessment (detection bias) All outcomes	High risk	Quote (page 216): "Blinding of the study was not considered possible due to the staining properties of tar and dithranol." Comment: no blinding of outcome assessors was done

van de Kerkhof 2009

Methods	This was a multicentre, prospective, randomised, double-blind, active-controlled, 3-arm, parallel-group trial
Participants	**Inclusion criteria of the trial** • Age: at least 18 years • At least 10% scalp surface involvement amenable to topical treatment • History of psoriasis on trunk and/or limbs • 1 of the clinical signs of erythema, thickness and scaliness at least "moderate", others as at least "slight" • IGA: at least "mild" **Exclusion criteria of the trial** • Within 2 weeks prior to randomisation: topical treatment with very potent corticosteroids of the scalp (except medicated shampoos/emollients), face, trunk and limbs or UVB therapy • Within 4 weeks prior to randomisation: PUVA or Grenz ray therapy, planned exposure to the sun, or systemic treatment with any other therapy with a possible effect on scalp psoriasis • Within 6 months prior to the trial: biological therapy • Patients who planned initiation of/changes to concomitant medication that may affect scalp psoriasis • Erythrodermic, exfoliative or pustular psoriasis • Viral, bacterial, parasitic or fungal skin infection • Atrophic skin on the scalp • Known or suspected abnormality of calcium homeostasis (including hypercalcaemia) • Severe impaired renal or hepatic function **Washout period** • 2 weeks (as mentioned above) • 4 weeks (as mentioned above) • 6 months (as mentioned above) **Baseline characteristics** • Age (years, mean ± SD): A: 48.5 ± 16.4, B: 47.9 ± 16.4, C: 48.7 ± 16.2 • Females N (%): A: 330 (58.1), B: 303 (53.8), C: 149 (52.1) • Total sign score (TSS, mean ± SD): A: 6.8 ± 1.9, B: 6.9 ± 1.8, C: 6.8 ± 1.8
Interventions	A: calcipotriol 50 µg/g plus betamethasone dipropionate 0.5 mg/g gel, once daily for 8 weeks (N = 568 participants) B: betamethasone dipropionate 0.5 mg/g (same vehicle as A), once daily for 8 weeks (N = 563 participants) C: calcipotriol 50 µg/g (same vehicle as A), once daily for 8 weeks (N = 286 participants) Patients with "absence of disease" according to the IGA at weeks 1 to 8 could stop treatment with study medication
Outcomes	**Primary outcome of the trial** 1. Investigator global assessment (IGA): proportion of patients with 'absence of disease' or 'very mild disease' (week 8) **Secondary outcome of the trial** 1. IGA (week 2, 4) 2. TSS (week 8) 3. Patient's overall assessment of treatment response (PGA) (week 8)

	4. Redness (week 8) 5. Thickness (week 8) 6. Scaliness (week 8) 7. Adverse events (AE) (week 8) 8. Number of patients with at least 1 AE (week 8) 9. Withdrawal due to treatment failure (week 8) 10. Withdrawal due to adverse event (week 8) 11. Compliance (week 1, 2 4, 6 and 8) 12. Blood analysis (week 1, 4) Definition: *IGA (6-point scale):* rated as 'absence of disease', 'very mild disease', 'mild disease', 'moderate disease', 'severe disease', 'very severe disease' *PGA (7-point scale):* rated as 'worse', 'unchanged', 'slight improvement', 'moderate improvement', 'marked improvement', 'almost clear', 'clear' *Erythema, thickness, scaling score:* rated as 0 = complete lack of cutaneous involvement, 1 = slight, 2 = moderate, 3 = severe and 4 = severest possible involvement *TSS (0-12):* sum of erythema, thickness, scaling scores *Compliance:* self reported and weighting of returned medication *Blood analysis:* assessment of serum calcium and albumin Visits: baseline, weeks 1, 2, 4, 6 and 8
Notes	This study was sponsored by LEO Pharma A S, Ballerup, Denmark NCT00216840

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote (page 171): "randomized according to a computer-generated schedule" Comment: sequence generation considered as probably adequate
Allocation concealment (selection bias)	Unclear risk	This was not stated
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote (page 172): "All randomized patients were included in the full analysis set [...] for efficacy parameters, and all patients who had received any trial medication and from whom the presence or confirmed absence of adverse events was available were included in the safety analysis set [...] using last observation carried forward (LOCF)" Comment: incomplete outcome data sufficiently addressed
Selective reporting (reporting bias)	Low risk	All reported results were pre-specified outcomes in the methods section

van de Kerkhof 2009 (*Continued*)

Other bias	Low risk	No other source of bias identified
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote (page 170): "double-blind [...] same vehicle" Comment: blinding of participants and personnel probably sufficient
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote (page 170): "double-blind [...] same vehicle" Comment: insufficient information about how blinding of outcome assessor was ensured throughout the study

Van der Ploeg 1989

Methods	This was a multicentre, randomised, third-party-blind, active-controlled, parallel-group trial
Participants	**Inclusion criteria of the trial** • Diagnosis of moderate to severe scalp psoriasis **Exclusion criteria of the trial** This was not stated **Washout period** This was not stated **Baseline characteristics** • Age (years, range): 13 to 87 • > 25% scalp surface involvement in 45% of participants
Interventions	A: mometasone furoate 0.1% lotion, once daily for 3 weeks (N = 101 participants analysed) B: betamethasone valerate 0.1% lotion, twice daily for 3 weeks (N = 102 participants analysed)
Outcomes	1. Target area evaluation (day 8, 15 and 22) 2. Global evaluation of overall change (day 8, 15 and 22) matched with IGA 3. Local safety evaluation: skin atrophy (day 8, 15 and 22) 4. Adverse events (AE) (day 8, 15 and 22) Definition: *Target area evaluation:* based on 1) changes in individual disease sign/symptom scores erythema, scaling, induration and pruritus rated on a scale from 0 to 3; 2) percent improvement in total sign/symptom score *Outcomes 2 to 5 (0 to 3):* rated on a 4-point scale 0 = none, 1 = mild, 2 = moderate, 3 = severe *Global evaluation of overall change:* rated as 'clear' = 100% clearance of disease signs/symptoms, 'marked' = 75% to < 100% improvement, 'moderate' = 50% to < 75% improvement, 'slight' = < 50% improvement, 'no change' = no detectable improvement, or 'exacerbation' = flare of signs/symptoms Visits: baseline, day 8, 15 and 22

Van der Ploeg 1989 (*Continued*)

Notes	-

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote (page 146): "randomized" Comment: insufficient detail was reported about the method used to generate the allocation sequence
Allocation concealment (selection bias)	Unclear risk	This was not stated
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote (page 146): "study conducted in 207 patients [...] In order to compensate for any bias that may have been caused by the loss of patients due to missed visits, all analyses were also performed using the last valid visit (i.e., the Endpoint of treatment) for each patient, irrespective of visit timing." Comment: last observation carried forward (LOCF) method used, but only for 203 participants (ITT = 207) data reported, but amount of missing data considered as too small to introduce bias
Selective reporting (reporting bias)	Low risk	All reported results were pre-specified outcomes in the methods section
Other bias	Low risk	No other source of bias identified
Blinding of participants and personnel (performance bias) All outcomes	High risk	Quote (page 146): "third-party-blind" Comment: no blinding of participants or personnel was done.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote (page 146): "third-party-blind" Comment: insufficient information on how blinding of outcome assessor was ensured throughout the study

Wall 1999

Methods	This was an 8-week, multicentre, open-label, randomised, parallel-group trial
Participants	**Inclusion criteria of the trial** • Patients with mild to moderate scalp psoriasis **Exclusion criteria of the trial** This was not stated

	Washout period This was not stated **Baseline characteristics** • Total sign score (TSS, mean): A: 5.6, B: 5.4
Interventions	A: calcipotriol 50 µg/ml solution bid and coal tar twice weekly, for 8 weeks (N = 236 participants) B: calcipotriol 50 µg/ml solution bid plus non-medicated shampoo twice weekly, for 8 weeks (N = 225 participants)
Outcomes	**Primary outcome of the trial** 1. Proportion of patients achieving 'marked improvement' or 'clearance' (week 8) **Secondary outcome of the trial** 1. Thickness 2. Erythema 3. Scaling 4. TSS 5. Investigator assessments of time to achieve treatment success 6. Extent of scalp psoriasis 7. Patient assessments of severity 8. Patient assessments of skin flaking 9. Patient assessments of overall response 10. Patient assessments of acceptability 11. Patient assessments of quality of life 12. Patient assessments of pruritus 13. Adverse event (AE) Definition: TSS (0 to 12): sum of erythema, thickness and scaling scores Erythema, thickness and scaling scores (0 to 4): each rated as 0 = absent to 4 = severest possible Visits: baseline and week 8 (reported)
Notes	This study was sponsored by Leo Pharmaceutical This study was published as a conference abstract

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Quote (page S337): "randomised" Comment: insufficient detail was reported about the method used to generate the allocation sequence
Allocation concealment (selection bias)	Unclear risk	This was not stated
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Insufficient reporting of attrition or exclusions

Wall 1999 (*Continued*)

Selective reporting (reporting bias)	High risk	Quote (page S337): "There were no statistically significant differences in investigator assessments of time to achieve treatment success or extent of scalp psoriasis" Comment: no data reported. This abstract does not pre-specify any outcomes
Other bias	Low risk	No other source of bias identified
Blinding of participants and personnel (performance bias) All outcomes	High risk	Quote (page S337): "open-label" Comment: no blinding performed
Blinding of outcome assessment (detection bias) All outcomes	High risk	Quote (page S337): "open-label" Comment: no blinding performed

Wilhelm 2013

Methods	This was a multicentre, randomised, active-controlled, phase 2 trial
Participants	Unknown
Interventions	A: mometasone emulsion (LAS41002), for 3 weeks B: mometasone solution, for 3 weeks N = 70 participants
Outcomes	**Primary outcome of the trial** 1. Relative reduction from baseline in total sign score (TSS, week 3) **Secondary outcome of the trial** 1. Physician's Global Assessment (PGA) 2. Patient's self assessment questionnaire to evaluate the tolerability 3. Patient's self assessment questionnaire to evaluate the cosmetic acceptability 4. Adverse events 5. Serious adverse events Definition: TSS: compound evaluation of erythema, thickness and scaliness Visits: baseline and week 3
Notes	Full-text of this study was not available. Information was retrieved from a power-point presentation and an abstract

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**

Wilhelm 2013 (*Continued*)

Random sequence generation (selection bias)	Unclear risk	Quote: "randomised " Comment: insufficient detail was reported about the method used to generate the allocation sequence
Allocation concealment (selection bias)	Unclear risk	Only abstract and power-point presentation available, insufficient details
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Only abstract and power-point presentation available, insufficient details
Selective reporting (reporting bias)	Unclear risk	Only abstract and power-point presentation available, insufficient details
Other bias	Low risk	No other source of bias identified
Blinding of participants and personnel (performance bias) All outcomes	High risk	Quote: "observer-blind" Comment: participants were not blinded. Patient-assessed outcomes possibly biased
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote: "observer-blind" Comment: insufficient information about how blinding of outcome assessors was ensured throughout the study

Willis 1986

Methods	This was a multicentre, double-blind, randomised, active-controlled, parallel-group trial
Participants	**Inclusion criteria of the trial** • Diagnosis of scalp psoriasis **Exclusion criteria of the trial** • Topical corticosteroid treatment 1 week prior to the trial • Systemic or intralesional corticosteroid treatment 1 month prior to the trial • Concomitant therapy with systemic antimetabolites, immunosuppressives or immunostimulants 2 months prior to the trial **Washout period** This was not stated **Baseline characteristics** • Age (years, mean (range)): A: 55.7 (22 to 81); B: 54.7 (17 to 85) • Females N (%): A: 28 (45), B: 25 (41) • Mean disease status: A: 2.31, B: 2.28
Interventions	A: desoximetasone 0.05% gel, twice daily for 2 weeks (N = 62 participants) B: fluocinonide 0.05% gel, twice daily for 2 weeks (N = 61 participants)

Outcomes	1. Pruritus (day 4, 7 and 14) 2. Erythema (day 4, 7 and 14) 3. Scaling (day 4, 7 and 14) 4. Thickening (day 4, 7 and 14) 5. Investigator's overall evaluation (day 4, 7 and 14) matched with IGA 6. Adverse events (AE) (day 4, 7 and 14) 7. Patient's acceptability of preparation (day 4, 7 and 14) Definition: *Outcomes 1 to 4 (0 to 3):* rated on a 5-point scale 1 = none, 2 = mild, 3 = moderate, 4 = severe, 5 = very severe *Investigator's overall evaluation:* rated as 1 = 'excellent' (76% to 100% improvement), 2 = 'good' (51% to 75% improvement), 3 = 'fair' (26% to 50% improvement), 4 = 'poor' (≤ 25% improvement), or 5 = 'exacerbation' *AE:* severity of burning, stinging and itching were rated by the patient from 1 = none to 4 = severe *Mean disease status:* 1 = exacerbating rapidly, 2 = exacerbating slowly, 3 = stable Visits: baseline, day 4, 7 and 14
Notes	-

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote (page 274): "patients were randomly assigned" Comment: insufficient detail was reported about the method used to generate the allocation sequence
Allocation concealment (selection bias)	Unclear risk	This was not stated
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Quote (page 277): "Evaluation scores for patients with missing visits out of range were estimated by an averaging procedure" Quote (page 278, Table II): "Patients with signs/symptom clear at baseline and throughout study are excluded. Two patients did not return past the visit on day 4 (one in each group)" Comment: inconsistency between intended method of imputation and procedure/reported results. Data for 123/125 randomised participants reported. Not clear to which group the missing 2 participants were randomised

Willis 1986 (*Continued*)

Selective reporting (reporting bias)	Low risk	All reported results are pre-specified outcomes in the methods section
Other bias	Low risk	No other source of bias identified
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote (page 276): "double-blind" Comment: probably the same vehicle used
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote (page 276): "double-blind" Comment: insufficient reporting about how blinding of outcome assessor was ensured throughout the study

Wright 1985

Methods	This was a randomised, single-blind, active-controlled, parallel-group trial
Participants	**Inclusion criteria of the trial** • Moderate to severe scalp psoriasis **Exclusion criteria of the trial** • At least 16 years of age • Any present disease of the scalp other than psoriasis • Any form of concomitant systemic anti-psoriasis therapy • Patients known to be sensitive to coal tar or dithranol • Pregnancy **Washout period** This was not stated **Baseline characteristics** • Age (years, mean ± SD): 42.6 ± 18.4 • Females N (%): 11 (29) • Total sign score (TSS), mean: A: 4.7, B: 5.3 calculated by the review authors
Interventions	A: dithranol 0.1% in urea base 17%, once daily for 3 weeks (N = 18 participants) B: pomade of coal tar 6% solution plus salicylic acid 2% and Tween 20 1% and emulsifying ointment, once daily for 3 weeks (N = 20 participants) After each application, participants of both groups washed their hair with 17.5% cetrimide shampoo and covered the hair with a perforated shower cap until the next application
Outcomes	1. Clearance (day 14) 2. Erythema (day 4, 7, 11, 14) 3. Thickness/scaling (day 4, 7, 11, 14) 4. Pruritus (day 4, 7, 11, 14) 5. Area of involvement (day 14) 6. Adverse events (AE) (day 14) 7. Number of patients with at least 1 AE (day 14) 8. TSS (day 4, 7, 11, 14) 9. Patient's opinion about acceptability and effectiveness (day 14)

Wright 1985 (*Continued*)

	Definition: *Clearance: sum of sign scores* ≤ 3 *Erythema, thickness/scaling, pruritus score:* sign scores rated as 0 = none to 3 = severe *TSS (0 to 9):* sum of erythema, thickness/scaling, pruritus scores *Area of involvement:* assessed as 0 = none, 1 = 1% to 25%, 2 = 26% to 50%, 3 = 51% to 75% or 4 = 76% to 100% *Patient's opinion about acceptability and effectiveness:* at the end of treatment patients were asked whether they would be happy to use the treatment at home or not *AE:* assessment of stinging, burning and staining of the hair (4-point scale) Visits: baseline, day 4, 7, 11 and 14	
Notes	For this study patients were hospitalised	
Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Quote (page 375): "allocated at random" Comment: insufficient detail was reported about the method used to generate the allocation sequence
Allocation concealment (selection bias)	Unclear risk	This was not stated
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote (page 375): "Forty patients [...] were recruited to the study [...] and allocated at random" Quote (page 376): "Results were available from 38 patients [...] There were insufficient patients left in the study at days 18 and 21 make comparison meaningful." Comment: no ITT analysis performed, but number of drop-outs per group (< 10%) considered as too small to introduce significant bias
Selective reporting (reporting bias)	High risk	Quote (page 376): "There were insufficient patients left in the study at days 18 and 21 make comparison meaningful." Comment: outcomes for the pre-specified endpoint at week 3 not reported. Results for assessment of area of involvement not reported
Other bias	High risk	Quote (page 376): "Results were available from 38 patients [...] There were insufficient patients left in the study at days 18 and 21 make comparison meaningful." Comment: study stopped earlier than

Wright 1985 *(Continued)*

		scheduled. Thus, overestimation of effect possible
Blinding of participants and personnel (performance bias) All outcomes	High risk	Quote (page 375): "single blind comparison" Comment: no blinding of participants or personnel was done
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote (page 375): "single blind comparison" Comment: insufficient reporting of method used to blind the outcome assessor

Yilmaz 2005

Methods	This was a randomised, active-controlled, 3-arm, parallel-group trial
Participants	**Inclusion criteria of the trial** • Age at least 18 years • Moderate to severe scalp psoriasis • At least 10% scalp surface involvement amenable to topical treatment • History of psoriasis on trunk and/or limbs • 1 clinical sign of erythema, thickness and scaliness at least 'moderate', others as at least 'slight' • IGA: at least 'mild' **Exclusion criteria of the trial** • Severe psoriasis of the scalp • Pregnant and breastfeeding women • Inadequate contraception • Within 2 weeks prior to randomisation: topical treatment with corticosteroids of the scalp • Within 8 weeks prior to randomisation: UV therapy, systemic anti-psoriatic treatment, vitamin D analogue or calcium supplementation • Severe impaired renal or hepatic function • Abnormality of calcium homeostasis (including hypercalcaemia) • Hypersensitivity to the study medication **Washout period** • 2 weeks (as mentioned above) • 8 weeks (as mentioned above) **Baseline characteristics** • Age (years, mean ± SD): A: 41.7 ± 4.8, B: 39.7 ± 4.1, C: 48.9 ± 4.7 • Females N (%): A: 7 (46.7), B: 10 (66.7), C: 8 (53.3) • Psoriasis Scalp Severity Index (PSSI), mean ± SD: A: 9.6 ± 5.2, B: 10.5 ± 7.7, C: 9.4 ± 6.0
Interventions	A: calcipotriol lotion, twice daily for 4 weeks (N = 15 participants) B: mometasone furoate lotion, once daily for 4 weeks (N = 15 participants) C: calcipotriol lotion (morning) plus mometasone furoate lotion (evening), once daily for 4 weeks (N = 15 participants)

Outcomes	1. Extend (week 4) 2. Investigator global assessment (IGA) (week 4) 3. Patient global assessment (PGA) (week 4) 4. PSSI (week 4) 5. Percent improvement of PSSI (week 4) 6. TSS (week 4) 7. Redness (week 4) 8. Thickness (week 4) 9. Scaliness (week 4) 10. Pruritus (week 4) 11. Adverse events (AE) (week 4) 12. Number of patients with at least 1 AE (week 4) 13. Urine analysis (week 4) 14. Blood analysis (week 4) Definition: *Extend (1 to 5):* rated on a scale from 1 = < 20%, 2 = 20% to 39%, 3 = 40% to 59%, 4 = 60% to 79%, to 5 = 80% to 100% *IGA/ PGA (1 to 5):* 1 = worse, 2 = none, 3 = slight improvement, 4 = marked improvement, 5 = clear *PSSI:* = extend x TSS *Percent improvement of PSSI:* PSSI (pre-treatment) - PSSI (post-treatment)/PSSI (pre-treatment) x 100 *Erythema, thickness, scaling score:* rated as 0 = absent, 1 = slight, 2 = moderate, 3 = severe and 4 = severest possible *TSS (0 to 12):* sum of erythema, thickness, scaling scores *Pruritus score:* rated as 0 = absent, 1 = slight, 2 = moderate, 3 = severe and 4 = severest possible *Blood/urine analysis:* blood count, renal/hepatic function, glucose, calcium, phosphate Visits: baseline, week 1 and 4
Notes	This Turkish article was translated for the review author

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Quote (page 110): "randomized into three groups of equal number" Comment: insufficient detail was reported about the method used to generate the allocation sequence
Allocation concealment (selection bias)	Unclear risk	This was not stated
Incomplete outcome data (attrition bias) All outcomes	Low risk	No ITT analysis mentioned, but results for all randomised participants reported (no attrition or exclusions)

Yilmaz 2005 (*Continued*)

Selective reporting (reporting bias)	Low risk	All reported results were pre-specified outcomes in the methods section
Other bias	Low risk	No other source of bias identified
Blinding of participants and personnel (performance bias) All outcomes	High risk	Due to difference in application, no blinding of participants considered as possible
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	No blinding of outcome assessors reported

ADR: adverse drug reaction
AE: adverse event
bid: twice daily
BTM: betamethasone
BSA: body surface area
DLQI: Dermatology Life Quality Index
DSS: dermatologic sum score
GSS: global severity score
HPA: hypothalamic-pituitary-adrenal
IGA: investigator's global assessment
IGSA: Investigator's Static Global Assessment
ITT: intention-to-treat
LOCF: last observation carried forward
LS: lesion score
NSAID: nonsteroidal anti-inflammatory drug
opd: once per day
PASI: Psoriasis Area and Severity Index
PGA: patient global assessment
PSSI: Psoriasis Scalp Severity Index
PUVA: psoralen and ultraviolet A
QOL: quality of life
SAPASI: self administered PASI
SD: standard deviation
TSS: total sign score
UV: ultraviolet

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

Study	Reason for exclusion
Andreassi 2003	Treatment of control group not specified
Bohnsack 2004	Study assessed different scalp disorders and did not assess scalp psoriasis separately
Cassano 2007	Not a RCT
Cunliffe 1974	Not a RCT
Elie 1983	This study assessed erythematous squamous dermatoses
Fallica 1989	Not a RCT
Feng 1997	Not a RCT
Heydendael 2004	Not a RCT
Jakubowicz 1981	Not a RCT
Kar 2000	Both groups were treated with concomitant PUVA therapy
Kose 1995	Not a RCT
Kostarelos 2000	Not a RCT
Lassus 1985	Not a RCT
Lassus 1991	Study investigated body psoriasis and did not assess the scalp separately
Lecewicz-Torun 2001	Not a RCT
Liu 1994	Not a RCT
Nolting 1983	Study investigated body psoriasis and did not assess the scalp separately
Rex 1973	Study investigated body psoriasis and did not assess the scalp separately
Ross 1981	Not a RCT
Saraceno 2014	Study assesses maintenance treatment. Participants received the same medication during induction therapy
Singh 2013	Not a RCT
Taneja 2004	No topical treatment
Texier 1978	Not a RCT

(*Continued*)

Tsankov 1995	Not a RCT
Tsankov 1998	Not a RCT
Williams 1967	Not a RCT
Wulff-Woesten 2004	Systemic concomitant treatment was allowed during the study

PUVA: psoralen and ultraviolet A
RCT: randomised controlled trial

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

Andres 2005

Methods	Unknown
Participants	Unknown
Interventions	A: clobetasol propionate 0.05% shampoo (number of participants unclear)
Outcomes	Hypothalamic-pituitary-adrenal axis suppression, atrophogenicity and ocular safety
Notes	The text of this poster abstract was not available

Augustin 2014

Methods	Single-centre, randomised, active-controlled, investigator-blinded, parallel-group trial
Participants	**Inclusion criteria of the trial** • Participants at least 18 years of age • Having a diagnosis of chronic psoriasis capitis (scalp psoriasis) with or without the involvement of other body areas and with or without psoriatic arthritis • PSSI $\geq$ 5 (range 0 to 72) • Scaling $\geq$ 2 (on an scale from 0 to 4) • At least 10% of scalp area affected • Premenopausal women must use an established oral, injected or implanted hormonal method of contraception, intrauterine device (IUD) or intrauterine system (IUS) **Exclusion criteria of the trial** • Participants having a solely non-plaque form of psoriasis (e.g. erythrodermic, guttate, pustular) • Participants with uncontrolled psoriasis under the current treatment • Participants having received topical keratolytic agents for the scalp within the past 2 weeks and topical steroids for the scalp within the past week (prior to inclusion) • Participants receiving systemic antipsoriatic drugs, immunosuppressants or systemic corticosteroids (within 4 weeks prior to inclusion)

Augustin 2014 (*Continued*)

	• Women who are pregnant or breastfeeding or planning to become pregnant during the observational period • Known hypersensitivity to any ingredient in the investigational products' formulations **Washout period** • 1 weeks prior to randomisation: topical steroids on the scalp • 2 weeks prior to randomisation: topical keratolytic agents on the scalp • 4 weeks prior to randomisation: systemic antipsoriatic drugs, immunosuppressants or systemic corticosteroids **Baseline characteristics** This was not yet stated
Interventions	A: dimethicone formulation, once daily for 2 weeks (number of participants unclear) B: 10% salicylic acid gel, once daily for 2 weeks (number of participants unclear) Total estimated number of participants enrolled: 90
Outcomes	**Primary outcome of the trial** 1. Change from baseline in scaling (day 14) **Secondary outcomes of the trial** 1. Psoriasis Scalp Severity Index (PSSI) (day 3, 7 and 14) 2. Psoriasis Area Severity Index (PASI) (day 3, 7 and 14) 3. Body Surface Area (BSA) (day 3, 7 and 14) 4. Physician Global Assessment (PGA) (= IGA) (day 3, 7 and 14) 5. Scalp Physician Global Assessment (sPGA) (day 3, 7 and 14) 6. Dermatology Life Quality Index (DLQI) (day 3, 7 and 14) 7. Patient Benefit Index (PBI) (day 3, 7 and 14) 8. EuroQol Questionnaire (EQ-5D) (IAGI) (day 3, 7 and 14) 9. Adverse events (day 14) 10. Serious AEs (day 14) Definition: Detailed definition of the outcomes insufficiently addressed Visits: baseline, day 3, 7 and 14
Notes	This trial was identified on clinicaltrials.gov (NCT01914627, http://www.clinicaltrials.gov/ct2/show/NCT01914627 This study was supported by G. Pohl-Boskamp GmbH & Co. KG

Berth-Jones 1998

Methods	Multicentre, randomised, double-blinded, vehicle-controlled, parallel-group trial
Participants	Age between 18 and 80 years Diagnosis of mild to moderate scalp psoriasis
Interventions	A: tacalcitol lotion 4 mg/g, once daily B: vehicle N = 250 participants
Outcomes	Assessment of efficacy and safety. The abstract did not address the outcomes in detail

Berth-Jones 1998 (*Continued*)

Notes	Full-text of this study was not available

Bewley 2001

Methods	Multicentre, randomised, controlled, phase 3 study
Participants	Diagnosis of mild to moderate scalp psoriasis
Interventions	A: clobetasol propionate 0.05% shampoo B: Polytar Liquid N = 160 participants
Outcomes	Assessment of efficacy and safety. The abstract did not address the outcomes in detail
Notes	Full text of this study was not available

Combemale 2009

Methods	International, multicentre, randomised, vehicle-controlled, phase 3 trial
Participants	**Inclusion criteria of the trial** • Scalp psoriasis amenable to topical treatment • Psoriasis vulgaris on trunk and/or limbs • Extent of scalp psoriasis involving more than 10% of the total scalp area • Disease severity on the scalp graded as mild or worse by the investigator • Consenting out-patients of 18 years or above **Exclusion criteria of the trial** • Current diagnosis of erythrodermic, exfoliative or pustular psoriasis **Washout period** • 2 weeks prior to randomisation: UVB therapy, any topical treatment of the scalp (except for medicated shampoos and emollients), topical treatment of the face, trunk and/or limbs with very potent WHO group IV corticosteroids • 4 weeks prior to randomisation: PUVA or Grenz ray therapy, systemic anti-psoriatic treatment with all other therapies than biologicals • 6 months prior to randomisation: systematic anti-psoriatic treatment with biological therapies **Baseline characteristics** This was not stated
Interventions	A: calcipotriol 50 µg/g and betamethasone dipropionate 0.5 mg/g gel (Xamiol®), for 8 weeks B: calcipotriol 50 µg/g gel, for 8 weeks C: betamethasone dipropionate 0.5 mg/g gel, for 8 weeks D: vehicle, for 8 weeks N = 1485 participants
Outcomes	**Primary outcome of the trial** 1. Overall disease severity according to investigator's assessment (week 8) **Secondary outcomes of the trial**

Combemale 2009 *(Continued)*

	1. Total sign score (week 8) 2. Score for scaliness, redness and thickness (week 8) 3. Extent of scalp psoriasis (week 8) 4. Overall disease severity according to investigator's assessment (week 2 and 4) 5. Overall disease severity according to patients (week 8) 6. Adverse events 7. Laboratory data Definition: Detailed definition of the outcomes insufficiently addressed
Notes	Full text of this study was not available Study ID: MBL 0405 INT ClinicalTrials.gov-ID: NCT00216827 This study is sponsored by LEO Pharma

Graham-Brown 2001

Methods	Unknown
Participants	Unknown
Interventions	A: clobetasol propionate 0.5% shampoo B: Polytar Liquid
Outcomes	Efficacy and safety. The abstract did not address the outcomes in detail
Notes	Full text of this study was not available

Groves 2001

Methods	Randomised controlled trial
Participants	Diagnosis of moderate to severe scalp psoriasis
Interventions	A: agent A 0.05% shampoo B: agent B shampoo/liquid N = 8 participants
Outcomes	Efficacy and safety. The abstract did not address the outcomes in detail
Notes	Full text of this study was not available

Hutchinson 1995

Methods	Unknown
Participants	Unknown
Interventions	A: calcitriol solution B: Capasal (tar preparation)
Outcomes	Efficacy. The abstract did not address the outcomes in detail
Notes	Full text of this study was not available

Hutchinson 1997

Methods	Multicentre, double-blinded, randomised, vehicle-controlled, parallel-group trial
Participants	Unknown
Interventions	A: Tacalcitol lotion (4 µg/g) B: Vehicle
Outcomes	Efficacy and safety. The abstract did not address the outcomes in detail
Notes	Full text of this study was not available

Lebwohl 2015

Methods	Multicentre, randomised, active-controlled, double-blinded, parallel-group, phase 2 trial
Participants	Adult patients (= 18 years) with plaque psoriasis (psoriasis vulgaris) of at least mild severity by Physician's Global Assessment (PGA)
Interventions	A: calcipotriene 0.005% plus betamethasone dipropionate 0.064% foam, once daily for up to 4 weeks B: betamethasone dipropionate 0.064% foam, once daily for up to 4 weeks C: calcipotriene 0.005% foam, once daily for up to 4 weeks
Outcomes	Treatment success of the involved scalp according to modified Psoriasis Area Severity Index (mPASI) and safety
Notes	The information was derived from a conference abstract. It was presented at the 73rd Annual Meeting of the American Academy of Dermatology San Francisco, CA United States. Conference start: 20 March 2015, Conference end: 24 March 2015. The full text of this study was not available

Messenger 2011

Methods	Multicentre, randomised, active-controlled, investigator-blinded, parallel-group, phase 3 trial
Participants	Diagnosis of moderate to severe scalp psoriasis
Interventions	A: clobetasol propionate 0.05% shampoo B: Plytar liquid
Outcomes	Efficacy (global severity score and total severity score) and safety. The abstract did not address the outcomes in more detail
Notes	Full-text of this study was not available

Nishiyama 2010

Methods	Unknown
Participants	Unknown
Interventions	A: first month: camellia oil-containing shampoo alone, second month: camellia oil spray plus camellia oil-containing shampoo (2-step care) B: first month: camellia oil spray plus camellia oil-containing shampoo (2-step care), second month: camellia oil-containing shampoo alone
Outcomes	Scalp PASI, scaling, itching, number of adverse events. The abstract did not address the outcomes in more detail
Notes	Full text of this study was not available. The abstract does not provide sufficient information on study design

Pye 1995

Methods	Multicentre, randomised, prospective, double-blinded, parallel-group trial
Participants	Unknown
Interventions	A: calcipotriol cream, twice daily, for 6 weeks B: vehicle, twice daily, for 6 weeks
Outcomes	Efficacy and safety. The abstract did not address the outcomes in detail
Notes	Full text of this study was not available

Pye 1997

Methods	Multicentre, prospective, open-label, randomised, parallel-group trial
Participants	Unknown
Interventions	A: calcipotriol solution, for 8 weeks B: Capasal shampoo, for 8 weeks
Outcomes	Assessment of treatment response until week 24 of patients that cleared or responded to calcipotriol after 8 weeks of treatment. The abstract did not address the outcomes in more detail
Notes	Full text of this study was not available

AE: adverse event
BSA: body surface area
DLQI: Dermatology Life Quality Index
IGA: investigator's global assessment
mPASI: modified Psoriasis Area Severity Index
PASI: Psoriasis Area and Severity Index
PBI: Patient Benefit Index
PGA: Physician Global Assessment
PSSI: Psoriasis Scalp Severity Index
PUVA: psoralen and ultraviolet A
sPGA: Scalp Physician Global Assessment
WHO: World Health Organization

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

EUCTR2010-024033-24-DE

Trial name or title	'Double-blind, randomised, clinical study to compare the efficacy and safety of betamethasone 0.05% salicylic acid 2% vs. Diprosalic solution vs. vehicle for the treatment of psoriasis capitis'
Methods	This is a randomised, active and vehicle-controlled, double-blinded, 3-arm trial
Participants	**Inclusion criteria of the trial** • Men or women • At least 18 years • Diagnosis of psoriasis of the scalp • At least 20% of the scalp affected • Less than 50% of the body surface affected • Less than 30% of the body surface affected if the dermatosis was progressive within the last 4 weeks • Activity parameter erythema, desquamation, thickening and pruritus (score 0 to 3): sum score equal to or more than 6 and desquamation and erythema equal to or more than 4 and desquamation equal to or more than 2 **Exclusion criteria of the trial** • Known intolerance or hypersensitivity against betamethasone, salicylic acid or other components of

	the vehicle • Severe heart failure, severe insufficiency of the circulatory system, severe hepatic or renal insufficiency, severe respiratory insufficiency, neoplasm • Severe acute or chronic concomitant disease seriously affecting the general condition • Concomitant diseases which may - taking the present knowledge into account - influence the parameters evaluated in the study in a way that an objective evaluation would be impossible • Concomitant medication which may - taking the present knowledge into account - influence the methods of measurement used in this study or the resulting data • Pregnant women or planned pregnancy or lactating women **Washout period** • Within 2 weeks prior to screening: topical treatment or other therapies (e.g. UV exposure) of the psoriasis capitis • Within 4 weeks prior to screening: systemic psoriasis therapy
Interventions	A: betamethasone dipropionate 0.05% plus salicylic acid 2% solution for 3 weeks (number of participants unclear) B: betamethasone dipropionate plus salicylic acid solution (diprosalic acid) for 3 weeks (number of participants unclear) C: vehicle for 3 weeks (number of participants unclear) Total estimated number of participants enrolled: 225
Outcomes	**Primary outcome of the trial** 1. Difference of the sum score between start and end of therapy (day 21) **Secondary outcomes of the trial** 1. Course of the clinical signs and the sum score between baseline and final examination or early termination 2. Percentage of participants without symptoms (sum score = 0) at end of therapy and at the end of the observation phase 3. Global evaluation of therapeutic success by the investigator and the participant in the course of the study Definition: *Sum score (0 to 12):* consists of the activity parameters (clinical signs) erythema, desquamation, thickening of the skin and pruritus each rated on a scale from 0 to 3 Visits: baseline, day 7, 14, 21 and 35
Starting date	31/05/2011 (first enrolment)
Contact information	Lil-Dagover-Ring 7, 82031 Grünwald, Germany, Telephone: 004908964186121, Email: gabriele.bast@dermapharm.de
Notes	This study is sponsored by Dermapharm AG http://apps.who.int/trialsearch/trial.aspx?trialid=EUCTR2010-024033-24-DE

NCT01368887

Trial name or title	'Phase II study of a non-steroidal novel treatment for scalp psoriasis'
Methods	This is a randomised, active and vehicle-controlled, double-blind, 4-arm trial
Participants	**Inclusion criteria of the trial** • Male or female of age 18 or older • Participant with a personal history of scalp psoriasis • participant with treatable lesions • Participant with a TSS score equal or lower than 9 • Participant with a PGA score equal or lower than 5 • Participant with a negative urine pregnancy test at inclusion for women of childbearing potential and using an efficient contraceptive (oral contraceptives, IUD or tubal ligation) • Participant agreeing to participate to the study and to sign a written informed consent and comply with study requirements **Exclusion criteria of the trial** • Participant with PEG (poly ethylene glycol) allergy • Pregnant or breastfeeding female or female who do not use contraception • Participant with an history of hypersensitivity to Dovonex/Daivonex • Participant who has participated in a clinical trial within 3 months prior inclusion • Participants on carbamazepine and primidone (the clearance of primidone and carbamazepine may be reduced with the concomitant use of nicotinamide) • Participant who is under guardianship, or unable to understand the information (for linguistic or mental reason), or unwilling to give her/his informed consent to participate in the study **Washout period** • Within 2 weeks prior to randomisation: topical scalp treatment for scalp psoriasis (corticoids, retinoids, vitamin D derivatives) or systemic niacin and multivitamins • Within 4 weeks prior to randomisation: systemic treatment for psoriasis (biologics, methotrexate, cyclosporine, retinoids) or start or modification of treatment with beta-blocker
Interventions	A: calcipotriol plus nicotinamide (DermiPsor's DPS-102), twice daily for 12 weeks (number of participants unclear) B: vehicle, twice daily for 12 weeks (number of participants unclear) C: calcipotriol, twice daily for 12 weeks (number of participants unclear) D: nicotinamide, twice daily for 12 weeks (number of participants unclear) Total estimated number of participants to be enrolled: 160
Outcomes	**Primary outcome of the trial** 1. The number of participants at each Physician's Global Assessment (PGA = IGA) scale level (week 2, 4, 8 and 12) 2. Comparison of each individual's scale assessments over the 12-week period to assess any changes (week 2, 4, 8 and 12) **Secondary outcomes of the trial** 1. Review of haematology and blood chemistry test results (week 12) 2. Adverse events (AEs) (week 12) 3. Number of participants who experience AEs and type of AE in each case (week 12) Definition: *PGA*: investigator (physician) rating scalp psoriasis on a 6-point scale (clear, minimal, mild, moderate, severe and very severe) Visits: baseline, week 2, 4, 8 and 12

NCT01368887 (*Continued*)

Starting date	April 2013
Contact information	Shay Marcus, VP Business Development & Marketing, DermiPsor Ltd ClinicalTrials.gov-ID: NCT01368887
Notes	Recruitment is currently suspended (April 2014) This study is sponsored by DermiPsor, Ltd.

NCT01582932

Trial name or title	'A multicenter, randomised, double-blind, phase 3 study of the safety, efficacy, systemic exposure, and pharmacodynamics of calcipotriene foam, 0.005%, versus vehicle foam in paediatric subjects (ages 2 to 11 years) with plaque psoriasis'
Methods	This is a multicentre, randomised, active-controlled, double-blind, parallel-group trial
Participants	**Inclusion criteria of the trial** • Male or female participants • Age between 2 and 11 years • Clinical diagnosis of mild to moderate plaque psoriasis, as defined by body ISGA score of 2 or 3 on a scale of 0 to 4 • Mild to moderate plaque psoriasis involving at least 5% BSA and at least 5% scalp involvement (excluding the face) • Identification of a target lesion (> 2 cm^2) on the trunk or extremities with a score of 2 or 3 on a 0 to 5 scale for erythema, scaling and plaque thickness **Exclusion criteria of the trial** • Any inflammatory skin disease in the treatment area that may confound the evaluation of the plaque psoriasis • Current diagnosis of unstable forms of psoriasis in the treatment area, including guttate, erythrodermic, exfoliative or pustular psoriasis • Known difficult venous access beyond that expected for participant age • Average daily ingestion of more than 2000 mg of elemental calcium or more than 1000 IU of vitamin D within 2 weeks prior to enrolment • History of hypersensitivity, known allergy or other adverse reaction to calcipotriene or other vitamin D analogues or to any component of the study product • Current or past history of hypercalcaemia, vitamin D toxicity, severe renal insufficiency or severe hepatic disorders • Pregnant or breastfeeding female or females who do not use contraception • Current immunosuppression • Albumin-adjusted serum calcium at screening that is above the upper limit of normal **Washout period** • Within 2 weeks prior to randomisation: use of topical treatments that have a known beneficial effect on psoriasis, including but not limited to corticosteroids, retinoids, vitamin D derivatives, coal tar, tazarotene, medicated shampoos or anthralin • Within 4 weeks prior to randomisation: use of non biologic systemic antipsoriatic therapy (e.g. corticosteroids, psoralen, retinoids, methotrexate, cyclosporine, other immunosuppressive agents), biologic therapy (e.g. adalimumab, etanercept, golimumab, infliximab, ustekinumab), or phototherapy (e.g. psoralen

NCT01582932 (*Continued*)

	and ultraviolet A (PUVA), ultraviolet B (UVB)) • Within 4 weeks prior to randomisation: use of or need for initiation of any non psoriatic therapy that might affect psoriasis (including antimalarials, β-blockers, interferon, or lithium) • Within 4 weeks prior to randomisation: use of medications that affect or change calcium and parathyroid hormone (PTH) concentrations or interfere with the measurement of calcium or PTH concentrations • Within 4 weeks prior to randomisation: use of any investigational therapy
Interventions	A: calcipotriene 0.005% foam (STF 115469), twice daily for 8 weeks (number of participants unclear) B: vehicle foam, twice daily for 8 weeks (number of participants unclear) Total estimated number of participants to be enrolled: 180 Participants will be randomly assigned in a 2:1 ratio
Outcomes	**Primary outcome of the trial** 1. Treatment success (week 8) **Secondary outcomes of the trial** 1. Improvement of clinical signs from baseline (week 8) Definition: *Treatment success:* treatment success = ISGA score 0 or 1, and a minimum improvement in the ISGA score of 2 grades from baseline to week 8 *Improvement of clinical signs:* erythema, scaling and plaque thickness. Target lesion score of 0 or 1 for all 3 signs and at least to 2-grade improvement from baseline for erythema and scaling Visits: baseline, week 2 and 8
Starting date	April 2013
Contact information	US GSK Clinical Trials Call Center 877-379-3718 GSKClinicalSupportHD@gsk.com ClinicalTrials.gov-ID: NCT01582932
Notes	This trial may only be eligible for inclusion, if the authors report outcomes for the scalp separately This study is sponsored by GlaxoSmithKline

NCT01707043

Trial name or title	'Patient preference of Taclonex ointment to Taclonex scalp suspension in adult subjects with psoriasis vulgaris'
Methods	This is a monocentre, open-label, randomised, investigator-blinded, cross-over trial
Participants	**Inclusion criteria of the trial** • Male or female, age 18 or older • Participant has plaque-type psoriasis - no history of or current pustular, erythrodermic or guttate psoriasis • The percentage of overall body surface involvement is between 1% and 10% on the trunk or extremities and is amenable to topical treatment with less than 100 g of topical medication per week • The participant has an investigator global assessment of mild to moderate plaque psoriasis (severity index between 2 and 3 on a 5-point scale) **Exclusion criteria of the trial**

NCT01707043 (*Continued*)

	• Participant has other serious skin disorder or any chronic medical condition that is not well controlled • Participant has clinically relevant abnormal vital signs or findings on the physical examination • Participant has major illness within 30 days prior to the baseline visit • Participant has history of any immunocompromising disease • Participant has a skin condition or disease that may require concurrent therapy or may confound the evaluation; a history of hypersensitivity to any of the formulation components; or atopic dermatitis **Washout period** • Within 1 month prior to randomisation: systemic corticosteroid, phototherapy, retinoids, methotrexate, cyclosporine, or other immunosuppressive agents or biologics therapy (i.e. alefacept, etanercept, efalizumab) • Within two weeks prior to randomisation: topical therapy, corticosteroid therapy, topical vitamin D analogue or calcineurin inhibitors or tazarotene • Within 2 weeks prior to randomisation: tar, anthralin, salicylic acid, lactic acid, urea preparations
Interventions	A: calcipotriene 0.005% and betamethasone dipropionate 0.064% within an ointment (Taclonex®), once daily for 3 days B: calcipotriene 0.005% and betamethasone dipropionate 0.064% within a suspension (Taclonex Scalp®), once daily for 3 days Participants will be randomised to use either the ointment or the scalp suspension for 3 days, then cross over to use the other product for 3 days Estimated enrolment: 20 participants
Outcomes	**Primary outcome of the trial** 1. Patient preference 2. Adverse events Definition: Patient preference: participants will complete a questionnaire about their psoriasis treatment preferences Visits: baseline, day 3 and 6
Starting date	October 2012
Contact information	Steven R. Feldman, Professor of Dermatology, Wake Forest University
Notes	Sponsor: Wake Forest University, Collaborator: LEO Pharma Other study ID number: 21361 This study will only be eligible for inclusion if the authors report one of the safety outcomes of this review: the number of withdrawals due to adverse events or the number of patients with at least one adverse event

NCT02413229

Trial name or title	'A randomised double-blind vehicle controlled dose ranging multiple site phase 2 clinical study to evaluate the efficacy and safety of desoximetasone 0.25% shampoo in patients with moderate to severe scalp psoriasis'
Methods	This is a randomised, vehicle-controlled, double-blind, parallel-group trial
Participants	**Inclusion criteria of the trial** • Male or non-pregnant, non-lactating females age 12 and older • If female of child bearing potential, have a negative urine pregnancy test at baseline/randomisation

	visits and prepared to abstain from sexual intercourse or use a reliable method of contraception during the study. • Signed informed consent form. For patients under the age of majority in the state the study is being conducted, the parent or legal guardian signs consent and child signs a patient assent form. • Clinical diagnosis of moderate to severe scalp psoriasis, defined by a Investigator's Global Assessment score of at least 3 at screening. • Is in good general health. **Exclusion criteria of the trial** • Under 12 years of age • Females who are pregnant, lactating or likely to become pregnant during the study • Patients whose scalp and/or non-scalp psoriasis necessitates systemic or other concomitant topical therapies during the study • Has a scalp skin condition that would interfere with the diagnosis or assessment of plaque psoriasis of the scalp • Presence of pigmentation, extensive scarring, pigmented lesions or sunburn in the treatment areas, which could interfere with the rating of efficacy parameters • History of psoriasis unresponsive to topical treatments • Current immunosuppression • Changed brands/types or frequency of use of routine hair care products within 14 days prior to baseline, or intend to change during the study • Received any drug as part of a research study within 30 days prior to dosing • Significant history or current evidence of chronic infectious disease, system disorder, organ disorder or other medical condition that would place the study participant at undue risk by participation • History of allergy or hypersensitivity to desoximetasone or history of any drug hypersensitivity or intolerance which would compromise the safety of the patient or the study • Current evidence of drug abuse or history of drug abuse within 1 year before the first dose, including history of alcohol abuse or active alcoholism • Inability to understand the protocol requirements, instructions, and study-related restrictions, the nature, scope, and possible consequences of the clinical study • Unlikely to comply with the protocol requirements, instructions, and study-related restrictions **Washout period of the trial** • Within 2 weeks of screening: topical corticosteroids, topical anti-psoriatic medication, topical retinoids, beta blockers, lithium preparations, anti-malarial agents and non-steroidal anti-inflammatory drugs • Within 6 months: a biologic treatment for psoriasis • Within 3 months chemotherapy or radiation therapy • Within 1 month prior to screening: systemic steroids, systemic antibiotics, systemic antipsoriatic treatment, psoralen and ultraviolet A therapy, ultraviolet B therapy, systemic anti-inflammatory agents • Within 16 weeks of randomisation: systemic retinoids • Within 2 months prior to baseline of any immunosuppressive drugs or oral retinoids
Interventions	A: desoximetasone 0.25% shampoo, once daily for a total of 28 days B: vehicle shampoo, once daily for a total of 28 days Estimated enrolment: 180 participants
Outcomes	**Primary outcome of the trial** 1. Clinical success according to the Investigator's Global Assessment score (IGA) 2. Multiple treatment durations will be evaluated to determine the optimum duration of application Definition: Clinical success: IGA of 0 or 1

NCT02413229 (*Continued*)

	Visits: number of visits not reported
Starting date	March 2015
Contact information	Taro Pharmaceuticals USA, Inc. Hawthorne, New York, United States, 10532 Tel.: 914-345-9001 Study director: Natalie Yantovskiy
Notes	Sponsor: Taro Pharmaceuticals USA, Inc.

NCT02533973

Trial name or title	'Long-term treatment of scalp psoriasis with Xamiol® gel in a large adult Chinese population'
Methods	This is a randomised, investigator-blinded, active-controlled, parallel-group trial
Participants	**Inclusion criteria** : • Participants of either gender 18 years of age or older • At visit 1, a clinical diagnosis of scalp psoriasis which is: ○ of an investigator's assessment of clinical signs of the scalp of at least ≥ 2 in one of the clinical signs, redness, thickness and scaliness, and at least 1 in each of the other 2 clinical signs, and total score ≥ 4; ○ of an extent of 10% or more of the total scalp area; ○ of at least mild severity according the investigator's global assessment. • Clinical signs of psoriasis vulgaris on trunk and/or limbs, or participant earlier diagnosed with psoriasis vulgaris on trunk and/or limbs • Female of childbearing potential using a reliable method of contraception for at least 1 month before the trial start and during the course of the trial (e.g. oral contraceptive pill, intrauterine device, contraceptive patches, implantable contraception, condoms) or females of non-childbearing potential (i.e. postmenopausal (absence of menstrual bleeding for 2 years), hysterectomy, bilateral ovariectomy, or tubal section/ligation) **Exclusion criteria** : • Current diagnosis of guttate, erythrodermic, exfoliative or pustular psoriasis • Participants with any of the following conditions present on the scalp area: viral lesions, fungal and bacterial skin infections, parasitic infections, skin manifestations in relation to syphilis or tuberculosis, rosacea, acne vulgaris, acne rosacea, atrophic skin, striae atrophicae, fragility of skin veins, ichthyosis, ulcers and wound • Known or suspected renal insufficiency or hepatic disorders or severe heart disease • Clinical signs or symptoms of Cushing's disease or Addison's disease • Known or suspected hypersensitivity to component(s) of IMPs • Current participation in any other interventional clinical trial • Participants who have received treatment with any non-marketed drug substance (i.e. an agent which has not yet been made available for clinical use following registration) within 4 weeks/5 half-lives (whichever is longer) prior to randomisation • Previously participated in a clinical trial within 4 weeks prior to randomisation • In the opinion of the (sub) investigator, the subject is unlikely to comply with the clinical trial protocol (e.g. due to alcoholism, drug addiction or psychotic state) **Washout period** • Within 4 weeks prior to randomisation: etanercept (Yisaipu)

NCT02533973 (*Continued*)

	• Within 2 months prior to randomisation: infliximab (Remicade) • Within 4 weeks prior to randomisation: systemic treatment with all other therapies with a possible effect on psoriasis vulgaris (e.g., corticosteroids, retinoids, methotrexate, ciclosporin and other immunosuppressant's, TCM (traditional Chinese Medicine)) • Within 4 weeks prior to randomisation: PUVA therapy • Within 2 weeks prior to randomisation: UVB therapy • Within 2 weeks prior to randomisation: topical treatment of body psoriasis with very potent (WHO group IV) corticosteroids, topical treatment of face psoriasis with potent or very potent (WHO group III and IV) corticosteroids, any topical treatment of the scalp (except for non-steroid medicated shampoos and emollients)
Interventions	A: calcipotriol 50 µg/g plus betamethasone dipropionate 0.5 mg/g gel (Xamiol®), once daily as required for 28 weeks B: calcipotriol 50 µg/g solution (Daivonex®), twice daily as required for 28 weeks Estimated enrolment: 900 participants
Outcomes	**Primary outcome of the trial** 1. Number patients with adverse events associated with long-term corticosteroid use on the scalp **Secondary outcomes of the trial** 1. IGA: "treatment success" 2. PGA: "treatment success" Visits: number of visits not reported
Starting date	September 2015
Contact information	Annette Trotz, BSc, +61 7 3250 1200, annette.trotz@leo-pharma.com ClinicalTrials.gov-ID: NCT02533973
Notes	Sponsor: LEO Pharma, Collaborator: Hangzhou Tigermed Consulting Co. Ld Principle Investigator: Min Zheng, MD, PHD

BSA: body surface area
ISGA: Investigator's Static Global Assessment
IUD: intrauterine device
PGA: patient global assessment
PUVA: psoralen and ultraviolet A
TSS: total sign score
UV: ultraviolet
WHO: World Health Organization

DATA AND ANALYSES

Comparison 1. Steroid: once versus twice daily

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Mean score of the IGA	1		Mean Difference (IV, Random, 95% CI)	Totals not selected
1.1 Betamethasone valerate 0.12% (hydrophilic leave-on)	1		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
2 Mean score of the PGA	1		Mean Difference (IV, Random, 95% CI)	Totals not selected
2.1 Betamethasone valerate 0.12% (hydrophilic leave-on)	1		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]

Comparison 2. Steroid versus the vehicle

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Number of participants achieving 'clearance' by IGA	4	1315	Risk Ratio (M-H, Random, 95% CI)	14.58 [7.28, 29.17]
1.1 Amcinonide 0.1% (hydrophilic leave-on)	1	165	Risk Ratio (M-H, Random, 95% CI)	16.80 [2.29, 123.30]
1.2 Betamethasone dipropionate (hydrophilic leave-on)	1	692	Risk Ratio (M-H, Random, 95% CI)	10.15 [3.83, 26.88]
1.3 Clobetasol propionate (hydrophilic leave-on)	2	458	Risk Ratio (M-H, Random, 95% CI)	22.83 [7.31, 71.30]
2 Number of participants achieving 'response' by IGA	9	2114	Risk Ratio (M-H, Random, 95% CI)	5.24 [3.83, 7.17]
2.1 Betamethasone dipropionate (hydrophilic leave-on)	2	911	Risk Ratio (M-H, Random, 95% CI)	4.06 [2.85, 5.79]
2.2 Amcinonide 0.1% (hydrophilic leave-on)	1	165	Risk Ratio (M-H, Random, 95% CI)	5.19 [2.60, 10.36]
2.3 Betamethasone valerate 0.1% (hydrophilic leave-on)	2	250	Risk Ratio (M-H, Random, 95% CI)	2.96 [1.81, 4.85]
2.4 Clobetasol propionate (hydrophilic leave-on)	3	646	Risk Ratio (M-H, Random, 95% CI)	7.93 [5.46, 11.51]
2.5 Clobetasol propionate (rinse-off)	1	142	Risk Ratio (M-H, Random, 95% CI)	15.83 [2.23, 112.33]
3 Mean of the TSS			Other data	No numeric data
4 Improvement in quality of life	1		Mean Difference (IV, Random, 95% CI)	Totals not selected
4.1 Scalpdex	1		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
5 Number of participants withdrawing due to adverse events	4	1315	Risk Ratio (M-H, Random, 95% CI)	0.27 [0.11, 0.67]

5.1 Betamethasone dipropionate (hydrophilic leave-on)	1	692	Risk Ratio (M-H, Random, 95% CI)	0.21 [0.07, 0.61]
5.2 Amcinonide 0.1% (hydrophilic leave-on)	1	165	Risk Ratio (M-H, Random, 95% CI)	0.99 [0.06, 15.53]
5.3 Clobetasol propionate (hydrophilic leave-on)	2	458	Risk Ratio (M-H, Random, 95% CI)	0.33 [0.03, 3.13]
6 Number of participants achieving 'response' by PGA	5		Risk Ratio (M-H, Random, 95% CI)	Subtotals only
6.1 Betamethasone dipropionate (hydrophilic leave-on)	1	692	Risk Ratio (M-H, Random, 95% CI)	3.04 [2.17, 4.26]
6.2 Betamethasone valerate 0.1% (hydrophilic leave-on)	1	172	Risk Ratio (M-H, Random, 95% CI)	3.52 [1.97, 6.29]
6.3 Clobetasol propionate (hydrophilic leave-on)	2	565	Risk Ratio (M-H, Random, 95% CI)	6.92 [4.42, 10.83]
6.4 Clobetasol propionate (rinse-off)	1	142	Risk Ratio (M-H, Random, 95% CI)	14.35 [2.02, 102.12]
7 Mean score of the PGA	1		Mean Difference (IV, Random, 95% CI)	Totals not selected
7.1 Amcinonide 0.1% (hydrophilic leave-on)	1		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
8 Number of participants with at least one adverse event	7	1307	Risk Ratio (M-H, Random, 95% CI)	0.87 [0.70, 1.08]
8.1 Betamethasone valerate 0.1% (hydrophilic leave-on)	1	78	Risk Ratio (M-H, Random, 95% CI)	0.25 [0.01, 5.86]
8.2 Amcinonide 0.1% (hydrophilic leave-on)	1	157	Risk Ratio (M-H, Random, 95% CI)	1.39 [0.32, 5.99]
8.3 Betamethasone dipropionate (hydrophilic leave-on)	1	683	Risk Ratio (M-H, Random, 95% CI)	0.87 [0.69, 1.10]
8.4 Fluocinolone acetonide 0.01% (lipophilic leave-on)	1	84	Risk Ratio (M-H, Random, 95% CI)	3.0 [0.13, 71.61]
8.5 Clobetasol propionate (hydrophilic leave-on)	1	81	Risk Ratio (M-H, Random, 95% CI)	1.56 [0.56, 4.37]
8.6 Clobetasol propionate (rinse-off)	2	224	Risk Ratio (M-H, Random, 95% CI)	0.59 [0.29, 1.18]

Comparison 3. Vitamin D versus the vehicle

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Number of participants achieving 'clearance' by IGA	2		Risk Ratio (M-H, Random, 95% CI)	Subtotals only
1.1 Vitamin D (hydrophilic leave-on)	2	457	Risk Ratio (M-H, Random, 95% CI)	3.88 [1.49, 10.11]
2 Number of participants achieving 'response' by IGA	2		Risk Ratio (M-H, Random, 95% CI)	Subtotals only

2.1 Calcipotriene (hydrophilic leave-on)	2	771	Risk Ratio (M-H, Random, 95% CI)	2.11 [1.20, 3.69]
3 Mean of the TSS			Other data	No numeric data
4 Number of participants withdrawing due to adverse events	3		Risk Ratio (M-H, Random, 95% CI)	Subtotals only
4.1 Vitamin D (hydrophilic leave-on)	3	820	Risk Ratio (M-H, Random, 95% CI)	1.43 [0.72, 2.83]
5 Number of participants achieving 'clearance' by PGA	1		Risk Ratio (M-H, Random, 95% CI)	Totals not selected
5.1 Calcipotriol (hydrophilic leave-on)	1		Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
6 Number of participants achieving 'response' by PGA	1		Risk Ratio (M-H, Random, 95% CI)	Totals not selected
6.1 Calcipotriene (hydrophilic leave-on)	1		Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
7 Number of participants with at least one adverse event	3		Risk Ratio (M-H, Random, 95% CI)	Subtotals only
7.1 Vitamin D (hydrophilic leave-on)	3	813	Risk Ratio (M-H, Random, 95% CI)	1.12 [0.92, 1.36]

Comparison 4. Steroid plus vitamin D versus the vehicle

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Number of participants achieving 'clearance' by IGA	1		Risk Ratio (M-H, Random, 95% CI)	Totals not selected
1.1 Betamethasone dipropionate plus calcipotriene (hydrophilic leave-on)	1		Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
2 Number of participants achieving 'response' by IGA	2		Risk Ratio (M-H, Random, 95% CI)	Totals not selected
2.1 Betamethasone dipropionate plus calcipotriene (hydrophilic leave-on)	2		Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
3 Mean of the TSS			Other data	No numeric data
4 Number of participants withdrawing due to adverse events	2		Risk Ratio (M-H, Random, 95% CI)	Subtotals only
4.1 Betamethasone dipropionate plus calcipotriene (hydrophilic leave-on)	2	843	Risk Ratio (M-H, Random, 95% CI)	0.48 [0.08, 2.83]
5 Number of participants achieving 'response' by PGA	2		Risk Ratio (M-H, Random, 95% CI)	Totals not selected
5.1 Betamethasone dipropionate plus calcipotriene (hydrophilic leave-on)	2		Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]

6 Number of participants with at least one adverse event	2		Risk Ratio (M-H, Random, 95% CI)	Subtotals only
6.1 Betamethasone dipropionate plus calcipotriene (hydrophilic leave-on)	2	831	Risk Ratio (M-H, Random, 95% CI)	0.86 [0.68, 1.09]

Comparison 5. Steroid versus steroid: very high versus high potency

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Number of participants achieving 'clearance' by IGA	1		Risk Ratio (M-H, Random, 95% CI)	Totals not selected
1.1 Clobetasol propionate vs betamethasone dipropionate (hydrophilic leave-ons)	1		Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
2 Number of participants achieving 'response' by IGA	1		Risk Ratio (M-H, Random, 95% CI)	Totals not selected
2.1 Clobetasol propionate vs betamethasone dipropionate (hydrophilic leave-ons)	1		Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
3 Mean of the TSS			Other data	No numeric data
4 Number of participants with at least one adverse event	2		Risk Ratio (M-H, Random, 95% CI)	Subtotals only
4.1 Clobetasol propionate vs betamethasone dipropionate (hydrophilic leave-ons)	2	236	Risk Ratio (M-H, Random, 95% CI)	0.90 [0.32, 2.48]

Comparison 6. Steroid versus steroid: high versus moderate potency

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Number of participants achieving 'clearance' by IGA	2	190	Risk Ratio (M-H, Random, 95% CI)	1.16 [0.56, 2.39]
1.1 Betamethasone dipropionate vs hydrocortisone 17-butyrate 0.1% (hydrophilic leave-on)	1	150	Risk Ratio (M-H, Random, 95% CI)	0.76 [0.30, 1.93]
1.2 Fluocinolone acetonide 0.025% vs hydrocortisone 17-butyrate 0.1% (lipophilic leave-on)	1	40	Risk Ratio (M-H, Random, 95% CI)	1.57 [0.77, 3.22]
2 Number of participants achieving 'response' by IGA	1		Risk Ratio (M-H, Random, 95% CI)	Totals not selected

2.1 Fluocinonide 0.05% vs desoximetasone 0.05% (hydrophilic leave-ons)	1	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
3 Mean of the TSS		Other data	No numeric data
4 Number of participants with at least one adverse event	1	Risk Ratio (M-H, Random, 95% CI)	Totals not selected
4.1 Mometasone furoate vs triamcinolone acetonide 0.1% (hydrophilic leave-on)	1	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]

Comparison 7. Steroids versus steroid: both of high potency

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Number of participants achieving 'clearance' by IGA	1		Risk Ratio (M-H, Random, 95% CI)	Totals not selected
1.1 Mometasone furoate vs betamethasone valerate 0.1% (hydrophilic leave-ons)	1		Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
2 Number of participants achieving 'response' by IGA	1		Risk Ratio (M-H, Random, 95% CI)	Totals not selected
2.1 Mometasone furoate vs betamethasone valerate 0.1% (hydrophilic leave-ons)	1		Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
3 Mean of the TSS			Other data	No numeric data
4 Number of participants withdrawing due to adverse events	2		Risk Ratio (M-H, Random, 95% CI)	Totals not selected
4.1 Amcinonide 0.1% vs fluocinonide (hydrophilic leave-ons)	1		Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
4.2 Betamethasone vs fluocinonide (hydrophilic leave-ons)	1		Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
5 Number of participants with at least one adverse event	2		Risk Ratio (M-H, Random, 95% CI)	Totals not selected
5.1 Amcinonide 0.1% vs fluocinonide (hydrophilic leave-ons)	1		Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
5.2 Betamethasone dipropionate vs fluocinonide (hydrophilic leave-ons)	1		Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]

Comparison 8. Steroid versus vitamin D

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Number of participants achieving 'clearance' by IGA	4	2180	Risk Ratio (M-H, Random, 95% CI)	1.82 [1.52, 2.18]
1.1 Betamethasone valerate 1 mg/ml vs calcipotriol (hydrophilic leave-ons)	1	474	Risk Ratio (M-H, Random, 95% CI)	1.85 [1.31, 2.60]
1.2 Betamethasone dipropionate vs vitamin D (hydrophilic leave-ons)	2	1676	Risk Ratio (M-H, Random, 95% CI)	1.81 [1.46, 2.24]
1.3 Mometasone furoate vs calcipotriol (hydrophilic leave-ons)	1	30	Risk Ratio (M-H, Random, 95% CI)	2.0 [0.43, 9.32]
2 Number of participants achieving 'response' by IGA	3	1827	Risk Ratio (M-H, Random, 95% CI)	2.09 [1.80, 2.41]
2.1 Clobetasol propionate vs calcipotriol (rinse-off vs hydrophilic leave-on)	1	151	Risk Ratio (M-H, Random, 95% CI)	1.79 [1.17, 2.74]
2.2 Betamethasone dipropionate vs vitamin D (hydrophilic leave-ons)	2	1676	Risk Ratio (M-H, Random, 95% CI)	2.13 [1.82, 2.50]
3 Mean of the TSS			Other data	No numeric data
4 Number of participants withdrawing due to adverse events	4	2291	Risk Ratio (M-H, Random, 95% CI)	0.22 [0.11, 0.42]
4.1 Betamethasone valerate 1 mg/ml vs calcipotriol (hydrophilic leave-ons)	1	474	Risk Ratio (M-H, Random, 95% CI)	0.19 [0.04, 0.83]
4.2 Betamethasone dipropionate vs vitamin D (hydrophilic leave-ons)	2	1666	Risk Ratio (M-H, Random, 95% CI)	0.25 [0.08, 0.74]
4.3 Clobetasol propionate vs calcipotriol (rinse-off vs hydrophilic leave-on)	1	151	Risk Ratio (M-H, Random, 95% CI)	0.07 [0.00, 1.13]
5 Number of participants achieving 'clearance' by PGA	2	504	Risk Ratio (M-H, Random, 95% CI)	2.22 [1.47, 3.35]
5.1 Betamethasone valerate 1 mg/ml vs calcipotriol (hydrophilic leave-ons)	1	474	Risk Ratio (M-H, Random, 95% CI)	2.09 [1.36, 3.22]
5.2 Mometasone furoate vs calcipotriol (hydrophilic leave-ons)	1	30	Risk Ratio (M-H, Random, 95% CI)	4.0 [1.01, 15.81]
6 Number of participants achieving 'response' by PGA	3	1827	Risk Ratio (M-H, Random, 95% CI)	1.48 [1.28, 1.72]
6.1 Clobetasol propionate vs calcipotriol (rinse-off vs hydrophilic leave-on)	1	151	Risk Ratio (M-H, Random, 95% CI)	1.54 [1.02, 2.34]

6.2 Betamethasone dipropionate vs vitamin D (hydrophilic leave-ons)	2	1676	Risk Ratio (M-H, Random, 95% CI)	1.48 [1.21, 1.80]
7 Number of participants with at least one adverse event	5		Risk Ratio (M-H, Random, 95% CI)	Subtotals only
7.1 Betamethasone valerate 1 mg/ml vs calcipotriol (hydrophilic leave-ons)	1	474	Risk Ratio (M-H, Random, 95% CI)	0.37 [0.25, 0.53]
7.2 Betamethasone dipropionate vs vitamin D (hydrophilic leave-ons)	2	1652	Risk Ratio (M-H, Random, 95% CI)	0.82 [0.70, 0.97]
7.3 Clobetasol propionate vs calcipotriol (hydrophilic leave-on vs occlusive lipophilic leave-on)	1	43	Risk Ratio (M-H, Random, 95% CI)	0.48 [0.10, 2.34]
7.4 Clobetasol propionate vs calcipotriol (rinse-off vs hydrophilic leave-on)	1	151	Risk Ratio (M-H, Random, 95% CI)	0.34 [0.16, 0.72]

Comparison 9. Steroid plus salicylic acid versus steroid

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Number of participants achieving 'clearance' by IGA	1		Risk Ratio (M-H, Random, 95% CI)	Totals not selected
1.1 Betamethasone dipropionate plus SA vs betamethasone dipropionate (hydrophilic leave-on)	1		Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
2 Number of participants achieving 'response' by IGA	1		Risk Ratio (M-H, Random, 95% CI)	Totals not selected
2.1 Betamethasone dipropionate plus SA vs betamethasone dipropionate (hydrophilic leave-ons)	1		Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]

Comparison 10. Steroid plus vitamin D versus steroid

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Number of participants achieving 'clearance' by IGA	4	2474	Risk Ratio (M-H, Random, 95% CI)	1.22 [1.08, 1.36]

1.1 Betamethasone dipropionate plus vitamin D vs betamethasone dipropionate (hydrophilic leave-ons)	3	2444	Risk Ratio (M-H, Random, 95% CI)	1.21 [1.07, 1.36]
1.2 Mometasone furoate plus calcipotriol vs mometasone furoate (hydrophilic leave-ons)	1	30	Risk Ratio (M-H, Random, 95% CI)	2.0 [0.76, 5.24]
2 Number of participants achieving 'response' by IGA	3		Risk Ratio (M-H, Random, 95% CI)	Subtotals only
2.1 Betamethasone dipropionate plus vitamin D vs betamethasone dipropionate (hydrophilic leave-ons)	3	2444	Risk Ratio (M-H, Random, 95% CI)	1.15 [1.06, 1.25]
3 Mean of the TSS			Other data	No numeric data
4 Number of participants withdrawing due to adverse events	3		Risk Ratio (M-H, Random, 95% CI)	Subtotals only
4.1 Betamethasone dipropionate plus vitamin D vs betamethasone dipropionate (hydrophilic leave-ons)	3	2433	Risk Ratio (M-H, Random, 95% CI)	0.88 [0.42, 1.88]
5 Number of participants achieving 'clearance' by PGA	1		Risk Ratio (M-H, Random, 95% CI)	Totals not selected
5.1 Mometasone furoate plus calcipotriol vs mometasone furoate (hydrophilic leave-ons)	1		Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
6 Number of participants achieving 'response' by PGA	2		Risk Ratio (M-H, Random, 95% CI)	Subtotals only
6.1 Betamethasone dipropionate plus vitamin D vs betamethasone dipropionate (hydrophilic leave-ons)	2	2226	Risk Ratio (M-H, Random, 95% CI)	1.13 [1.06, 1.20]
7 Number of participants with at least one adverse event	3		Risk Ratio (M-H, Random, 95% CI)	Subtotals only
7.1 Betamethasone dipropionate plus vitamin D vs betamethasone dipropionate (hydrophilic leave-ons)	3	2414	Risk Ratio (M-H, Random, 95% CI)	0.97 [0.87, 1.07]

Comparison 11. Steroid plus vitamin D versus vitamin D

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Number of participants achieving 'clearance' by IGA	4	2008	Risk Ratio (M-H, Random, 95% CI)	2.28 [1.87, 2.78]

1.1 Betamethasone dipropionate plus vitamin D vs vitamin D (hydrophilic leave-ons)	3	1978	Risk Ratio (M-H, Random, 95% CI)	2.25 [1.83, 2.77]
1.2 Mometasone furoate plus calcipotriol vs calcipotriol (hydrophilic leave-ons)	1	30	Risk Ratio (M-H, Random, 95% CI)	4.0 [1.01, 15.81]
2 Number of participants achieving 'response' by IGA	4	2222	Risk Ratio (M-H, Random, 95% CI)	2.31 [1.75, 3.04]
2.1 Betamethasone dipropionate plus vitamin D vs vitamin D (hydrophilic leave-on)	3	1978	Risk Ratio (M-H, Random, 95% CI)	2.56 [2.03, 3.22]
2.2 Betamethasone dipropionate plus calcipotriol vs calcipotriol (hydrophilic leave-on) - trial register study	1	244	Risk Ratio (M-H, Random, 95% CI)	1.72 [1.43, 2.07]
3 Mean of the TSS			Other data	No numeric data
4 Number of participants withdrawing due to adverse events (short-term)	4		Risk Ratio (M-H, Random, 95% CI)	Subtotals only
4.1 Betamethasone dipropionate plus vitamin D vs vitamin Dg (hydrophilic leave-on)	3	1970	Risk Ratio (M-H, Random, 95% CI)	0.19 [0.11, 0.36]
4.2 Betamethasone dipropionate plus calcipotriol vs calcipotriol (hydrophilic leave-on) - trial register study	1	244	Risk Ratio (M-H, Random, 95% CI)	2.07 [0.39, 11.07]
5 Number of participants withdrawing due to adverse events (long-term)	1		Risk Ratio (M-H, Random, 95% CI)	Totals not selected
5.1 Betamethasone dipropionate plus calcipotriol vs calcipotriol (hydrophilic leave-on)	1		Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
6 Number of participants achieving 'clearance' by PGA	1		Risk Ratio (M-H, Random, 95% CI)	Totals not selected
6.1 Mometasone furoate plus calcipotriol vs calcipotriol (hydrophilic leave-ons)	1		Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
7 Number of participants achieving 'response' by PGA	4	2222	Risk Ratio (M-H, Random, 95% CI)	1.76 [1.46, 2.12]
7.1 Betamethasone dipropionate plus vitamin D vs vitamin D (hydrophilic leave-on)	3	1978	Risk Ratio (M-H, Random, 95% CI)	1.89 [1.47, 2.42]
7.2 Betamethasone dipropionate plus calcipotriol vs calcipotriol (hydrophilic leave-on)	1	244	Risk Ratio (M-H, Random, 95% CI)	1.50 [1.29, 1.75]

8 Number of participants with at least one adverse event (short-term)	4	2193	Risk Ratio (M-H, Random, 95% CI)	0.70 [0.58, 0.85]
8.1 Betamethasone dipropionate plus vitamin D vs vitamin D (hydrophilic leave-on)	3	1951	Risk Ratio (M-H, Random, 95% CI)	0.74 [0.63, 0.88]
8.2 Betamethasone dipropionate plus calcipotriol vs calcipotriol (hydrophilic leave-on) - trial register study	1	242	Risk Ratio (M-H, Random, 95% CI)	0.44 [0.25, 0.76]
9 Number of participants with at least one adverse event (long-term)	1		Risk Ratio (M-H, Random, 95% CI)	Totals not selected
9.1 Betamethasone dipropionate plus calcipotriol vs calcipotriol (hydrophilic leave-on)	1		Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]

Comparison 12. Tar and dithranol

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Number of participants achieving 'clearance' by IGA	3		Risk Ratio (M-H, Random, 95% CI)	Totals not selected
1.1 Calcipotriol vs tar/dithranol combination (hydro/lipophilic leave-on combination)	1		Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
1.2 Tacrolimus vs pine tar (lipophilic leave-ons)	1		Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
1.3 Dithranol/urea combination vs coal tar plus salicylic acid combination (lipophilic leave-ons)	1		Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
2 Number of participants achieving 'response' by IGA	1		Risk Ratio (M-H, Random, 95% CI)	Totals not selected
2.1 Calcipotriol vs tar/dithranol combination (hydro/lipophilic leave-on combination)	1		Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
3 Mean of the TSS			Other data	No numeric data
4 Number of participants withdrawing due to adverse events	4		Risk Ratio (M-H, Random, 95% CI)	Totals not selected

4.1 Calcipotriol vs tar/dithranol combination (hydro/lipophilic leave-on combination)	1	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
4.2 Calcipotriol vs coal tar/coconut oil/salicylic acid (hydrophilic leave-on vs rinse-off)	1	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
4.3 Clobetasol propionate vs tar blend (rinse-offs)	1	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
4.4 Cocois vs coal tar (lipophilic leave-on vs rinse-off)	1	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
5 Number of participants achieving 'clearance' by PGA	1	Risk Ratio (M-H, Random, 95% CI)	Totals not selected
5.1 Calcipotriol vs tar/dithranol combination (hydro/lipophilic leave-on combination)	1	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
6 Number of participants achieving 'response' by PGA	1	Risk Ratio (M-H, Random, 95% CI)	Totals not selected
6.1 Calcipotriol vs tar/dithranol combination (hydro/lipophilic leave-on combination)	1	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
7 Number of participants with at least one adverse event	6	Risk Ratio (M-H, Random, 95% CI)	Totals not selected
7.1 Calcipotriol vs tar/dithranol combination (hydro/lipophilic leave-on combination)	1	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
7.2 Calcipotriol vs coal tar/coconut oil/salicylic acid (hydrophilic leave-on vs rinse-off)	1	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
7.3 Clobetasol propionate vs tar blend (rinse-offs)	1	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
7.4 Tacrolimus vs pine tar (lipophilic leave-ons)	1	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
7.5 Dithranol/urea combination vs coal tar plus salicylic acid combination (lipophilic leave-ons)	1	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
7.6 Cocois vs coal tar (lipophilic leave-on vs rinse-off)	1	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]

Comparison 13. Steroid: vehicle comparisons

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Number of participants achieving 'clearance' by IGA	1		Risk Ratio (M-H, Random, 95% CI)	Totals not selected
1.1 Betameth diprop (BP) + RV3423A shampoo/shampoo vs BP + shampoo	1		Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
2 Number of participants achieving 'response' by IGA	2		Risk Ratio (M-H, Random, 95% CI)	Totals not selected
2.1 Betamethasone valerate 0.1%: foam vs lotion	1		Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
2.2 Clobetasol propionate: foam vs solution	1		Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
3 Mean of the TSS			Other data	No numeric data
4 Number of participants achieving 'response' by PGA	2		Risk Ratio (M-H, Random, 95% CI)	Totals not selected
4.1 Betamethasone valerate 0.1%: foam vs lotion	1		Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
4.2 Clobetasol propionate: foam vs solution	1		Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
5 Number of participants with at least one adverse event	1		Risk Ratio (M-H, Random, 95% CI)	Totals not selected
5.1 Clobetasol: shampoo vs hydrophilic leave-on	1		Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]

Comparison 14. Other steroid plus salicylic acid comparisons

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Number of participants achieving 'clearance' by IGA	4		Risk Ratio (M-H, Random, 95% CI)	Subtotals only
1.1 Betamethasone dipropionate (BDP) plus SA vs triamcinolone acetonide 0.2% plus SA (hydrophilic leave-ons)	1	61	Risk Ratio (M-H, Random, 95% CI)	2.64 [1.47, 4.74]
1.2 Betamethasone dipropionate (BDP) plus SA vs betamethasone valerate 0.1% (hydrophilic leave-ons)	2	116	Risk Ratio (M-H, Random, 95% CI)	1.40 [0.59, 3.32]
1.3 Betamethasone dipropionate (BDP) plus SA vs clobetasol propionate (hydrophilic leave-ons)	1	50	Risk Ratio (M-H, Random, 95% CI)	1.4 [0.97, 2.01]

1.4 Betamethasone dipropionate (BDP) vs triamcinolone acetonide 0.2% plus SA (hydrophilic leave-on)	1	60	Risk Ratio (M-H, Random, 95% CI)	2.26 [1.23, 4.16]
2 Number of participants achieving 'response' by IGA	1		Risk Ratio (M-H, Random, 95% CI)	Totals not selected
2.1 Betameth diprop plus SA vs triamcin acet 0.2% plus SA (hydrophilic leave-ons)	1		Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
2.2 Betameth diprop vs triamcin acet 0.2% plus SA (hydrophilic leave-ons)	1		Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
3 Number of participants withdrawing due to adverse events	1		Risk Ratio (M-H, Random, 95% CI)	Totals not selected
3.1 Betamethasone dipropionate plus SA vs clobetasol propionate (hydrophilic leave-ons)	1		Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
4 Number of participants with at least one adverse event	2		Risk Ratio (M-H, Random, 95% CI)	Totals not selected
4.1 Betamethasone dipropionate plus SA vs betamethasone valerate 0.1% (hydrophilic leave-ons)	1		Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
4.2 Betamethasone dipropionate plus SA vs clobetasol propionate (hydrophilic leave-ons)	1		Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]

Comparison 15. Antifungals versus vehicle

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Mean score of the IGA	1		Mean Difference (IV, Random, 95% CI)	Subtotals only
2 Number of participants withdrawing due to adverse events	1		Risk Ratio (M-H, Random, 95% CI)	Totals not selected
2.1 Ciclopirox olamine (hydrophilic leave-on)	1		Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
3 Mean score of the PGA	1		Mean Difference (IV, Random, 95% CI)	Subtotals only
4 Number of participants with at least one adverse event	1		Risk Ratio (M-H, Random, 95% CI)	Totals not selected
4.1 Ciclopirox olamine (hydrophilic leave-on) vs placebo	1		Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]

Analysis 1.1. Comparison 1 Steroid: once versus twice daily, Outcome 1 Mean score of the IGA.

Review: Topical treatments for scalp psoriasis

Comparison: 1 Steroid: once versus twice daily

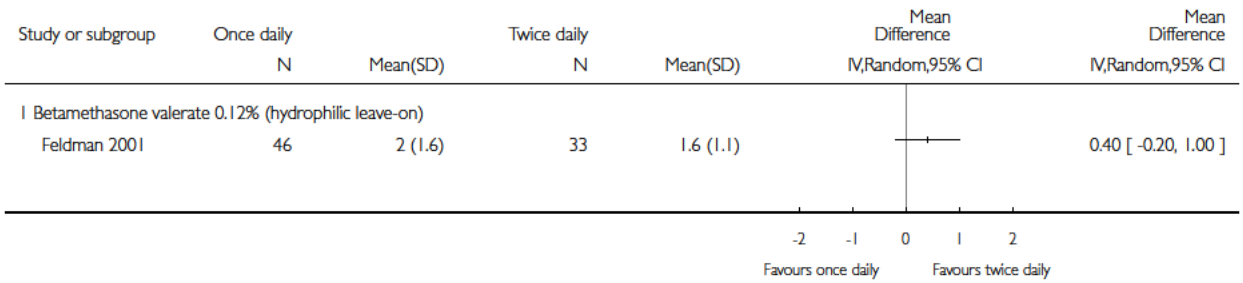
Outcome: 1 Mean score of the IGA

Analysis 1.2. Comparison 1 Steroid: once versus twice daily, Outcome 2 Mean score of the PGA.

Review: Topical treatments for scalp psoriasis

Comparison: 1 Steroid: once versus twice daily

Outcome: 2 Mean score of the PGA

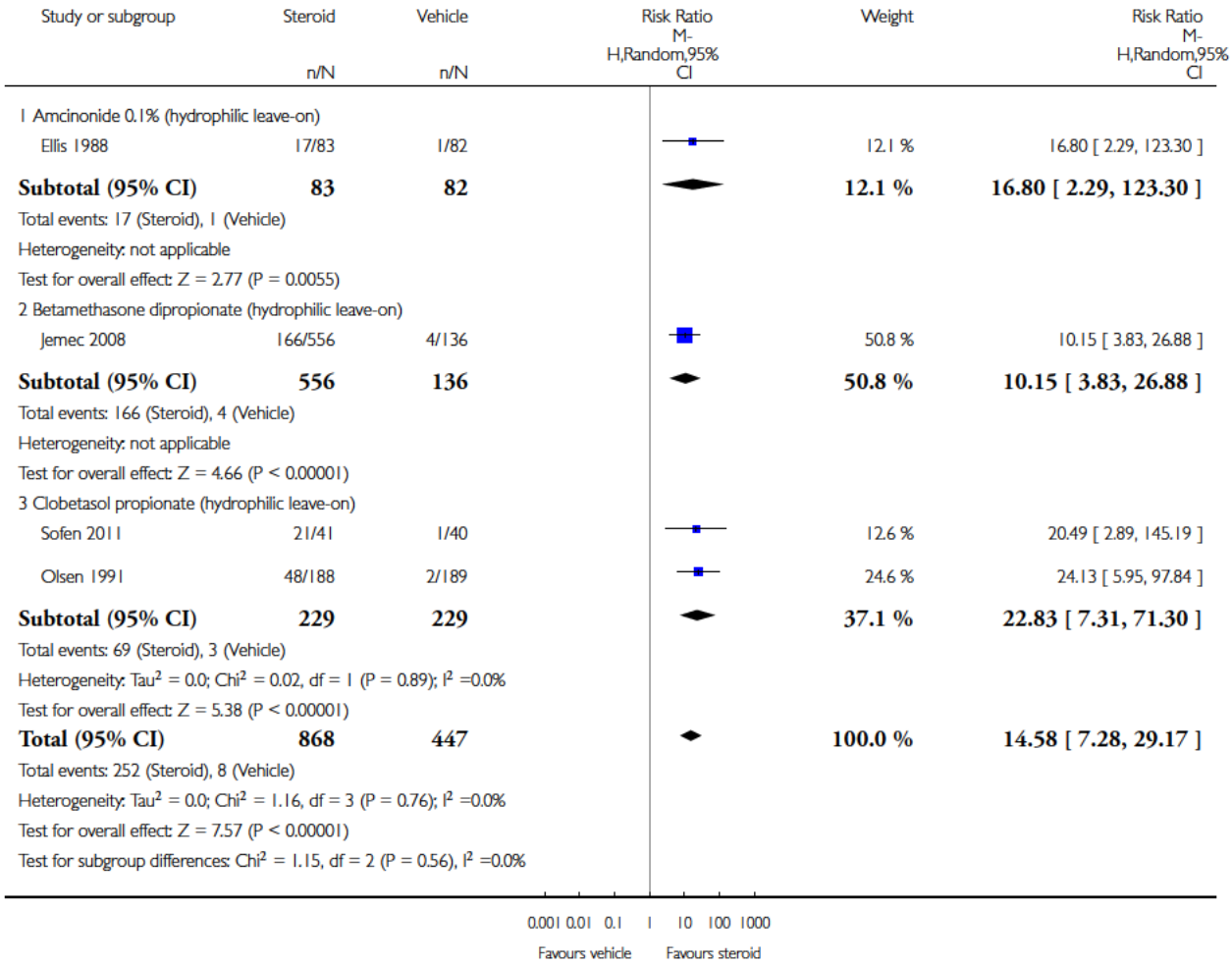


Analysis 2.1. Comparison 2 Steroid versus the vehicle, Outcome 1 Number of participants achieving 'clearance' by IGA.

Review: Topical treatments for scalp psoriasis

Comparison: 2 Steroid versus the vehicle

Outcome: 1 Number of participants achieving 'clearance' by IGA



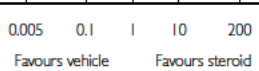
Analysis 2.2. Comparison 2 Steroid versus the vehicle, Outcome 2 Number of participants achieving 'response' by IGA.

Review: Topical treatments for scalp psoriasis

Comparison: 2 Steroid versus the vehicle

Outcome: 2 Number of participants achieving 'response' by IGA

Study or subgroup	Steroid n/N	Vehicle n/N	Risk Ratio M-H,Random,95% CI	Weight	Risk Ratio M-H,Random,95% CI
1 Betamethasone dipropionate (hydrophilic leave-on)					
Jemec 2008	304/556	20/136		18.8 %	3.72 [2.46, 5.61]
Medansky 1974	48/117	8/102		11.7 %	5.23 [2.60, 10.53]
Subtotal (95% CI)	**673**	**238**		**30.5 %**	**4.06 [2.85, 5.79]**
Total events: 352 (Steroid), 28 (Vehicle)					
Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 0.68$, df = 1 (P = 0.41); $I^2 = 0.0\%$					
Test for overall effect: Z = 7.74 (P < 0.00001)					
2 Amcinonide 0.1% (hydrophilic leave-on)					
Ellis 1988	42/83	8/82		11.8 %	5.19 [2.60, 10.36]
Subtotal (95% CI)	**83**	**82**		**11.8 %**	**5.19 [2.60, 10.36]**
Total events: 42 (Steroid), 8 (Vehicle)					
Heterogeneity: not applicable					
Test for overall effect: Z = 4.66 (P < 0.00001)					
3 Betamethasone valerate 0.1% (hydrophilic leave-on)					
Franz 1999	68/115	12/57		15.7 %	2.81 [1.66, 4.75]
Harris 1972	12/45	2/33		4.1 %	4.40 [1.06, 18.35]
Subtotal (95% CI)	**160**	**90**		**19.8 %**	**2.96 [1.81, 4.85]**
Total events: 80 (Steroid), 14 (Vehicle)					
Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 0.34$, df = 1 (P = 0.56); $I^2 = 0.0\%$					
Test for overall effect: Z = 4.32 (P = 0.000016)					
4 Clobetasol propionate (hydrophilic leave-on)					
Franz 2000	86/125	5/63		9.2 %	8.67 [3.71, 20.27]
Olsen 1991	129/188	16/189		16.9 %	8.11 [5.02, 13.08]
Sofen 2011	35/41	5/40		9.4 %	6.83 [2.98, 15.66]
Subtotal (95% CI)	**354**	**292**		**35.5 %**	**7.93 [5.46, 11.51]**
Total events: 250 (Steroid), 26 (Vehicle)					
Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 0.18$, df = 2 (P = 0.92); $I^2 = 0.0\%$					
Test for overall effect: Z = 10.89 (P < 0.00001)					
5 Clobetasol propionate (rinse-off)					
Jarratt 2004	32/95	1/47		2.3 %	15.83 [2.23, 112.33]



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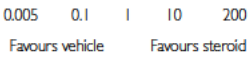
Study or subgroup	Steroid n/N	Vehicle n/N	Risk Ratio M-H,Random,95% CI	Weight	Risk Ratio M-H,Random,95% CI
Subtotal (95% CI)	**95**	**47**		**2.3 %**	**15.83 [2.23, 112.33]**
Total events: 32 (Steroid), 1 (Vehicle)					
Heterogeneity: not applicable					
Test for overall effect: Z = 2.76 (P = 0.0057)					
Total (95% CI)	**1365**	**749**		**100.0 %**	**5.24 [3.83, 7.17]**
Total events: 756 (Steroid), 77 (Vehicle)					
Heterogeneity: Tau^2 = 0.09; Chi^2 = 14.30, df = 8 (P = 0.07); I^2 =44%					
Test for overall effect: Z = 10.35 (P < 0.00001)					
Test for subgroup differences: Chi^2 = 12.89, df = 4 (P = 0.01), I^2 =69%					



Analysis 2.3. Comparison 2 Steroid versus the vehicle, Outcome 3 Mean of the TSS.

Mean of the TSS

Study	Comparison: Steroid vs vehicle	Steroid	Placebo
Franz 1999	Betamethasone valerate (hydrophilic leave-on) vs placebo	-57%	-24%
Franz 2000	Clobetasol propionate (hydrophilic leave-on) vs placebo	-72%	-37%
Jarratt 2004	Clobetasol propionate (rinse-off) vs placebo vs placebo	-49%	-18%
Jemec 2008	Betamethasone dipropionate (hydrophilic leave-on) vs placebo	-64%	-36%
Olsen 1991	Clobetasol propionate (hydrophilic leave-on) vs placebo	-72%	-30%
Pauporte 2004	Fluocinolone acetonide (hydrophilic leave-on) vs placebo	-59%	-32%
Sofen 2011	Clobetasol propionate (hydrophilic leave-on) vs placebo	-79%	-25%

Analysis 2.4. Comparison 2 Steroid versus the vehicle, Outcome 4 Improvement in quality of life.

Review: Topical treatments for scalp psoriasis
Comparison: 2 Steroid versus the vehicle
Outcome: 4 Improvement in quality of life

Study or subgroup	Clobetasol N	Mean(SD)	Vehicle N	Mean(SD)	Mean Difference IV,Random,95% CI	Mean Difference IV,Random,95% CI
1 Scalpdex						
Sofen 2011	41	30 (22)	40	50.7 (22.8)		-20.70 [-30.46, -10.94]

Analysis 2.5. Comparison 2 Steroid versus the vehicle, Outcome 5 Number of participants withdrawing due to adverse events.

Review: Topical treatments for scalp psoriasis
Comparison: 2 Steroid versus the vehicle
Outcome: 5 Number of participants withdrawing due to adverse events

Study or subgroup	Steroid n/N	Vehicle n/N	Risk Ratio M-H,Random,95% CI	Weight	Risk Ratio M-H,Random,95% CI
1 Betamethasone dipropionate (hydrophilic leave-on)					
Jemec 2008	6/556	7/136		72.5 %	0.21 [0.07, 0.61]
Subtotal (95% CI)	**556**	**136**		**72.5 %**	**0.21 [0.07, 0.61]**
Total events: 6 (Steroid), 7 (Vehicle)					
Heterogeneity: not applicable					
Test for overall effect: Z = 2.85 (P = 0.0044)					
2 Amcinonide 0.1% (hydrophilic leave-on)					
Ellis 1988	1/83	1/82		11.0 %	0.99 [0.06, 15.53]
Subtotal (95% CI)	**83**	**82**		**11.0 %**	**0.99 [0.06, 15.53]**
Total events: 1 (Steroid), 1 (Vehicle)					
Heterogeneity: not applicable					
Test for overall effect: Z = 0.01 (P = 0.99)					
3 Clobetasol propionate (hydrophilic leave-on)					

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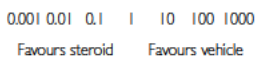
Study or subgroup	Steroid n/N	Vehicle n/N	Risk Ratio M-H,Random,95% CI	Weight	Risk Ratio M-H,Random,95% CI
Olsen 1991	0/188	1/189		8.2 %	0.34 [0.01, 8.17]
Sofen 2011	0/41	1/40		8.3 %	0.33 [0.01, 7.76]
Subtotal (95% CI)	**229**	**229**		**16.5 %**	**0.33 [0.03, 3.13]**
Total events: 0 (Steroid), 2 (Vehicle)					
Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 0.00$, df = 1 (P = 0.99); $I^2 = 0.0\%$					
Test for overall effect: Z = 0.97 (P = 0.33)					
Total (95% CI)	**868**	**447**		**100.0 %**	**0.27 [0.11, 0.67]**
Total events: 7 (Steroid), 10 (Vehicle)					
Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 1.11$, df = 3 (P = 0.77); $I^2 = 0.0\%$					
Test for overall effect: Z = 2.82 (P = 0.0048)					
Test for subgroup differences: $Chi^2 = 1.10$, df = 2 (P = 0.58), $I^2 = 0.0\%$					

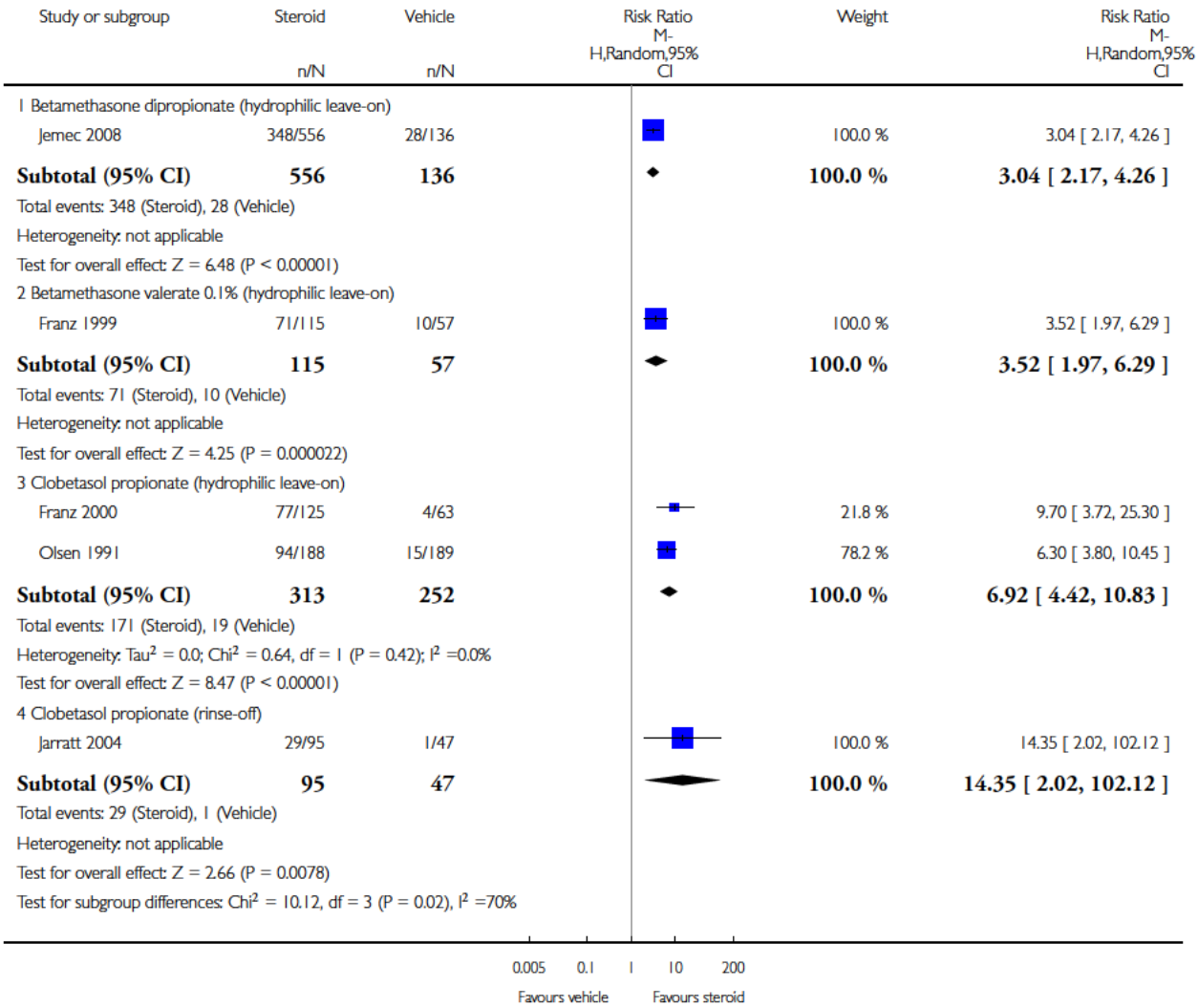


Analysis 2.6. Comparison 2 Steroid versus the vehicle, Outcome 6 Number of participants achieving 'response' by PGA.

Review: Topical treatments for scalp psoriasis

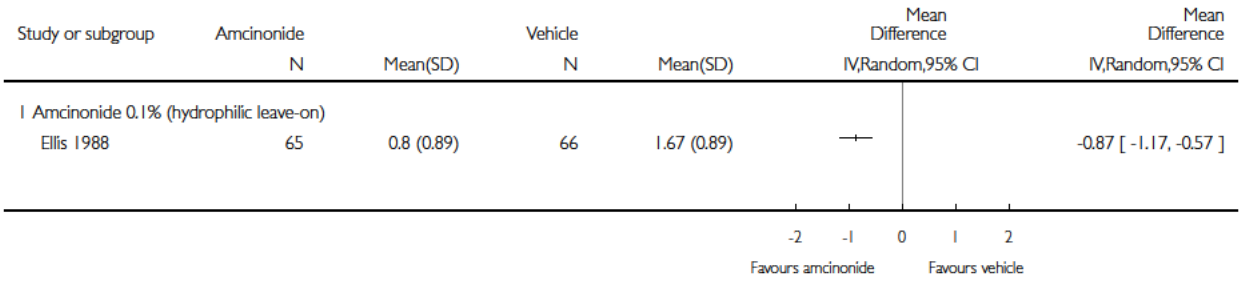
Comparison: 2 Steroid versus the vehicle

Outcome: 6 Number of participants achieving 'response' by PGA



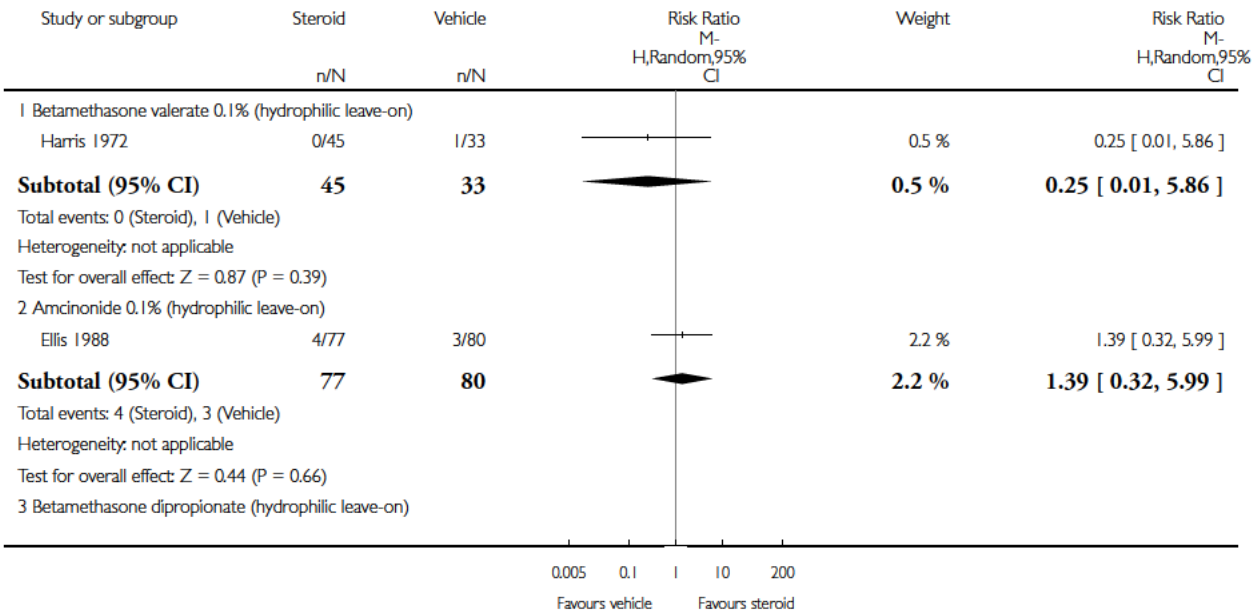
Analysis 2.7. Comparison 2 Steroid versus the vehicle, Outcome 7 Mean score of the PGA.

Review: Topical treatments for scalp psoriasis
Comparison: 2 Steroid versus the vehicle
Outcome: 7 Mean score of the PGA



Analysis 2.8. Comparison 2 Steroid versus the vehicle, Outcome 8 Number of participants with at least one adverse event.

Review: Topical treatments for scalp psoriasis
Comparison: 2 Steroid versus the vehicle
Outcome: 8 Number of participants with at least one adverse event



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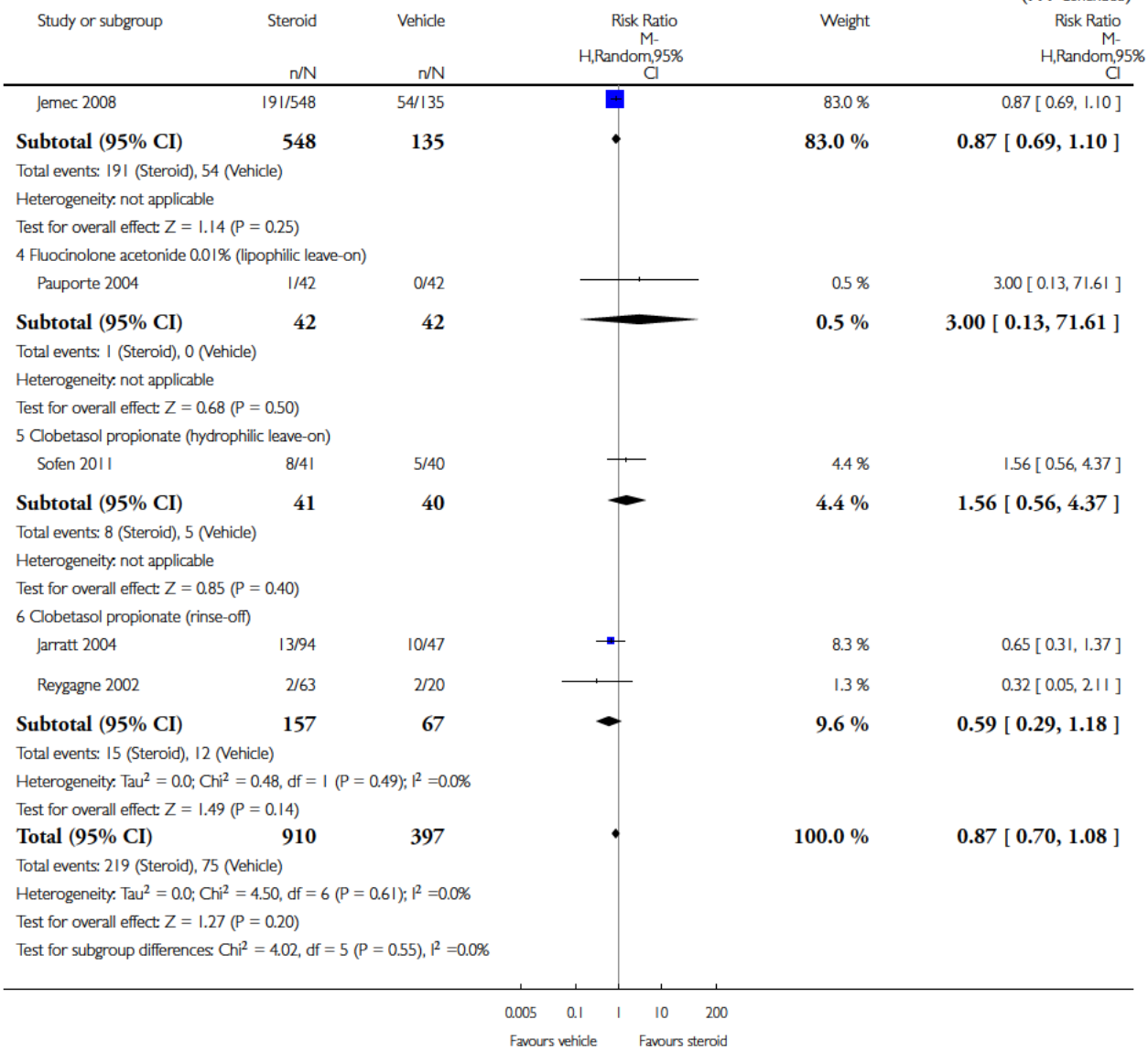
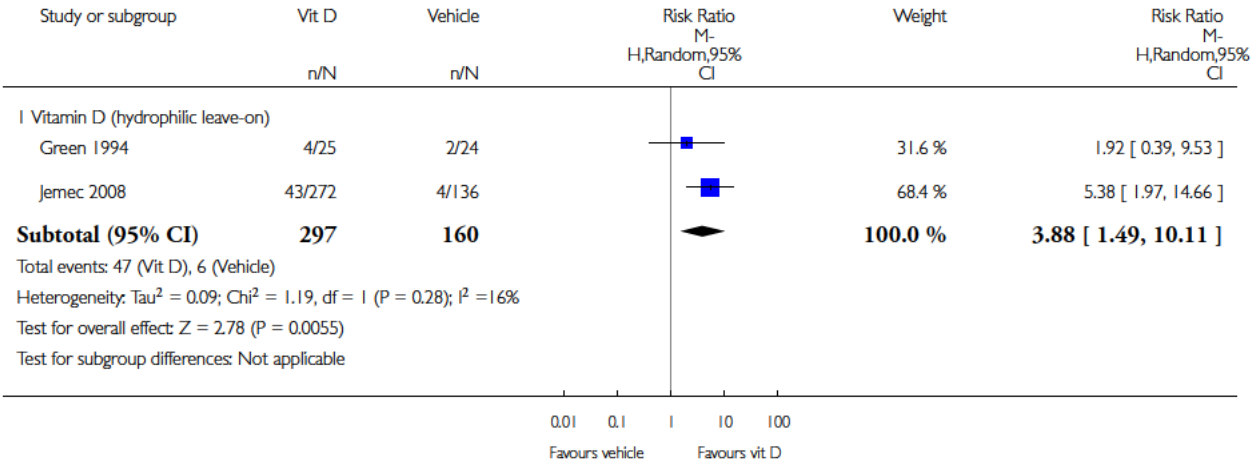


Analysis 3.1. Comparison 3 Vitamin D versus the vehicle, Outcome 1 Number of participants achieving 'clearance' by IGA.

Review: Topical treatments for scalp psoriasis

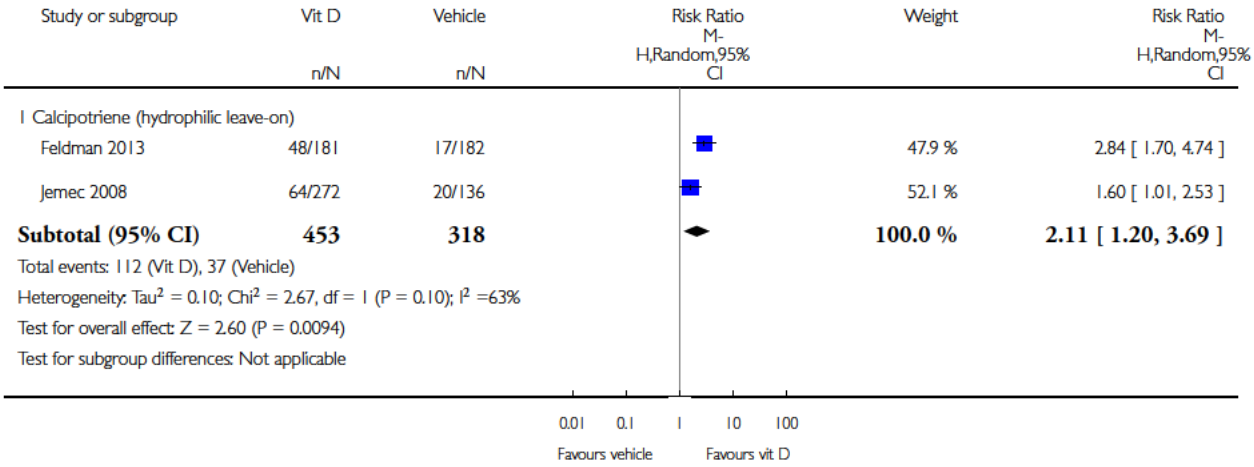
Comparison: 3 Vitamin D versus the vehicle

Outcome: 1 Number of participants achieving 'clearance' by IGA



Analysis 3.2. Comparison 3 Vitamin D versus the vehicle, Outcome 2 Number of participants achieving 'response' by IGA.

Review: Topical treatments for scalp psoriasis
Comparison: 3 Vitamin D versus the vehicle
Outcome: 2 Number of participants achieving 'response' by IGA



Analysis 3.3. Comparison 3 Vitamin D versus the vehicle, Outcome 3 Mean of the TSS.

Mean of the TSS

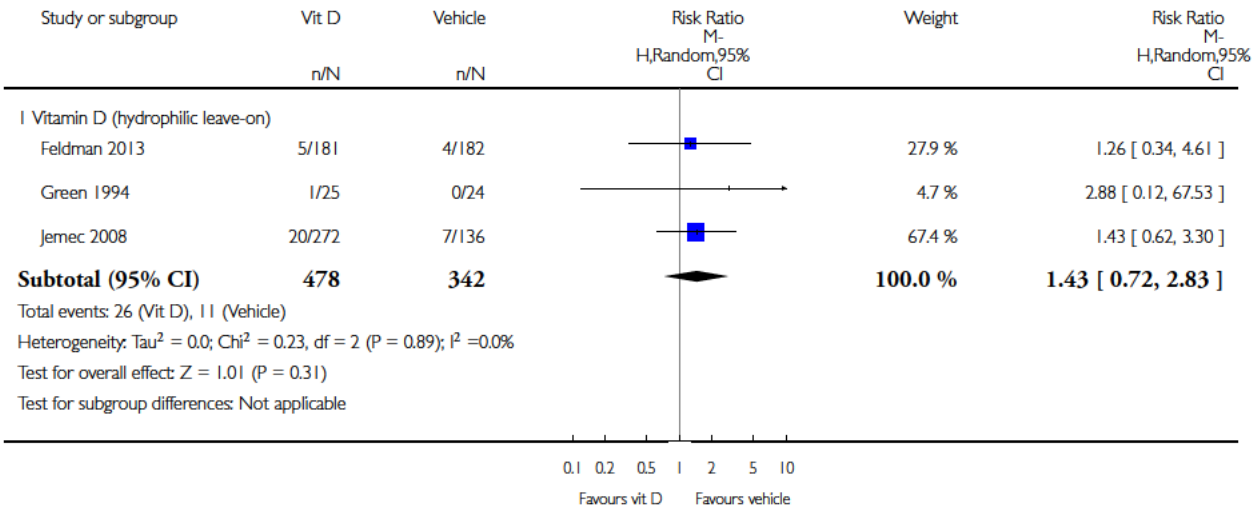
Study	Vitamin D vs vehicle	Vitamin D	Vehicle
Green 1994	Calcipotriol vs vehicle	-52%	-24%
Jemec 2008	Calcipotriene vs vehicle	-54%	-36%
Ruzicka 2004	Tacalcitol vs vehicle	-53%	-30%

Analysis 3.4. Comparison 3 Vitamin D versus the vehicle, Outcome 4 Number of participants withdrawing due to adverse events.

Review: Topical treatments for scalp psoriasis

Comparison: 3 Vitamin D versus the vehicle

Outcome: 4 Number of participants withdrawing due to adverse events

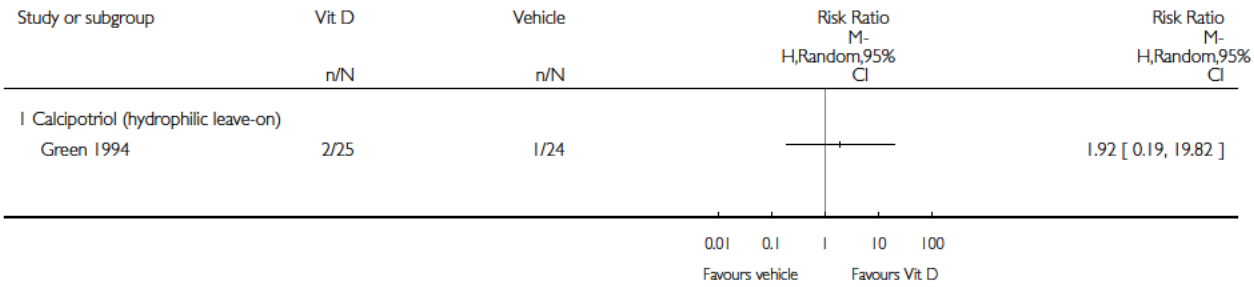


Analysis 3.5. Comparison 3 Vitamin D versus the vehicle, Outcome 5 Number of participants achieving 'clearance' by PGA.

Review: Topical treatments for scalp psoriasis

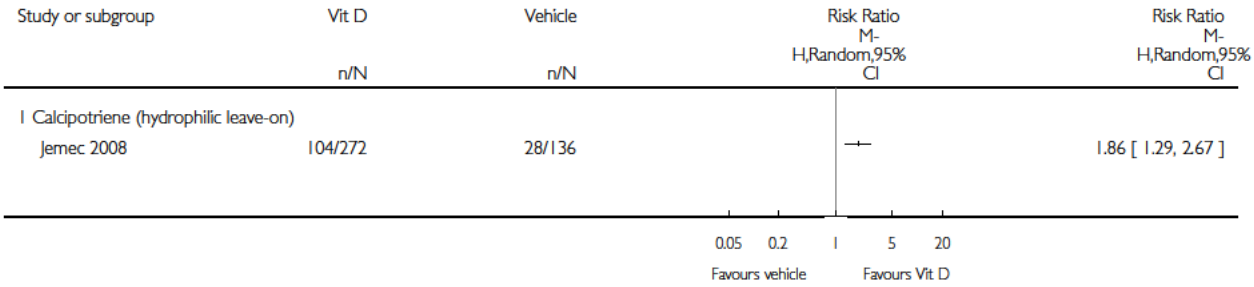
Comparison: 3 Vitamin D versus the vehicle

Outcome: 5 Number of participants achieving 'clearance' by PGA



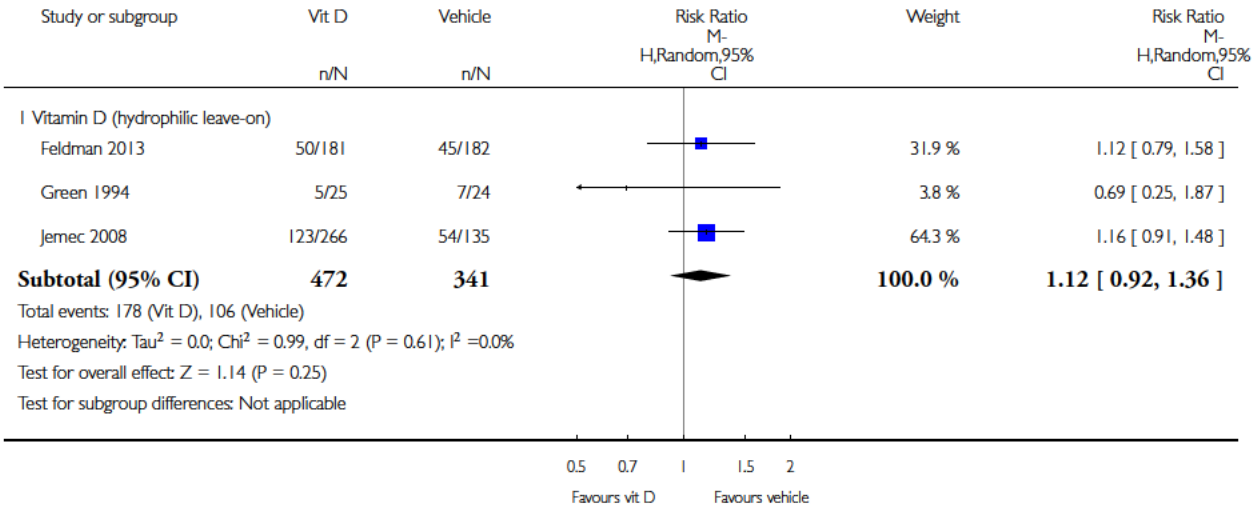
Analysis 3.6. Comparison 3 Vitamin D versus the vehicle, Outcome 6 Number of participants achieving 'response' by PGA.

Review: Topical treatments for scalp psoriasis
Comparison: 3 Vitamin D versus the vehicle
Outcome: 6 Number of participants achieving 'response' by PGA



Analysis 3.7. Comparison 3 Vitamin D versus the vehicle, Outcome 7 Number of participants with at least one adverse event.

Review: Topical treatments for scalp psoriasis
Comparison: 3 Vitamin D versus the vehicle
Outcome: 7 Number of participants with at least one adverse event

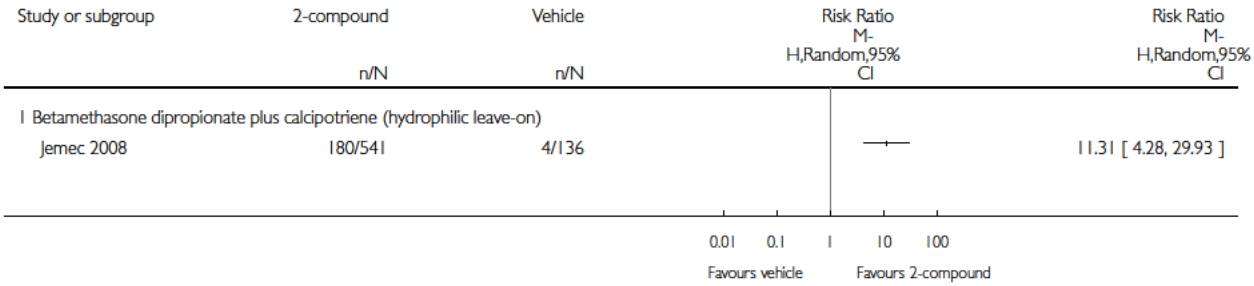


Analysis 4.1. Comparison 4 Steroid plus vitamin D versus the vehicle, Outcome 1 Number of participants achieving 'clearance' by IGA.

Review: Topical treatments for scalp psoriasis

Comparison: 4 Steroid plus vitamin D versus the vehicle

Outcome: 1 Number of participants achieving 'clearance' by IGA

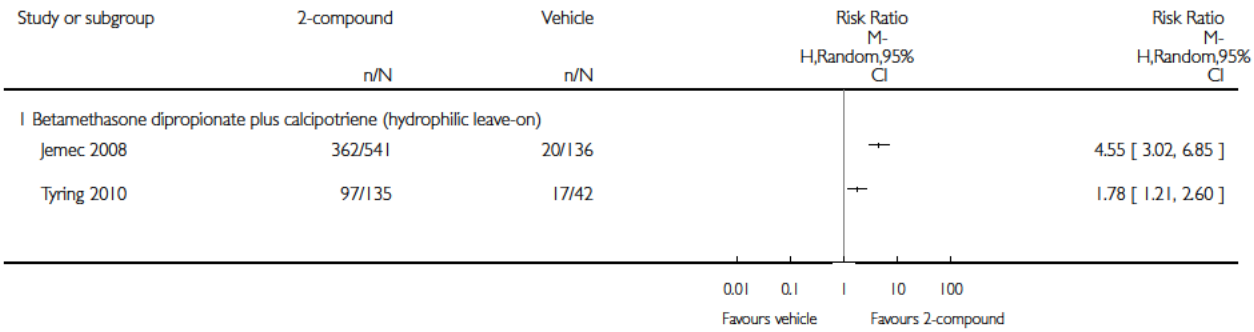


Analysis 4.2. Comparison 4 Steroid plus vitamin D versus the vehicle, Outcome 2 Number of participants achieving 'response' by IGA.

Review: Topical treatments for scalp psoriasis

Comparison: 4 Steroid plus vitamin D versus the vehicle

Outcome: 2 Number of participants achieving 'response' by IGA



Analysis 4.3. Comparison 4 Steroid plus vitamin D versus the vehicle, Outcome 3 Mean of the TSS.

Mean of the TSS

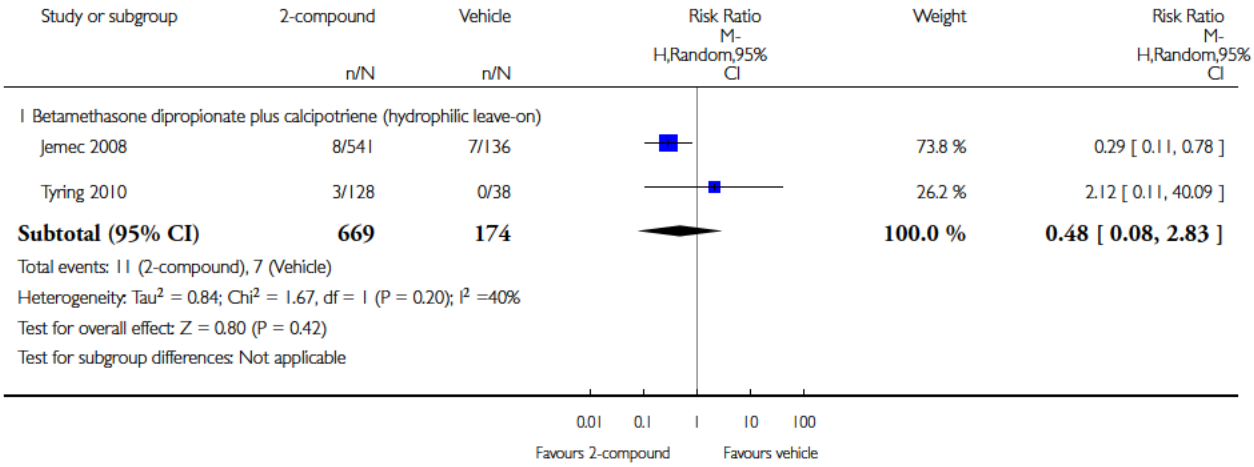
Study	Betamethasone dipropionate/calcipotriene combination	Placebo (vehicle)
Jemec 2008	-70%	-36%

Analysis 4.4. Comparison 4 Steroid plus vitamin D versus the vehicle, Outcome 4 Number of participants withdrawing due to adverse events.

Review: Topical treatments for scalp psoriasis

Comparison: 4 Steroid plus vitamin D versus the vehicle

Outcome: 4 Number of participants withdrawing due to adverse events

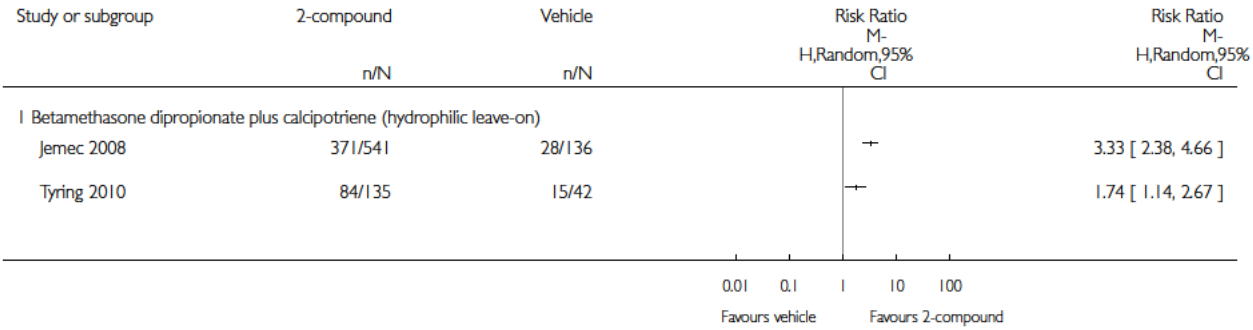


Analysis 4.5. Comparison 4 Steroid plus vitamin D versus the vehicle, Outcome 5 Number of participants achieving 'response' by PGA.

Review: Topical treatments for scalp psoriasis

Comparison: 4 Steroid plus vitamin D versus the vehicle

Outcome: 5 Number of participants achieving 'response' by PGA

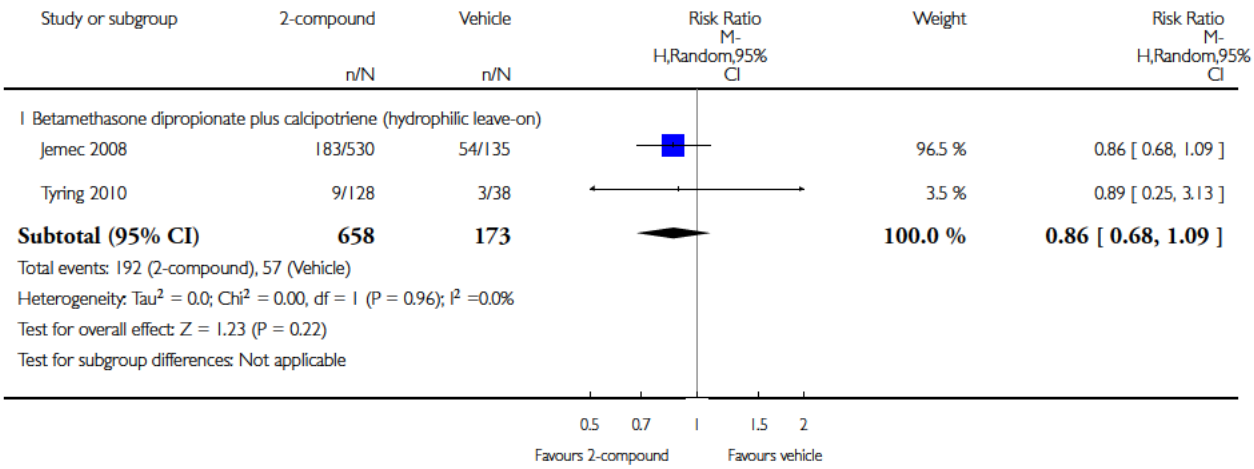


Analysis 4.6. Comparison 4 Steroid plus vitamin D versus the vehicle, Outcome 6 Number of participants with at least one adverse event.

Review: Topical treatments for scalp psoriasis

Comparison: 4 Steroid plus vitamin D versus the vehicle

Outcome: 6 Number of participants with at least one adverse event

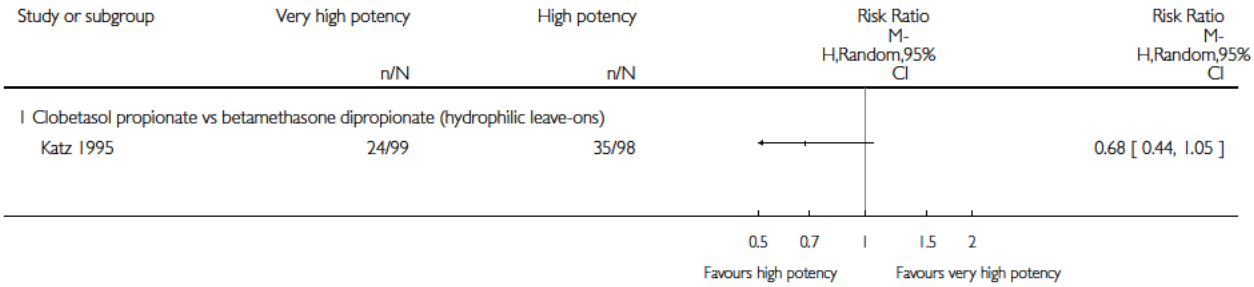


Analysis 5.1. Comparison 5 Steroid versus steroid: very high versus high potency, Outcome 1 Number of participants achieving 'clearance' by IGA.

Review: Topical treatments for scalp psoriasis

Comparison: 5 Steroid versus steroid: very high versus high potency

Outcome: 1 Number of participants achieving 'clearance' by IGA

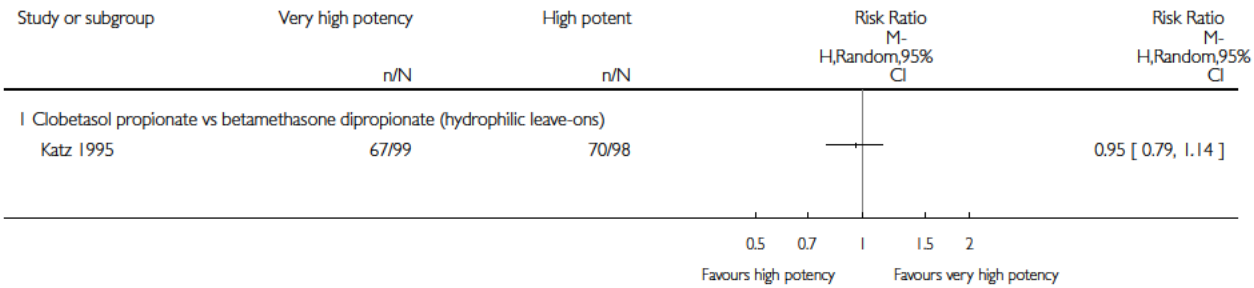


Analysis 5.2. Comparison 5 Steroid versus steroid: very high versus high potency, Outcome 2 Number of participants achieving 'response' by IGA.

Review: Topical treatments for scalp psoriasis

Comparison: 5 Steroid versus steroid: very high versus high potency

Outcome: 2 Number of participants achieving 'response' by IGA



Analysis 5.3. Comparison 5 Steroid versus steroid: very high versus high potency, Outcome 3 Mean of the TSS.

Mean of the TSS

Study	Clobetasol propionate	Betamethasone dipropionate
Katz 1995	-75%	-83%
Lassus 1976	-81%	-58%

Analysis 5.4. Comparison 5 Steroid versus steroid: very high versus high potency, Outcome 4 Number of participants with at least one adverse event.

Review: Topical treatments for scalp psoriasis

Comparison: 5 Steroid versus steroid: very high versus high potency

Outcome: 4 Number of participants with at least one adverse event

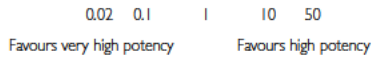
Study or subgroup	Favours very high potency n/N	High potency n/N	Risk Ratio M-H,Random,95% CI	Weight	Risk Ratio M-H,Random,95% CI
1 Clobetasol propionate vs betamethasone dipropionate (hydrophilic leave-ons)					
Katz 1995	36/99	33/97		89.5 %	1.07 [0.73, 1.56]
Lassus 1976	0/20	2/20		10.5 %	0.20 [0.01, 3.92]
Subtotal (95% CI)	**119**	**117**		**100.0 %**	**0.90 [0.32, 2.48]**

Total events: 36 (Favours very high potency), 35 (High potency)

Heterogeneity: $Tau^2 = 0.26$; $Chi^2 = 1.23$, df = 1 (P = 0.27); $I^2 = 18\%$

Test for overall effect: Z = 0.21 (P = 0.83)

Test for subgroup differences: Not applicable

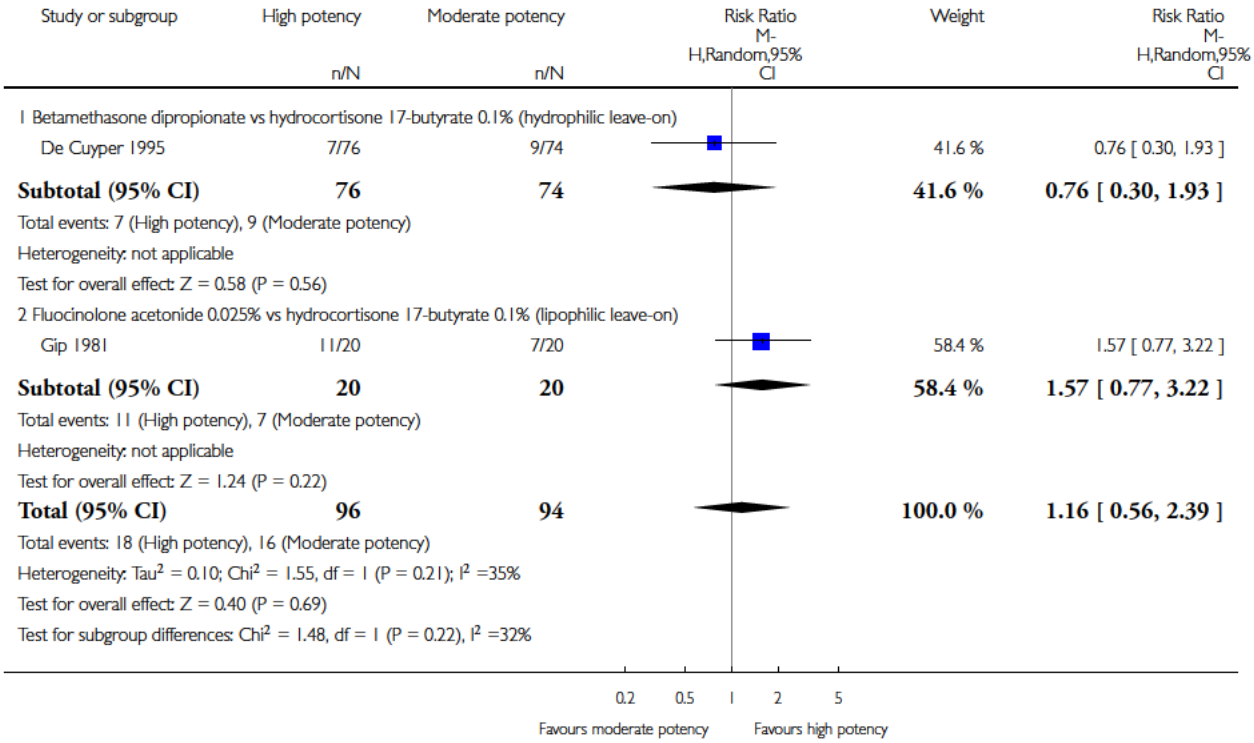


Analysis 6.1. Comparison 6 Steroid versus steroid: high versus moderate potency, Outcome 1 Number of participants achieving 'clearance' by IGA.

Review: Topical treatments for scalp psoriasis

Comparison: 6 Steroid versus steroid: high versus moderate potency

Outcome: 1 Number of participants achieving 'clearance' by IGA

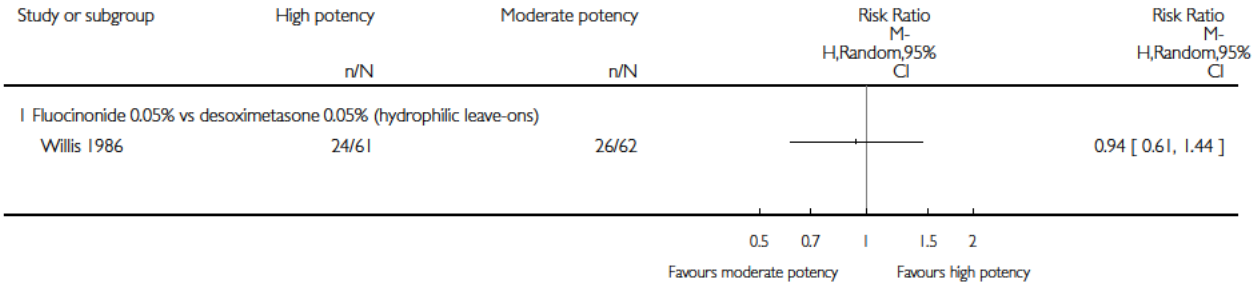


Analysis 6.2. Comparison 6 Steroid versus steroid: high versus moderate potency, Outcome 2 Number of participants achieving 'response' by IGA.

Review: Topical treatments for scalp psoriasis

Comparison: 6 Steroid versus steroid: high versus moderate potency

Outcome: 2 Number of participants achieving 'response' by IGA



Analysis 6.3. Comparison 6 Steroid versus steroid: high versus moderate potency, Outcome 3 Mean of the TSS.

Mean of the TSS

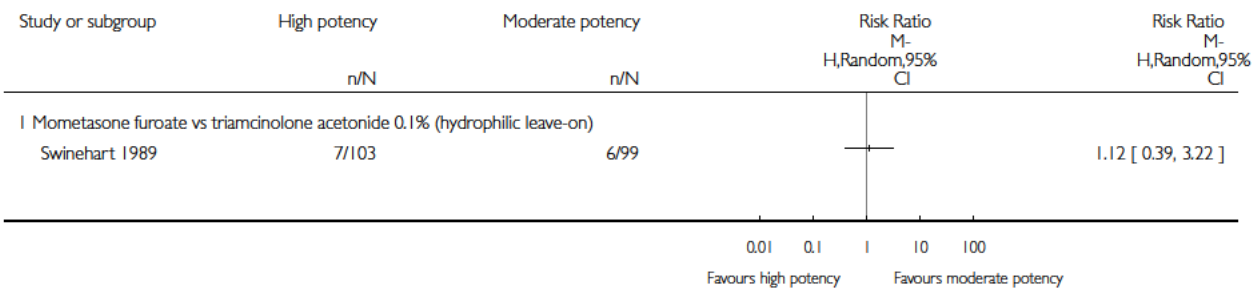
Study	Mometasone furoate	Triamcinolone acetonide
Swinehart 1989	-79%	-70%

Analysis 6.4. Comparison 6 Steroid versus steroid: high versus moderate potency, Outcome 4 Number of participants with at least one adverse event.

Review: Topical treatments for scalp psoriasis

Comparison: 6 Steroid versus steroid: high versus moderate potency

Outcome: 4 Number of participants with at least one adverse event

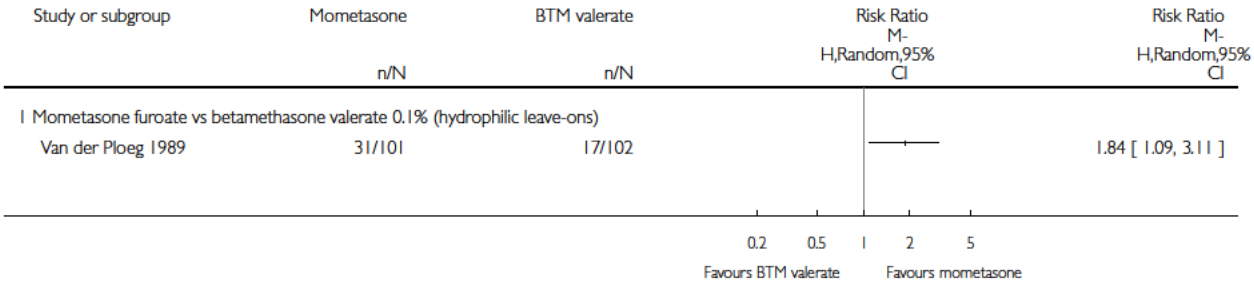


Analysis 7.1. Comparison 7 Steroids versus steroid: both of high potency, Outcome 1 Number of participants achieving 'clearance' by IGA.

Review: Topical treatments for scalp psoriasis

Comparison: 7 Steroids versus steroid: both of high potency

Outcome: 1 Number of participants achieving 'clearance' by IGA

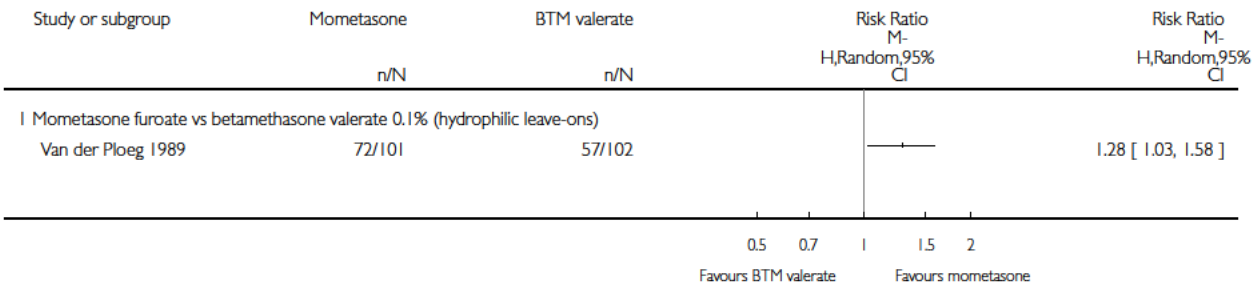


Analysis 7.2. Comparison 7 Steroids versus steroid: both of high potency, Outcome 2 Number of participants achieving 'response' by IGA.

Review: Topical treatments for scalp psoriasis

Comparison: 7 Steroids versus steroid: both of high potency

Outcome: 2 Number of participants achieving 'response' by IGA



Analysis 7.3. Comparison 7 Steroids versus steroid: both of high potency, Outcome 3 Mean of the TSS.

Mean of the TSS

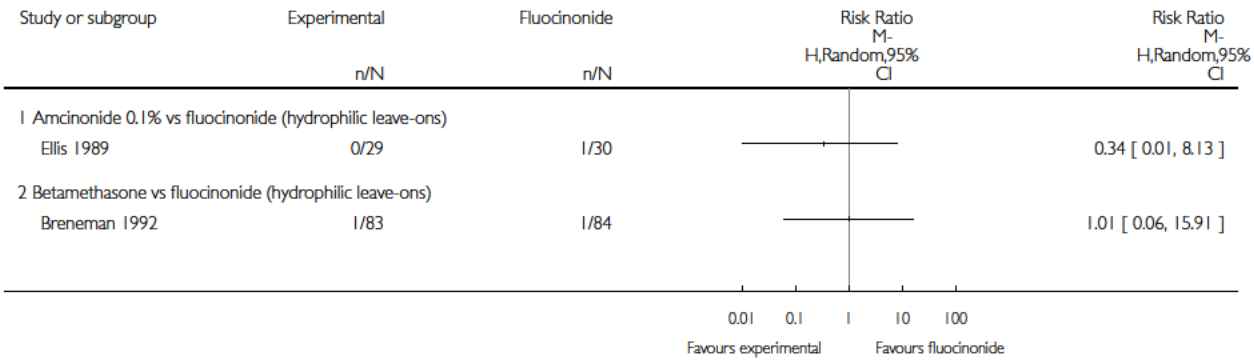
Study	Steroid vs steroid of high potency	Steroid (1)	Steroid (2)
Breneman 1992	Fluocinonide (1) vs BTM dipropionate (2)	-84%	-85%
Van der Ploeg 1989	Mometasone furoate (1) vs BTM valerate (2)	-85%	-70%

Analysis 7.4. Comparison 7 Steroids versus steroid: both of high potency, Outcome 4 Number of participants withdrawing due to adverse events.

Review: Topical treatments for scalp psoriasis

Comparison: 7 Steroids versus steroid: both of high potency

Outcome: 4 Number of participants withdrawing due to adverse events

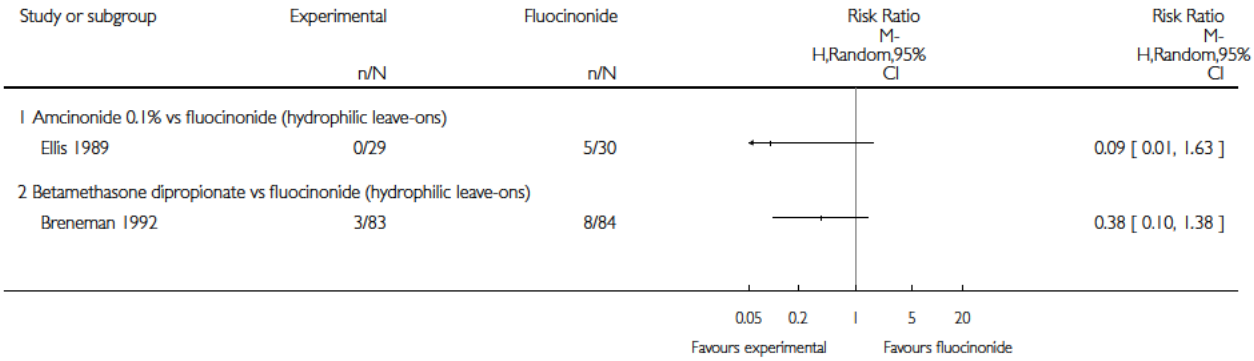


Analysis 7.5. Comparison 7 Steroids versus steroid: both of high potency, Outcome 5 Number of participants with at least one adverse event.

Review: Topical treatments for scalp psoriasis

Comparison: 7 Steroids versus steroid: both of high potency

Outcome: 5 Number of participants with at least one adverse event

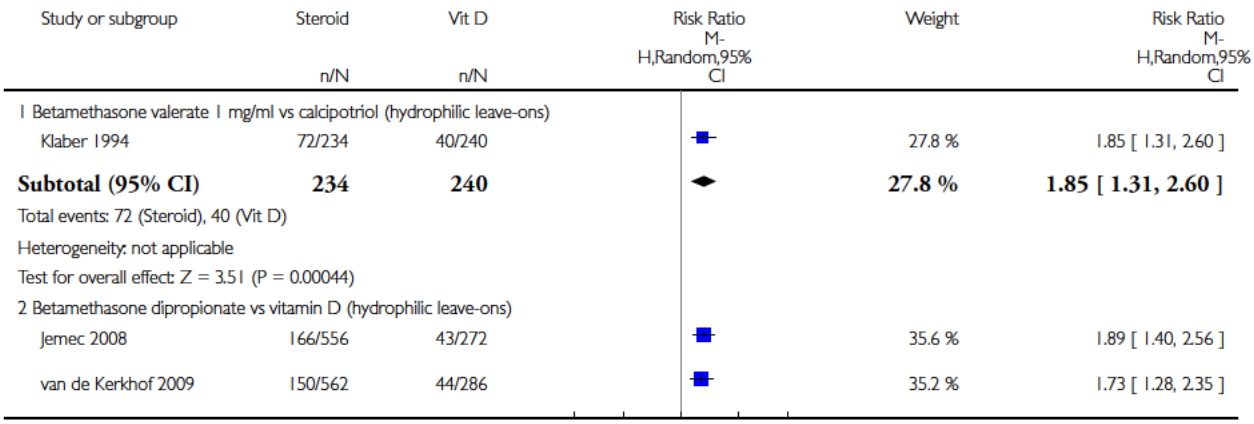


Analysis 8.1. Comparison 8 Steroid versus vitamin D, Outcome 1 Number of participants achieving 'clearance' by IGA.

Review: Topical treatments for scalp psoriasis

Comparison: 8 Steroid versus vitamin D

Outcome: 1 Number of participants achieving 'clearance' by IGA



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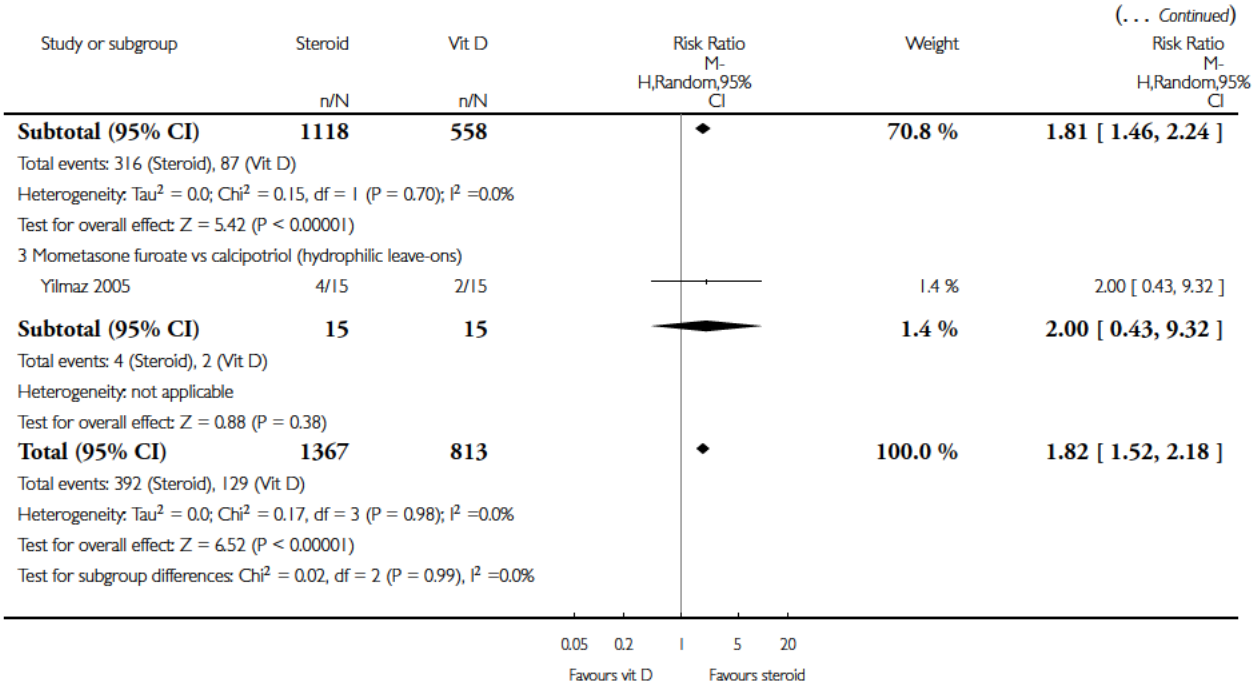
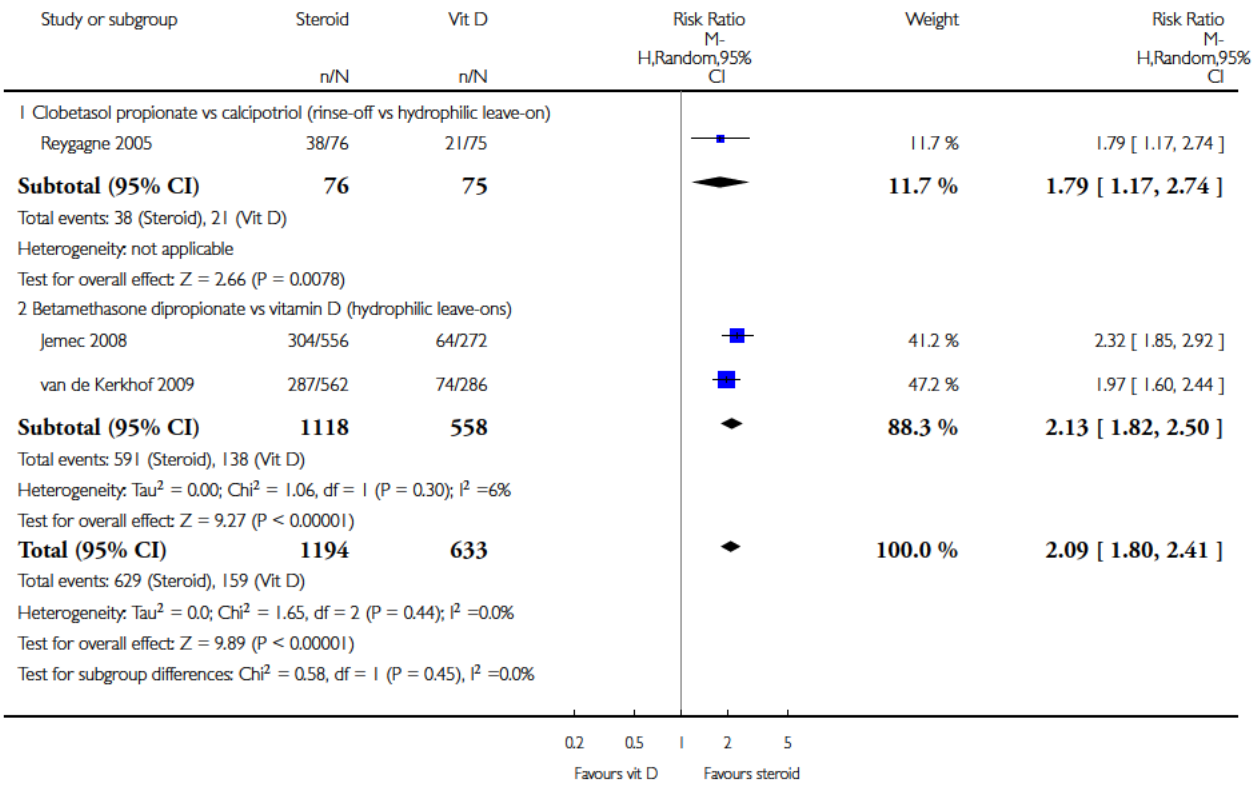


Analysis 8.2. Comparison 8 Steroid versus vitamin D, Outcome 2 Number of participants achieving 'response' by IGA.

Review: Topical treatments for scalp psoriasis
Comparison: 8 Steroid versus vitamin D
Outcome: 2 Number of participants achieving 'response' by IGA



Analysis 8.3. Comparison 8 Steroid versus vitamin D, Outcome 3 Mean of the TSS.

Mean of the TSS

Study	Corticosteroid vs vitamin D	Corticosteroid	Calcipotriol
Jemec 2008	Betamethasone dipropionate vs calcipotriene	-62%	-44%
Klaber 1994	Betamethasone valerate vs calcipotriol	-62%	-48%
Reygagne 2005	Clobetasol vs calcipotriol	-64%	-52%

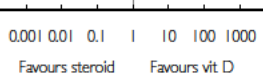
Mean of the TSS *(Continued)*

van de Kerkhof 2009	Betamethasone dipropionate vs calcipotriol	-57%	-43%
Yilmaz 2005	Mometasone vs calcipotriol	-52%	-49%

Analysis 8.4. Comparison 8 Steroid versus vitamin D, Outcome 4 Number of participants withdrawing due to adverse events.

Review: Topical treatments for scalp psoriasis
Comparison: 8 Steroid versus vitamin D
Outcome: 4 Number of participants withdrawing due to adverse events

Study or subgroup	Steroid n/N	Vit D n/N	Risk Ratio M-H,Random,95% CI	Weight	Risk Ratio M-H,Random,95% CI
1 Betamethasone valerate 1 mg/ml vs calcipotriol (hydrophilic leave-ons)					
Klaber 1994	2/234	11/240		17.8 %	0.19 [0.04, 0.83]
Subtotal (95% CI)	**234**	**240**		**17.8 %**	**0.19 [0.04, 0.83]**
Total events: 2 (Steroid), 11 (Vit D)					
Heterogeneity: not applicable					
Test for overall effect: Z = 2.20 (P = 0.028)					
2 Betamethasone dipropionate vs vitamin D (hydrophilic leave-ons)					
Jemec 2008	6/556	20/272		41.7 %	0.15 [0.06, 0.36]
van de Kerkhof 2009	7/556	8/282		35.2 %	0.44 [0.16, 1.21]
Subtotal (95% CI)	**1112**	**554**		**76.8 %**	**0.25 [0.08, 0.74]**
Total events: 13 (Steroid), 28 (Vit D)					
Heterogeneity: Tau^2 = 0.38; Chi^2 = 2.60, df = 1 (P = 0.11); I^2 =62%					
Test for overall effect: Z = 2.51 (P = 0.012)					
3 Clobetasol propionate vs calcipotriol (rinse-off vs hydrophilic leave-on)					
Reygagne 2005	0/76	7/75		5.3 %	0.07 [0.00, 1.13]
Subtotal (95% CI)	**76**	**75**		**5.3 %**	**0.07 [0.00, 1.13]**
Total events: 0 (Steroid), 7 (Vit D)					
Heterogeneity: not applicable					
Test for overall effect: Z = 1.87 (P = 0.061)					
Total (95% CI)	**1422**	**869**		**100.0 %**	**0.22 [0.11, 0.42]**
Total events: 15 (Steroid), 46 (Vit D)					
Heterogeneity: Tau^2 = 0.07; Chi^2 = 3.47, df = 3 (P = 0.32); I^2 =14%					
Test for overall effect: Z = 4.49 (P < 0.00001)					
Test for subgroup differences: Chi^2 = 0.75, df = 2 (P = 0.69), I^2 =0.0%					

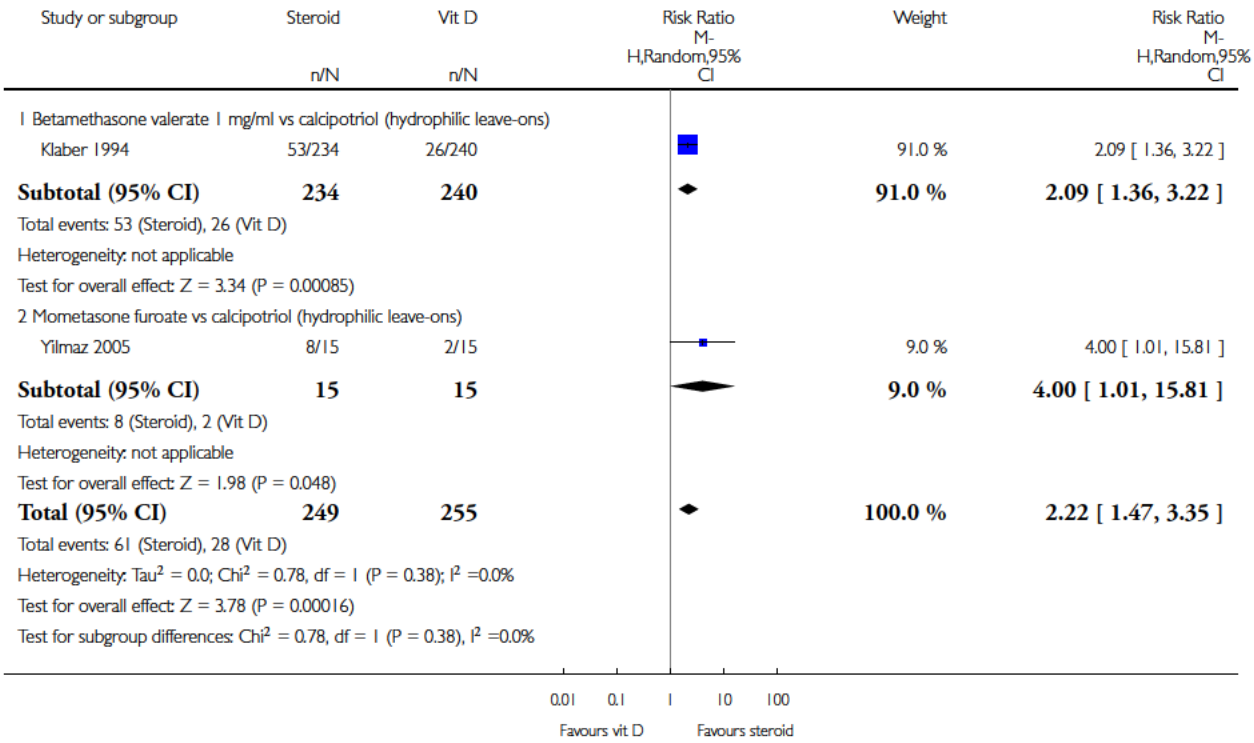


Analysis 8.5. Comparison 8 Steroid versus vitamin D, Outcome 5 Number of participants achieving 'clearance' by PGA.

Review: Topical treatments for scalp psoriasis

Comparison: 8 Steroid versus vitamin D

Outcome: 5 Number of participants achieving 'clearance' by PGA

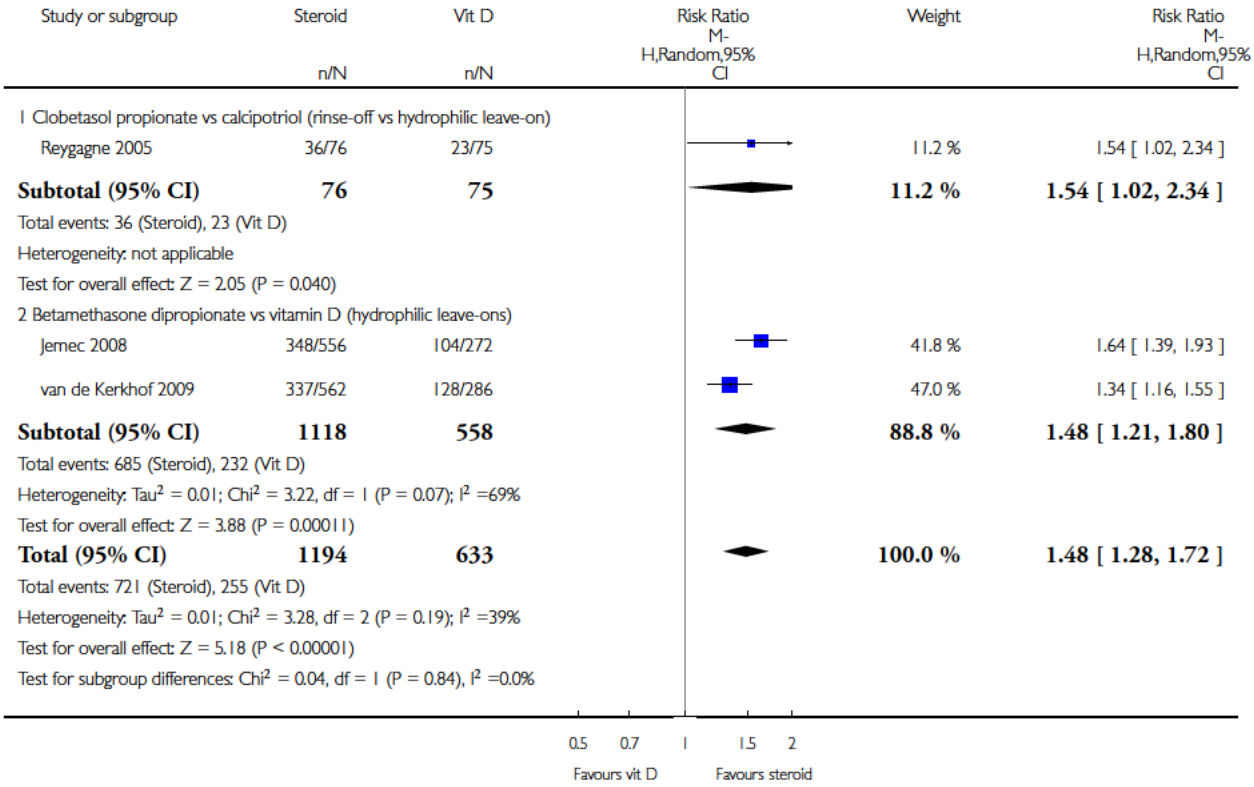


Analysis 8.6. Comparison 8 Steroid versus vitamin D, Outcome 6 Number of participants achieving 'response' by PGA.

Review: Topical treatments for scalp psoriasis

Comparison: 8 Steroid versus vitamin D

Outcome: 6 Number of participants achieving 'response' by PGA

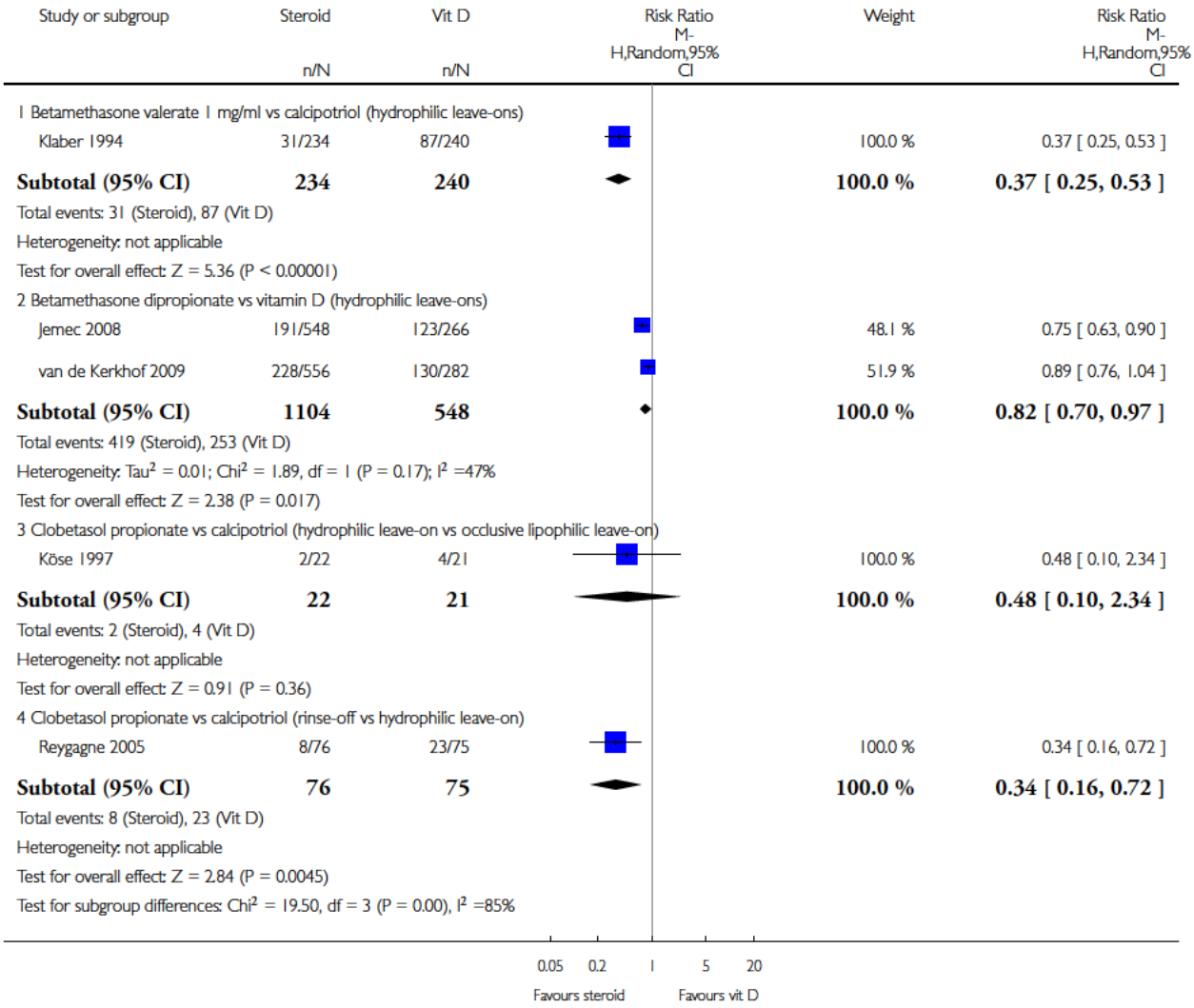


Analysis 8.7. Comparison 8 Steroid versus vitamin D, Outcome 7 Number of participants with at least one adverse event.

Review: Topical treatments for scalp psoriasis

Comparison: 8 Steroid versus vitamin D

Outcome: 7 Number of participants with at least one adverse event

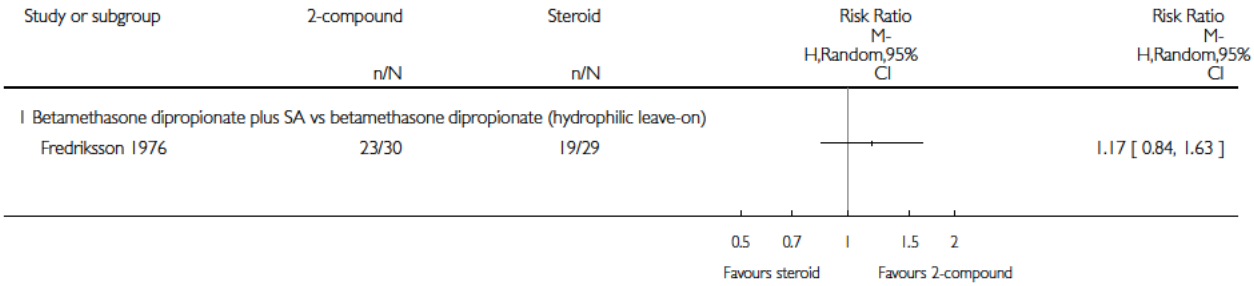


Analysis 9.1. Comparison 9 Steroid plus salicylic acid versus steroid, Outcome 1 Number of participants achieving 'clearance' by IGA.

Review: Topical treatments for scalp psoriasis

Comparison: 9 Steroid plus salicylic acid versus steroid

Outcome: 1 Number of participants achieving 'clearance' by IGA

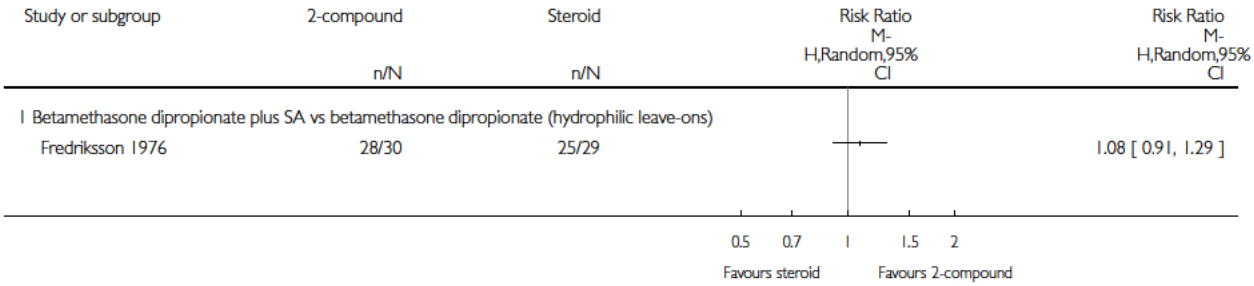


Analysis 9.2. Comparison 9 Steroid plus salicylic acid versus steroid, Outcome 2 Number of participants achieving 'response' by IGA.

Review: Topical treatments for scalp psoriasis

Comparison: 9 Steroid plus salicylic acid versus steroid

Outcome: 2 Number of participants achieving 'response' by IGA

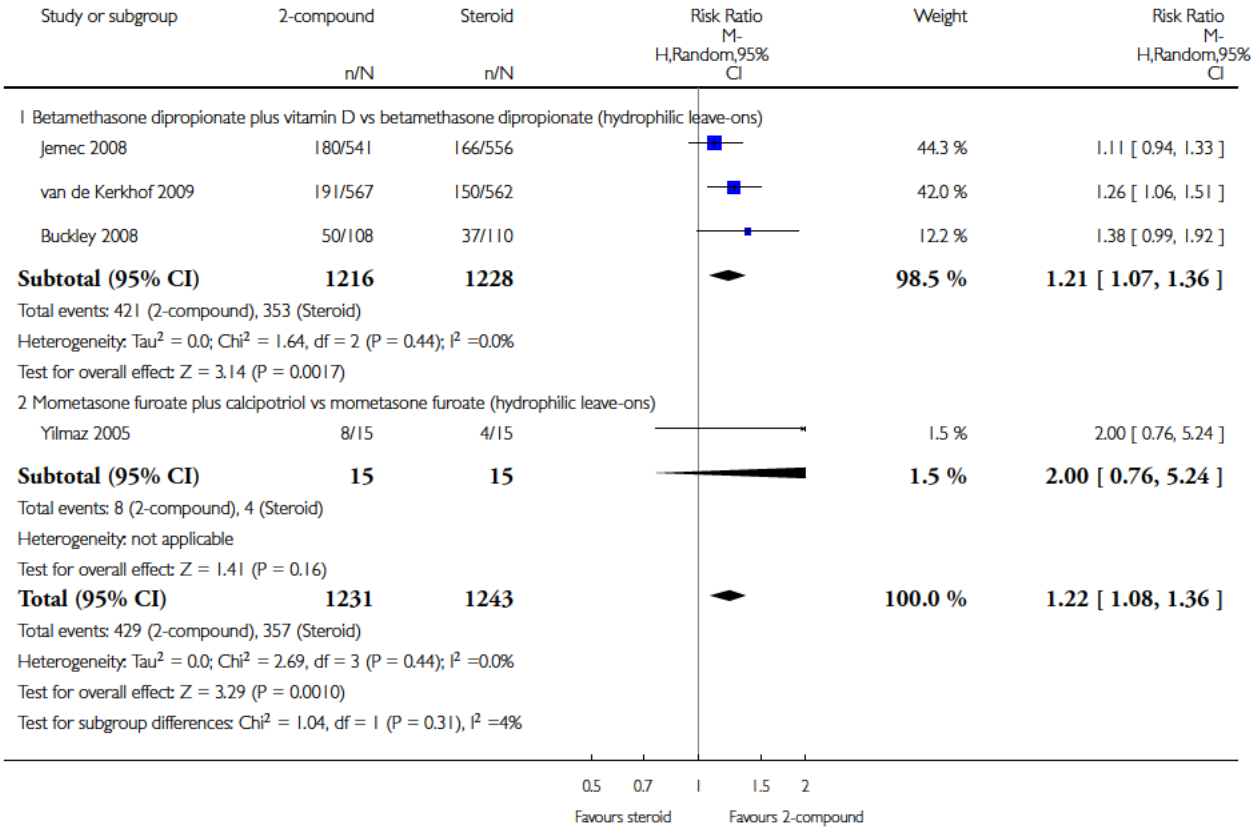


Analysis 10.1. Comparison 10 Steroid plus vitamin D versus steroid, Outcome 1 Number of participants achieving 'clearance' by IGA.

Review: Topical treatments for scalp psoriasis

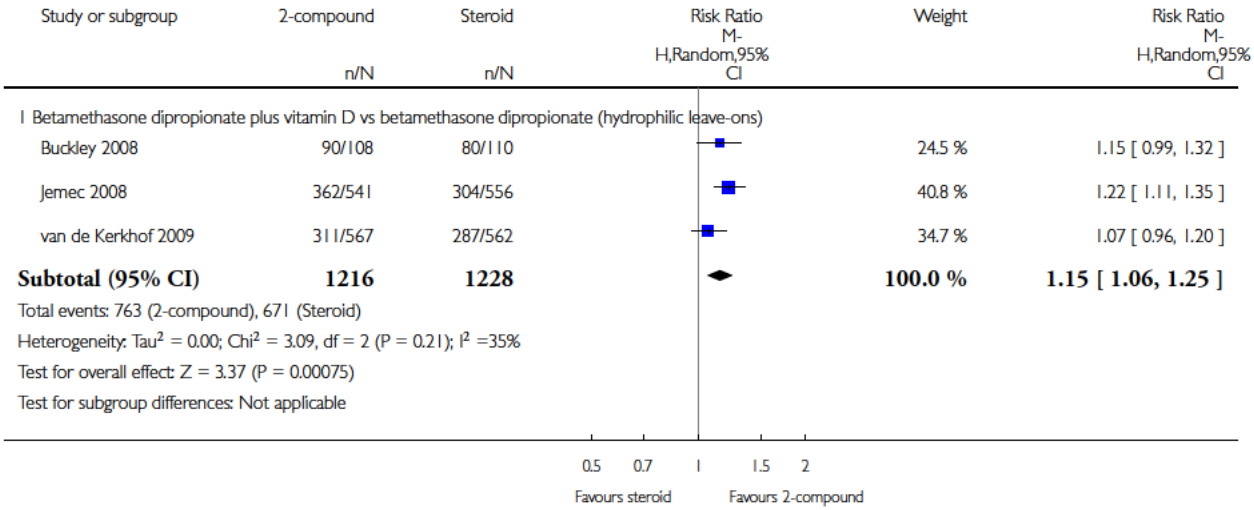
Comparison: 10 Steroid plus vitamin D versus steroid

Outcome: 1 Number of participants achieving 'clearance' by IGA



Analysis 10.2. Comparison 10 Steroid plus vitamin D versus steroid, Outcome 2 Number of participants achieving 'response' by IGA.

Review: Topical treatments for scalp psoriasis
Comparison: 10 Steroid plus vitamin D versus steroid
Outcome: 2 Number of participants achieving 'response' by IGA



Analysis 10.3. Comparison 10 Steroid plus vitamin D versus steroid, Outcome 3 Mean of the TSS.

Mean of the TSS

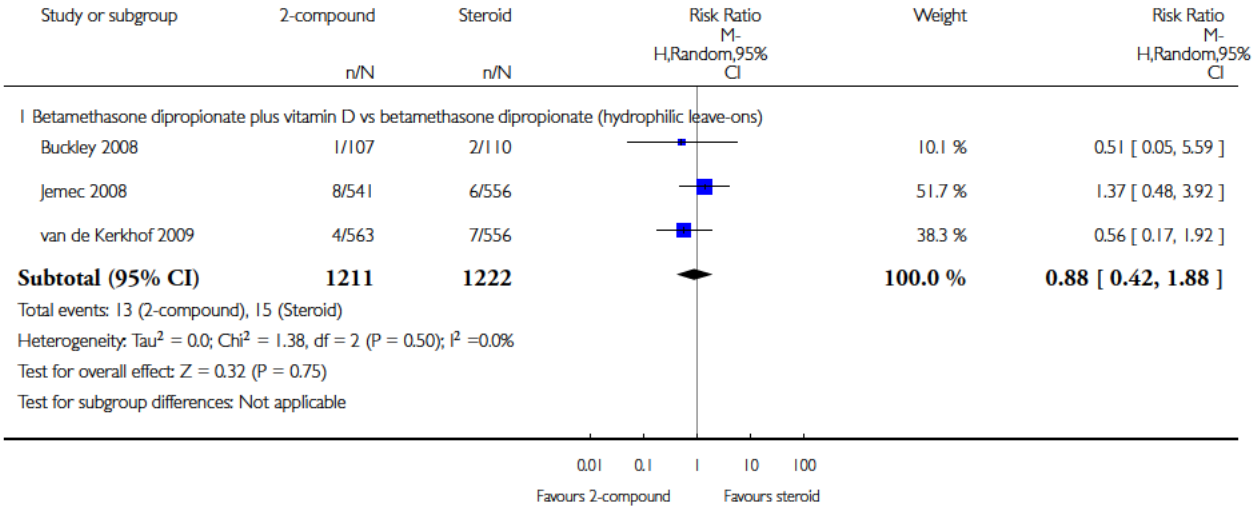
Study	Steroid/ vitamin D combination vs steroid	Steroid/calcipotriol	Steroid
Buckley 2008	Betamethasone dipropionate/calcipotriol vs betamethasone dipropionate	-69%	-62%
Jemec 2008	Betamethasone dipropionate/calcipotriene vs betamethasone dipropionate	-70%	-64%
van de Kerkhof 2009	Betamethasone dipropionate/calcipotriol vs betamethasone dipropionate	-62%	-57%
Yilmaz 2005	Mometasone/calcipotriol vs mometasone	-81%	-52%

Analysis 10.4. Comparison 10 Steroid plus vitamin D versus steroid, Outcome 4 Number of participants withdrawing due to adverse events.

Review: Topical treatments for scalp psoriasis

Comparison: 10 Steroid plus vitamin D versus steroid

Outcome: 4 Number of participants withdrawing due to adverse events

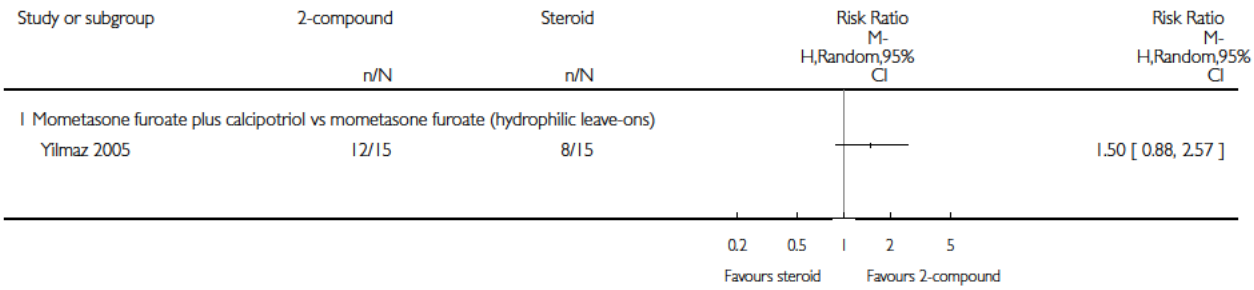


Analysis 10.5. Comparison 10 Steroid plus vitamin D versus steroid, Outcome 5 Number of participants achieving 'clearance' by PGA.

Review: Topical treatments for scalp psoriasis

Comparison: 10 Steroid plus vitamin D versus steroid

Outcome: 5 Number of participants achieving 'clearance' by PGA

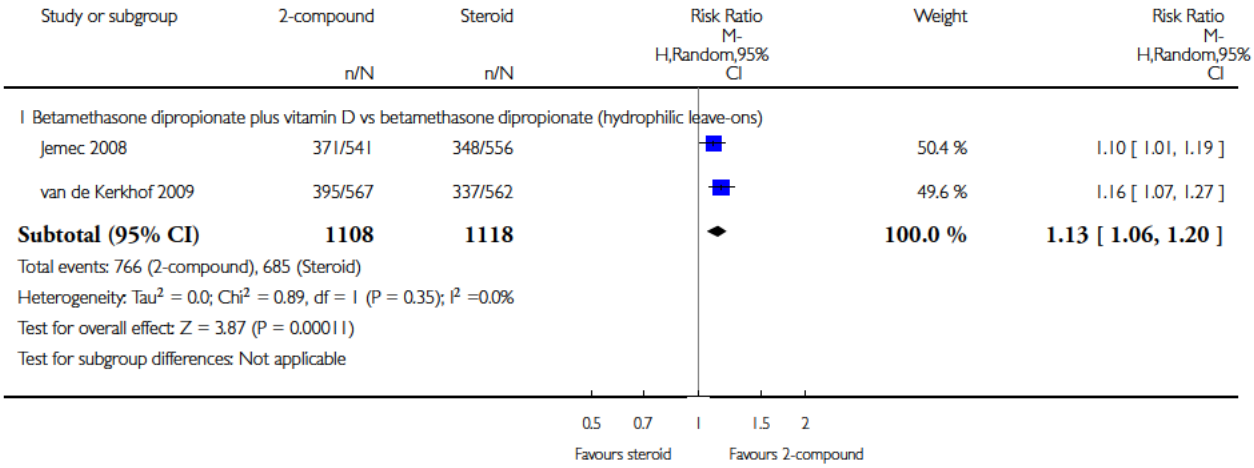


Analysis 10.6. Comparison 10 Steroid plus vitamin D versus steroid, Outcome 6 Number of participants achieving 'response' by PGA.

Review: Topical treatments for scalp psoriasis

Comparison: 10 Steroid plus vitamin D versus steroid

Outcome: 6 Number of participants achieving 'response' by PGA

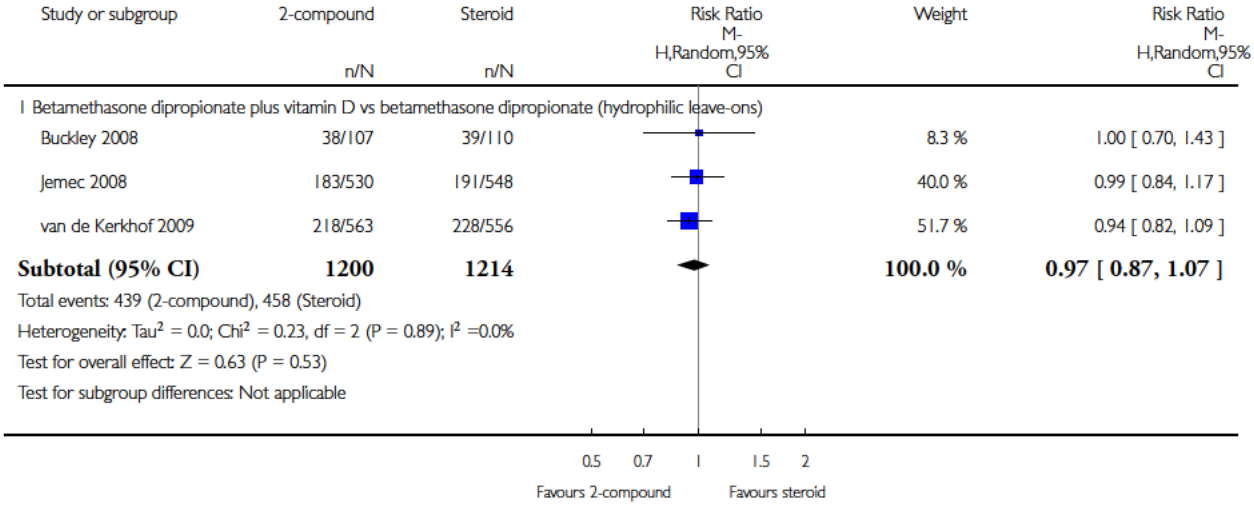


Analysis 10.7. Comparison 10 Steroid plus vitamin D versus steroid, Outcome 7 Number of participants with at least one adverse event.

Review: Topical treatments for scalp psoriasis

Comparison: 10 Steroid plus vitamin D versus steroid

Outcome: 7 Number of participants with at least one adverse event

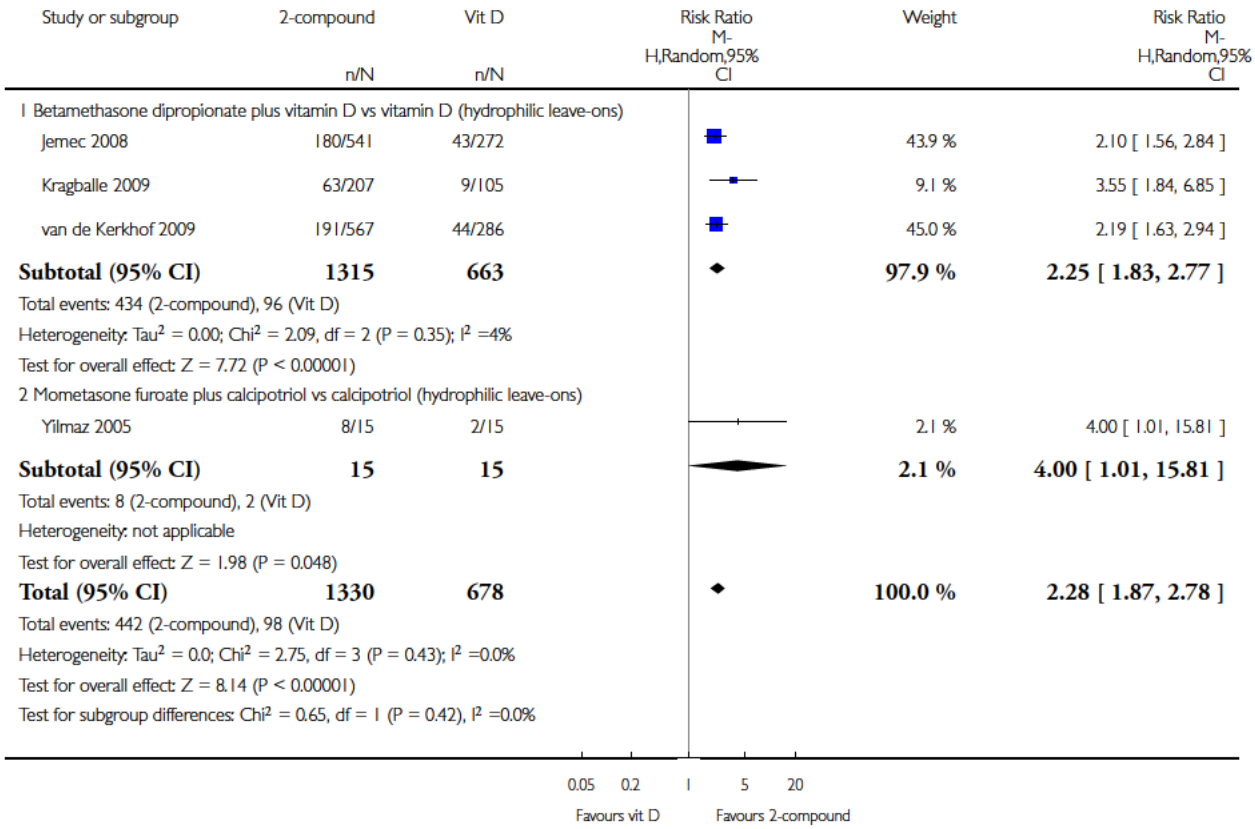


Analysis 11.1. Comparison 11 Steroid plus vitamin D versus vitamin D, Outcome 1 Number of participants achieving 'clearance' by IGA.

Review: Topical treatments for scalp psoriasis

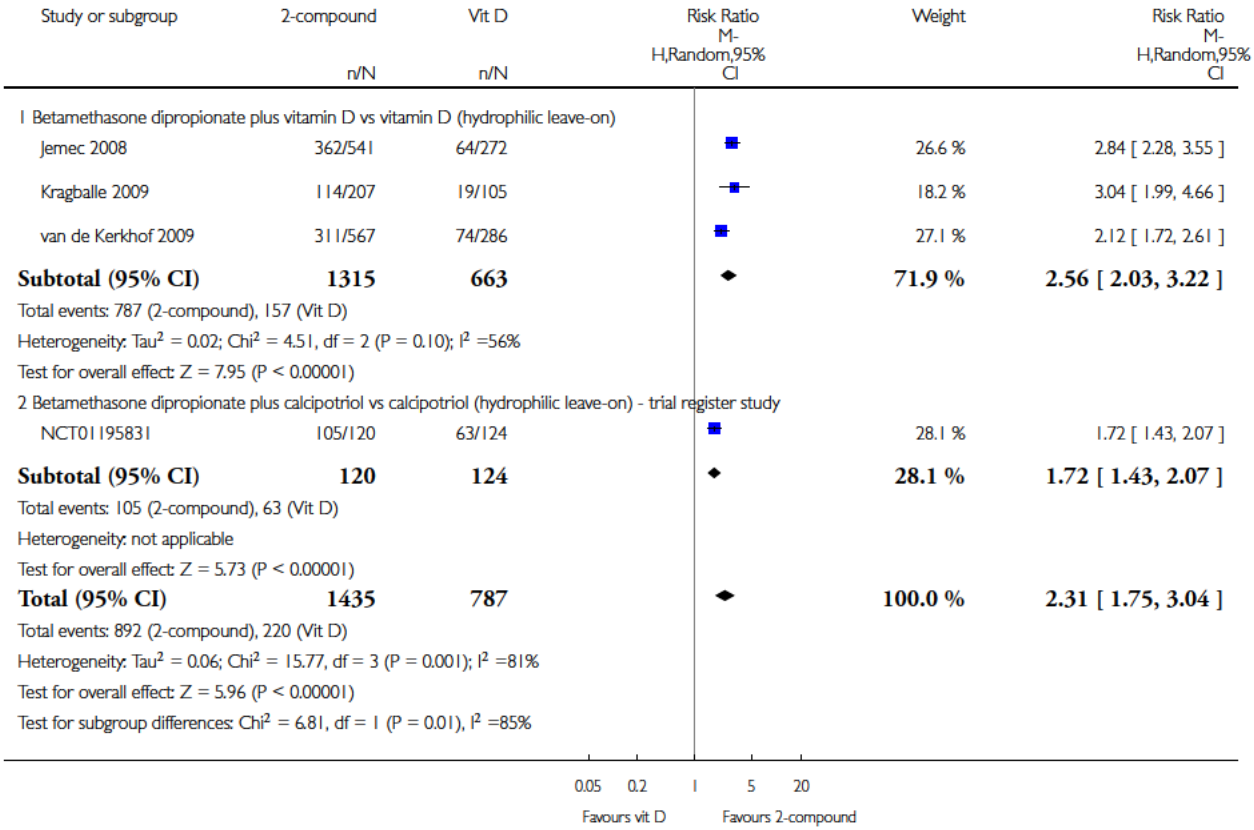
Comparison: 11 Steroid plus vitamin D versus vitamin D

Outcome: 1 Number of participants achieving 'clearance' by IGA



Analysis 11.2. Comparison 11 Steroid plus vitamin D versus vitamin D, Outcome 2 Number of participants achieving 'response' by IGA.

Review: Topical treatments for scalp psoriasis
Comparison: 11 Steroid plus vitamin D versus vitamin D
Outcome: 2 Number of participants achieving 'response' by IGA



Analysis 11.3. Comparison 11 Steroid plus vitamin D versus vitamin D, Outcome 3 Mean of the TSS.

Mean of the TSS

Study	Steroid/vitamin D combination vs vitamin D	Steroid/calcipotriol	Calcipotriol
Jemec 2008	Betamethasone dipropionate/calcipotriol vs calcipotriol	-70%	-54%
Kragballe 2009	Betamethasone dipropionate/calcipotriol vs calcipotriol	-64%	-38%

Mean of the TSS (*Continued*)

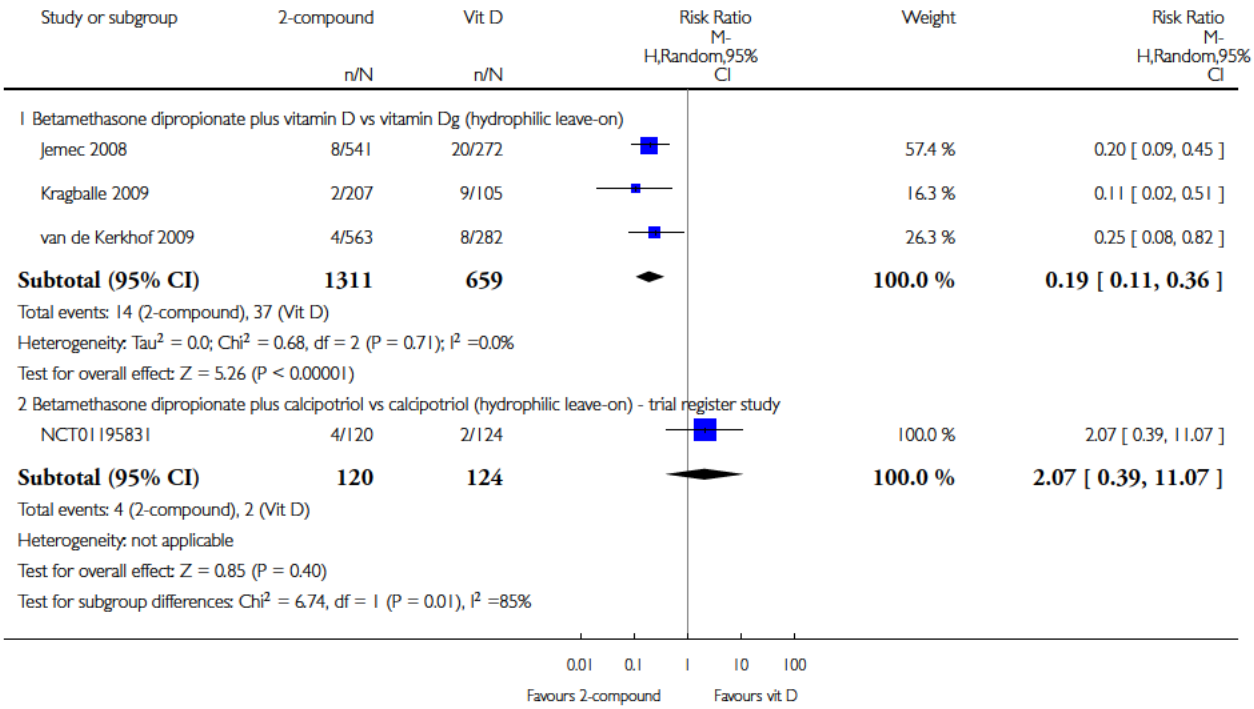
van de Kerkhof 2009	Betamethasone dipropionate/calcipotriol vs calcipotriol	-62%	-43%
Yilmaz 2005	Mometasone/calcipotriol vs calcipotriol	-81%	-49%

Analysis 11.4. Comparison 11 Steroid plus vitamin D versus vitamin D, Outcome 4 Number of participants withdrawing due to adverse events (short-term).

Review: Topical treatments for scalp psoriasis

Comparison: 11 Steroid plus vitamin D versus vitamin D

Outcome: 4 Number of participants withdrawing due to adverse events (short-term)

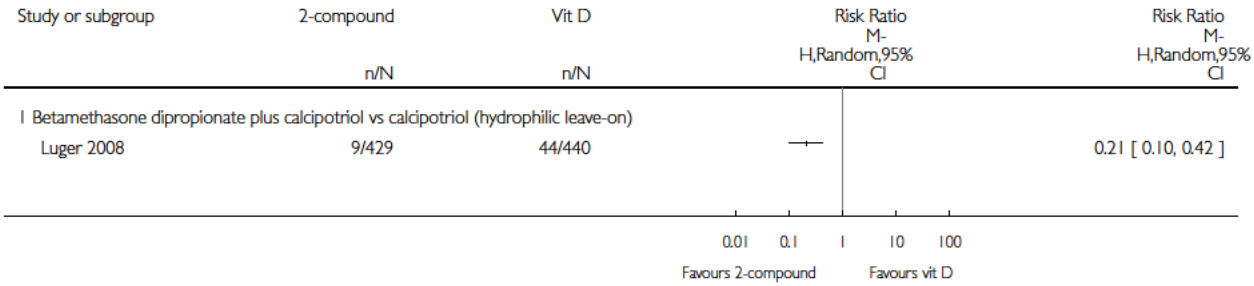


Analysis 11.5. Comparison 11 Steroid plus vitamin D versus vitamin D, Outcome 5 Number of participants withdrawing due to adverse events (long-term).

Review: Topical treatments for scalp psoriasis

Comparison: 11 Steroid plus vitamin D versus vitamin D

Outcome: 5 Number of participants withdrawing due to adverse events (long-term)

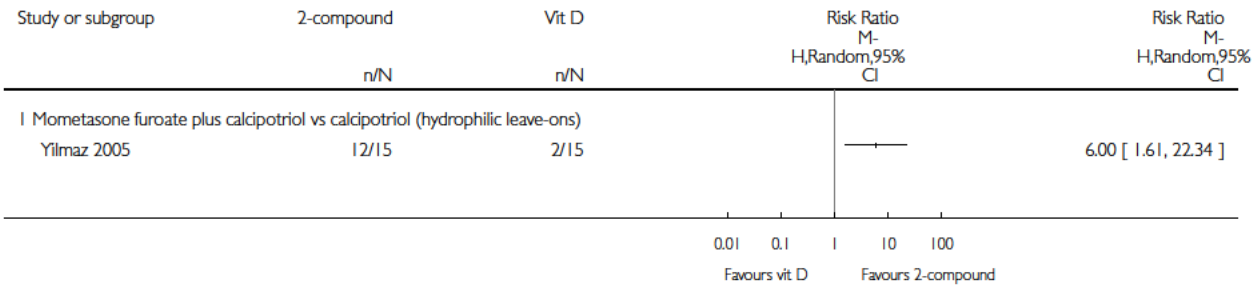


Analysis 11.6. Comparison 11 Steroid plus vitamin D versus vitamin D, Outcome 6 Number of participants achieving 'clearance' by PGA.

Review: Topical treatments for scalp psoriasis

Comparison: 11 Steroid plus vitamin D versus vitamin D

Outcome: 6 Number of participants achieving 'clearance' by PGA

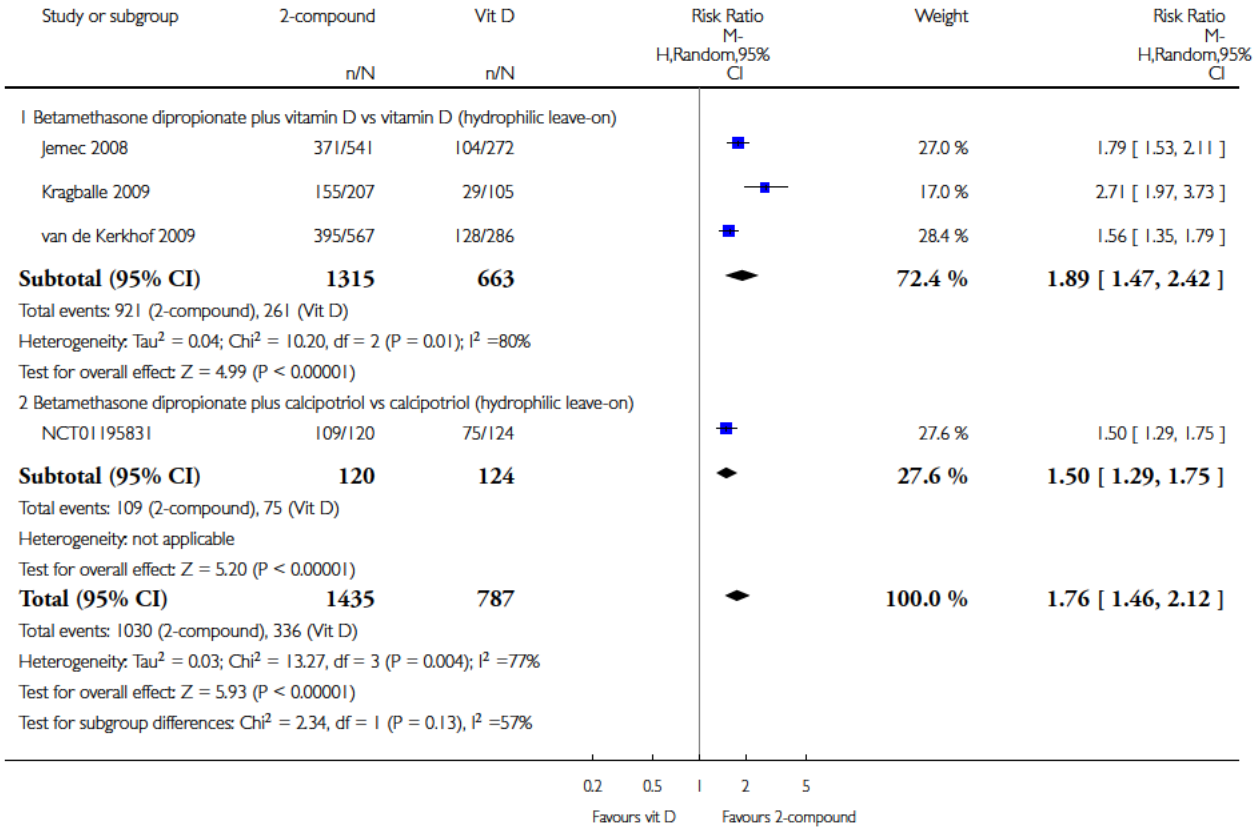


Analysis 11.7. Comparison 11 Steroid plus vitamin D versus vitamin D, Outcome 7 Number of participants achieving 'response' by PGA.

Review: Topical treatments for scalp psoriasis

Comparison: 11 Steroid plus vitamin D versus vitamin D

Outcome: 7 Number of participants achieving 'response' by PGA

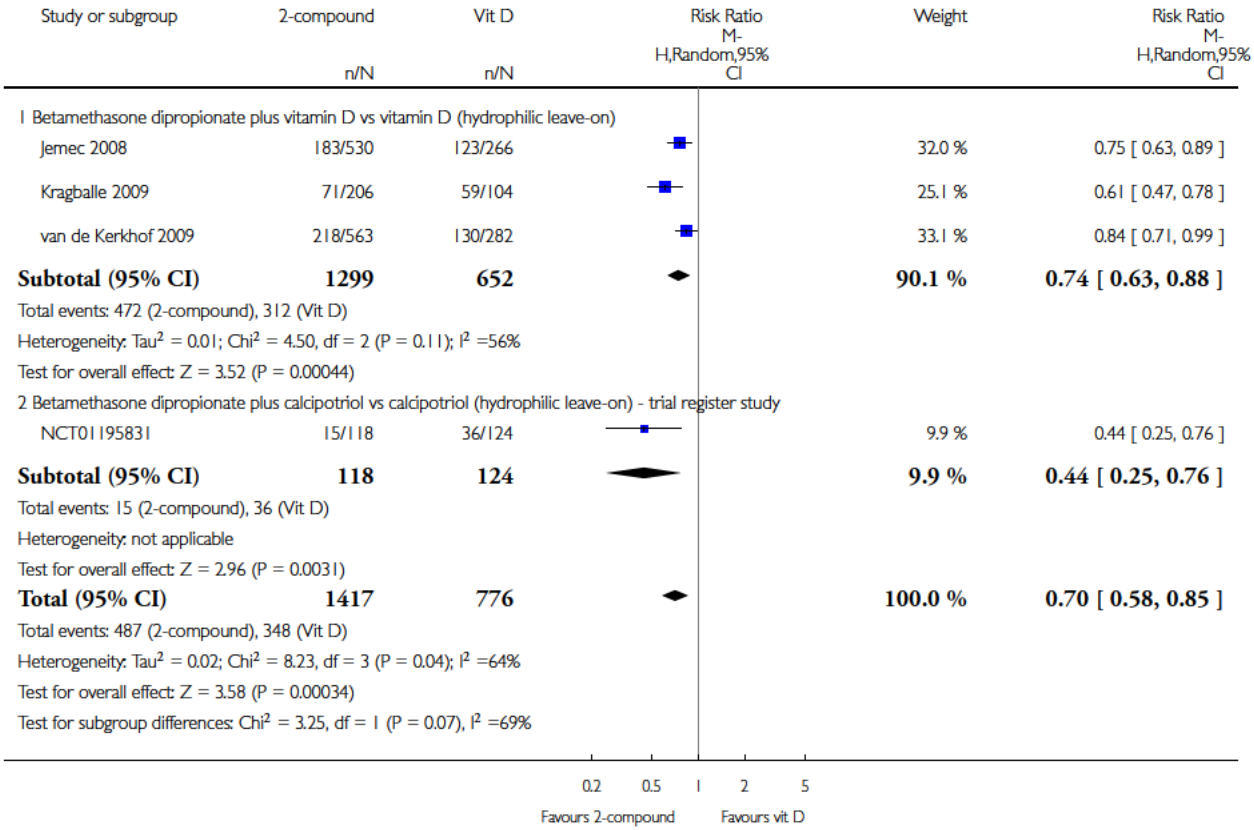


Analysis 11.8. Comparison 11 Steroid plus vitamin D versus vitamin D, Outcome 8 Number of participants with at least one adverse event (short-term).

Review: Topical treatments for scalp psoriasis

Comparison: 11 Steroid plus vitamin D versus vitamin D

Outcome: 8 Number of participants with at least one adverse event (short-term)

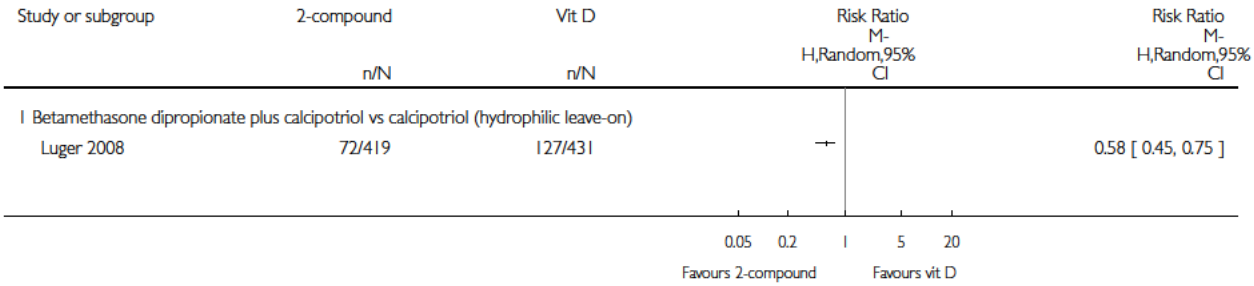


Analysis 11.9. Comparison 11 Steroid plus vitamin D versus vitamin D, Outcome 9 Number of participants with at least one adverse event (long-term).

Review: Topical treatments for scalp psoriasis

Comparison: 11 Steroid plus vitamin D versus vitamin D

Outcome: 9 Number of participants with at least one adverse event (long-term)

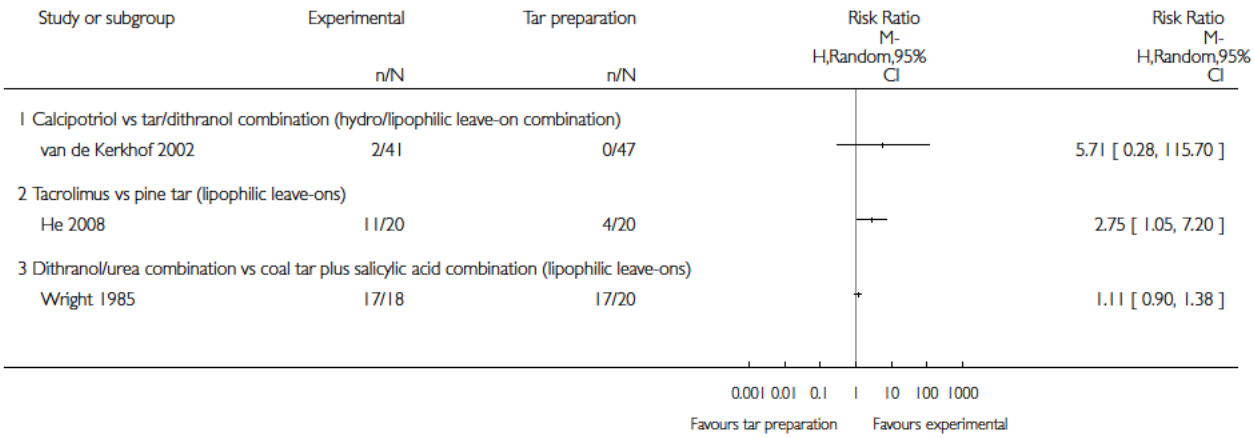


Analysis 12.1. Comparison 12 Tar and dithranol, Outcome 1 Number of participants achieving 'clearance' by IGA.

Review: Topical treatments for scalp psoriasis

Comparison: 12 Tar and dithranol

Outcome: 1 Number of participants achieving 'clearance' by IGA

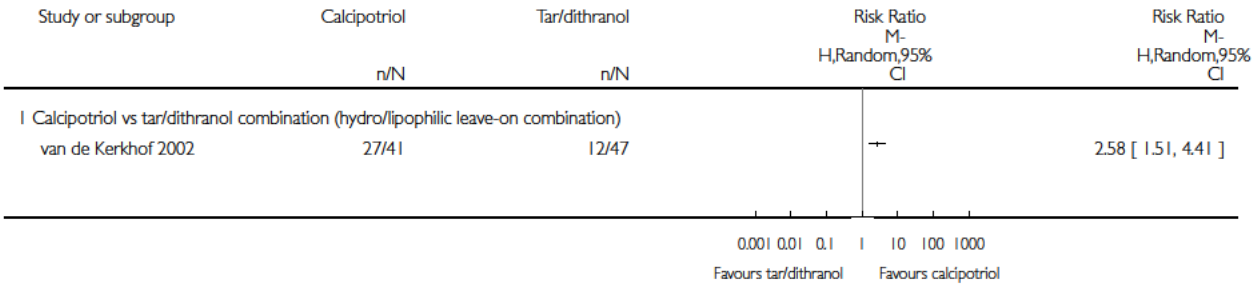


Analysis 12.2. Comparison 12 Tar and dithranol, Outcome 2 Number of participants achieving 'response' by IGA.

Review: Topical treatments for scalp psoriasis

Comparison: 12 Tar and dithranol

Outcome: 2 Number of participants achieving 'response' by IGA



Analysis 12.3. Comparison 12 Tar and dithranol, Outcome 3 Mean of the TSS.

Mean of the TSS

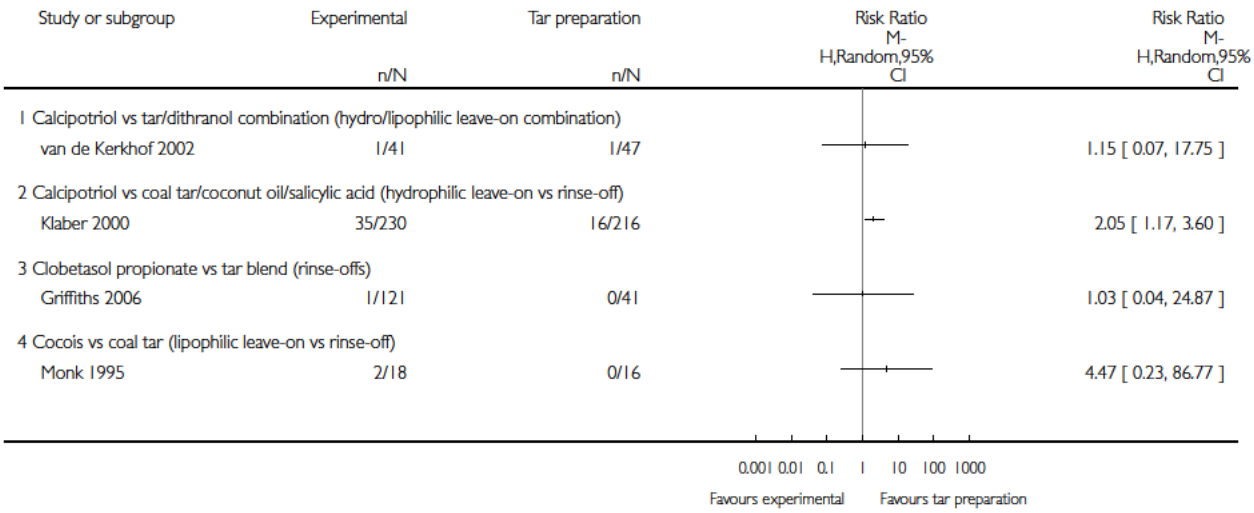
Study	Comparison	Other therapy	Tar containing product
Griffiths 2006	Clobetasol propionate vs tar blend	-48%	-16%
He 2008	Tacrolimus vs pine tar	-80%	-55%
Klaber 2000	Calcipotriol vs coal tar/coconut oil/salicylic acid combination	-28%	-23%
Monk 1995	Cocois vs coal tar	-67%	-14%
van de Kerkhof 2002	Calcipotriol vs tar/dithranol-combination	-51%	-17%
Wall 1999	Calcipotriol vs calcipotriol/coal tar combination	-41%	-48%
Wright 1985	Dithranol/urea vs coal tar	-51%	-47%

Analysis 12.4. Comparison 12 Tar and dithranol, Outcome 4 Number of participants withdrawing due to adverse events.

Review: Topical treatments for scalp psoriasis

Comparison: 12 Tar and dithranol

Outcome: 4 Number of participants withdrawing due to adverse events

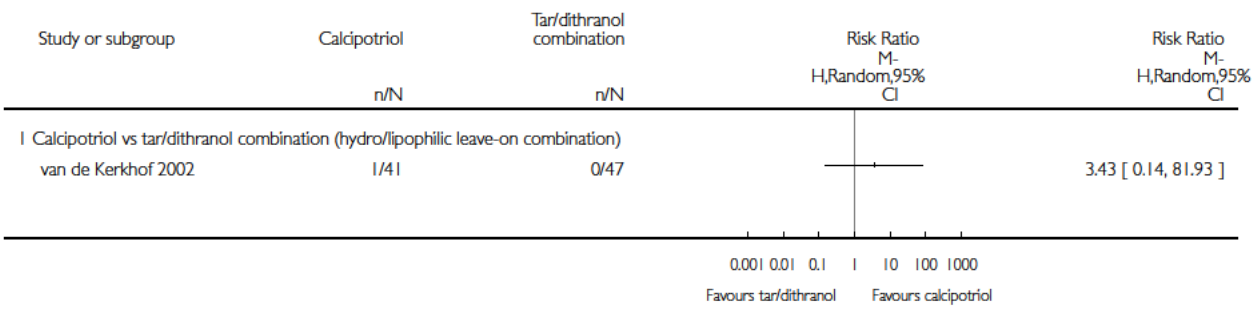


Analysis 12.5. Comparison 12 Tar and dithranol, Outcome 5 Number of participants achieving 'clearance' by PGA.

Review: Topical treatments for scalp psoriasis

Comparison: 12 Tar and dithranol

Outcome: 5 Number of participants achieving 'clearance' by PGA

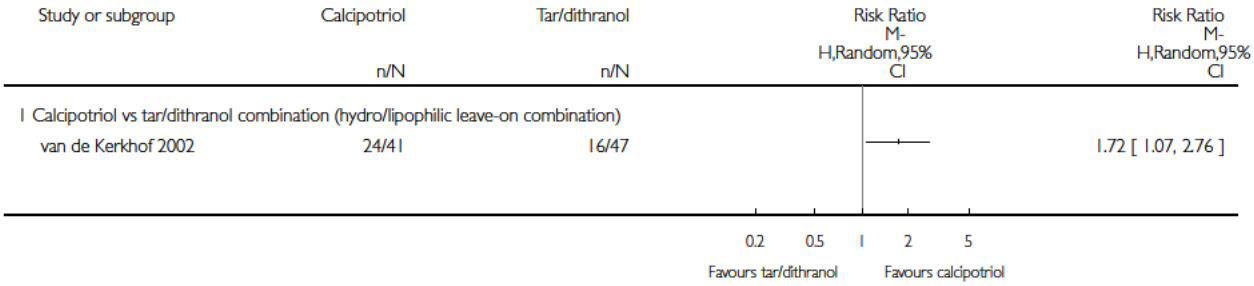


Analysis 12.6. Comparison 12 Tar and dithranol, Outcome 6 Number of participants achieving 'response' by PGA.

Review: Topical treatments for scalp psoriasis

Comparison: 12 Tar and dithranol

Outcome: 6 Number of participants achieving 'response' by PGA

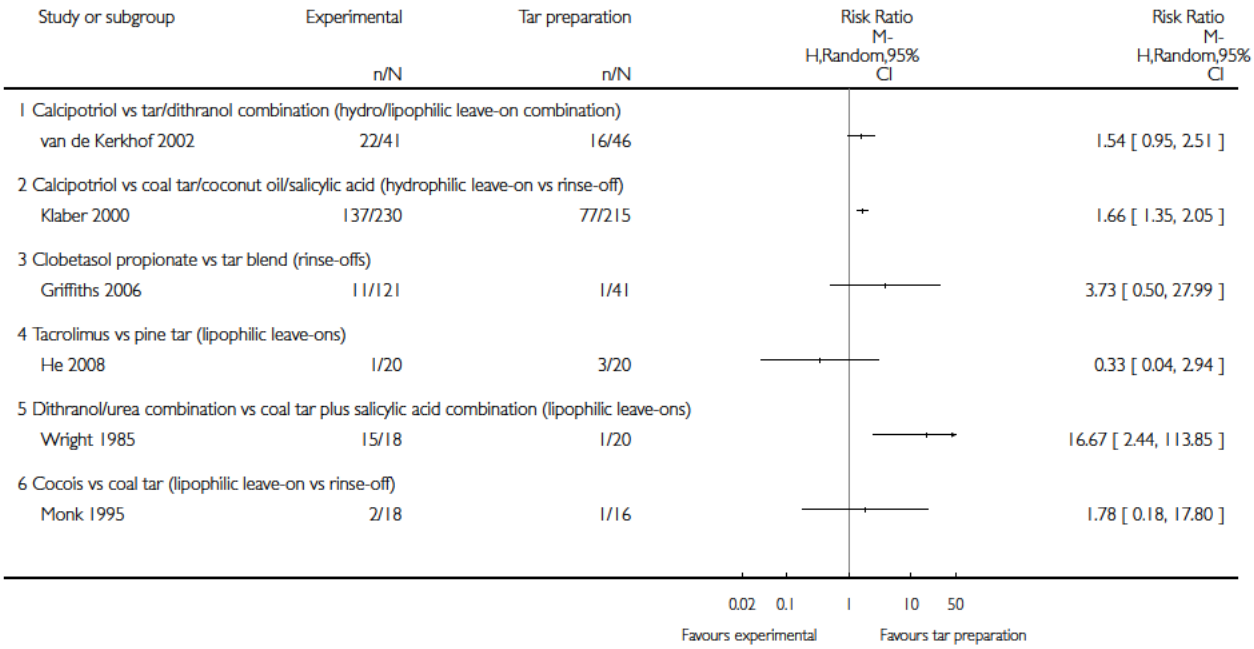


Analysis 12.7. Comparison 12 Tar and dithranol, Outcome 7 Number of participants with at least one adverse event.

Review: Topical treatments for scalp psoriasis

Comparison: 12 Tar and dithranol

Outcome: 7 Number of participants with at least one adverse event

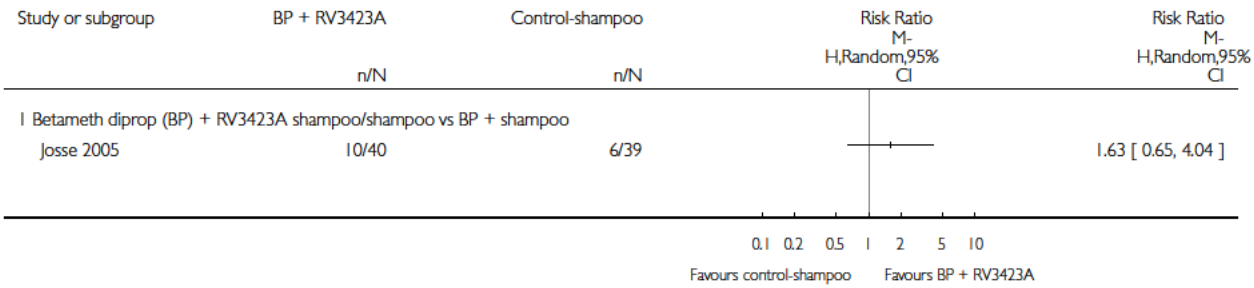


Analysis 13.1. Comparison 13 Steroid: vehicle comparisons, Outcome 1 Number of participants achieving 'clearance' by IGA.

Review: Topical treatments for scalp psoriasis

Comparison: 13 Steroid: vehicle comparisons

Outcome: 1 Number of participants achieving 'clearance' by IGA

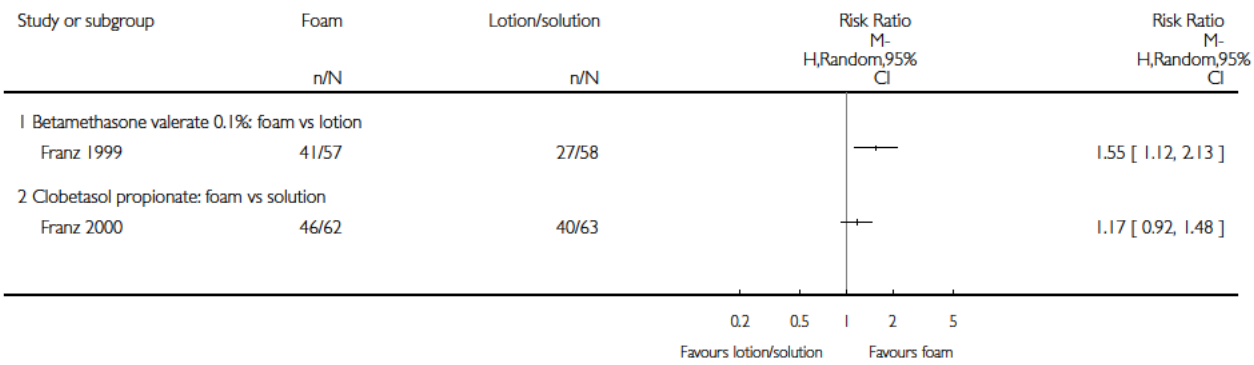


Analysis 13.2. Comparison 13 Steroid: vehicle comparisons, Outcome 2 Number of participants achieving 'response' by IGA.

Review: Topical treatments for scalp psoriasis

Comparison: 13 Steroid: vehicle comparisons

Outcome: 2 Number of participants achieving 'response' by IGA



Analysis 13.3. Comparison 13 Steroid: vehicle comparisons, Outcome 3 Mean of the TSS.

Mean of the TSS

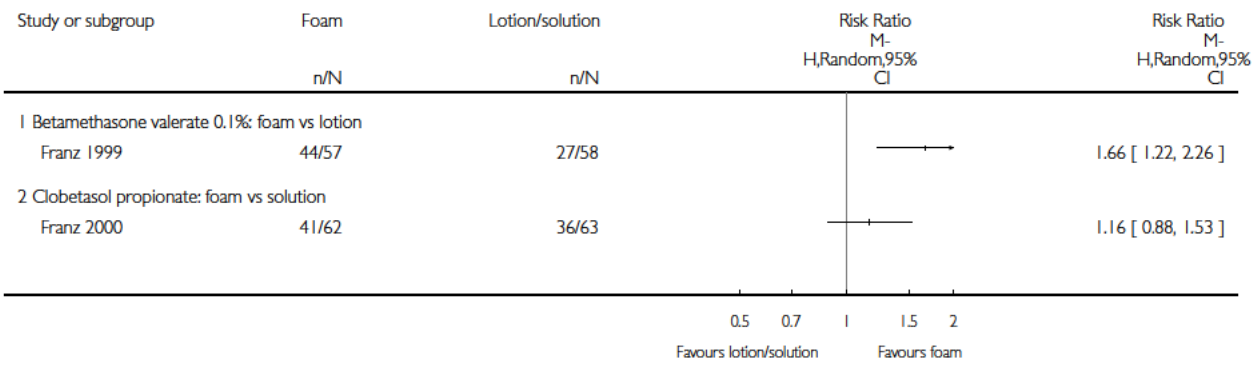
Study	Comparison: vehicle (1) vs (2)	Vehicle 1	Vehicle 2
Andres 2006	Clobetasol propionate: rinse-off (1) vs hydrophilic leave-on (2)	-70%	-75%
Franz 1999	Betamethasone valerate: foam (1) vs lotion (2)	-65%	-49%
Franz 2000	Clobetasol propionate: foam (1) vs solution (2)	-75%	-68%
Josse 2005	Betamethasone dipropionate: RV3423A/extra gentle shampoo (1) vs extra gentle shampoo (2)	-63%	-53%
Reygagne 2002	Clobetasol propionate: rinse-off (1) vs hydrophilic leave-on (2)	-67%	-80%
Wilhelm 2013	Mometasone: emulsion (LAS41002) (1) vs solution (2)	-81.82%	-84.55%

Analysis 13.4. Comparison 13 Steroid: vehicle comparisons, Outcome 4 Number of participants achieving 'response' by PGA.

Review: Topical treatments for scalp psoriasis

Comparison: 13 Steroid: vehicle comparisons

Outcome: 4 Number of participants achieving 'response' by PGA

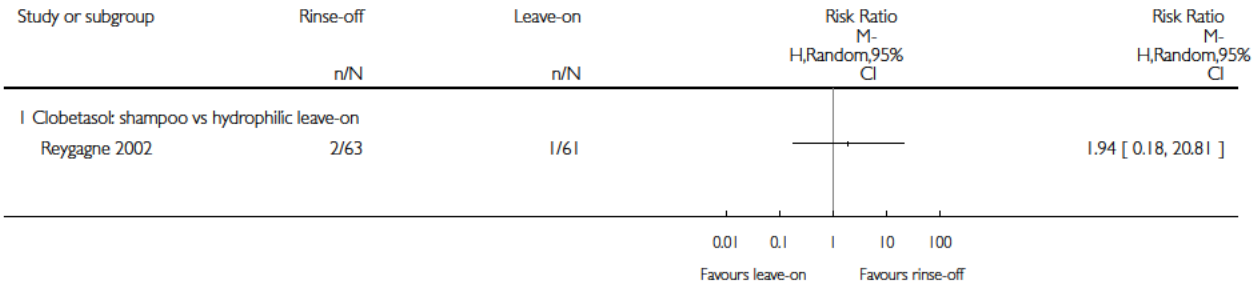


Analysis 13.5. Comparison 13 Steroid: vehicle comparisons, Outcome 5 Number of participants with at least one adverse event.

Review: Topical treatments for scalp psoriasis

Comparison: 13 Steroid: vehicle comparisons

Outcome: 5 Number of participants with at least one adverse event

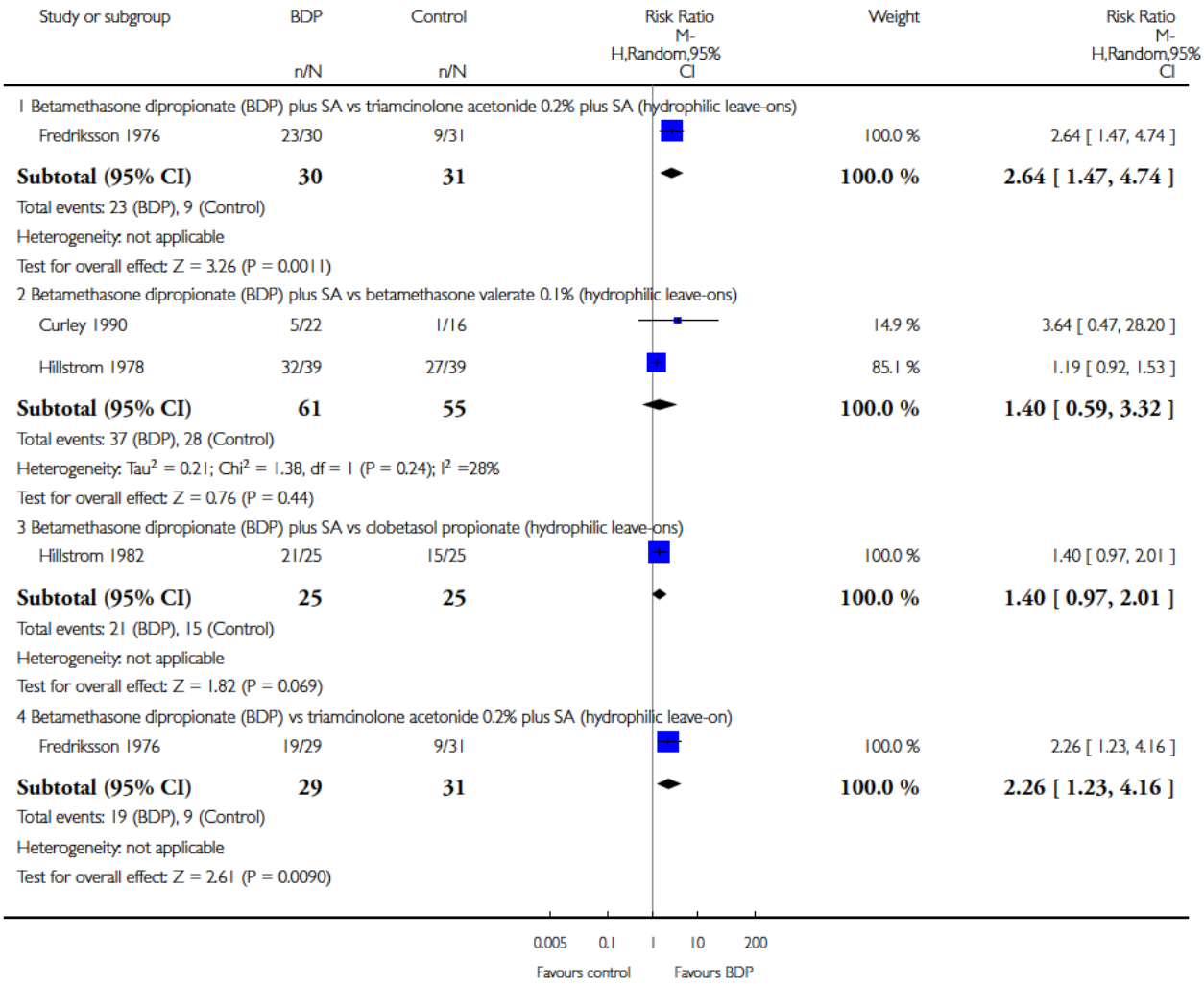


Analysis 14.1. Comparison 14 Other steroid plus salicylic acid comparisons, Outcome 1 Number of participants achieving 'clearance' by IGA.

Review: Topical treatments for scalp psoriasis

Comparison: 14 Other steroid plus salicylic acid comparisons

Outcome: 1 Number of participants achieving 'clearance' by IGA

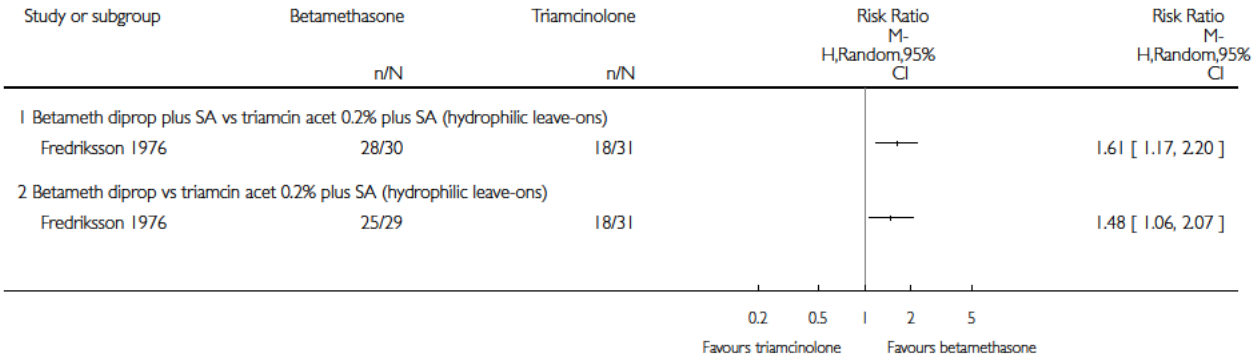


Analysis 14.2. Comparison 14 Other steroid plus salicylic acid comparisons, Outcome 2 Number of participants achieving 'response' by IGA.

Review: Topical treatments for scalp psoriasis

Comparison: 14 Other steroid plus salicylic acid comparisons

Outcome: 2 Number of participants achieving 'response' by IGA

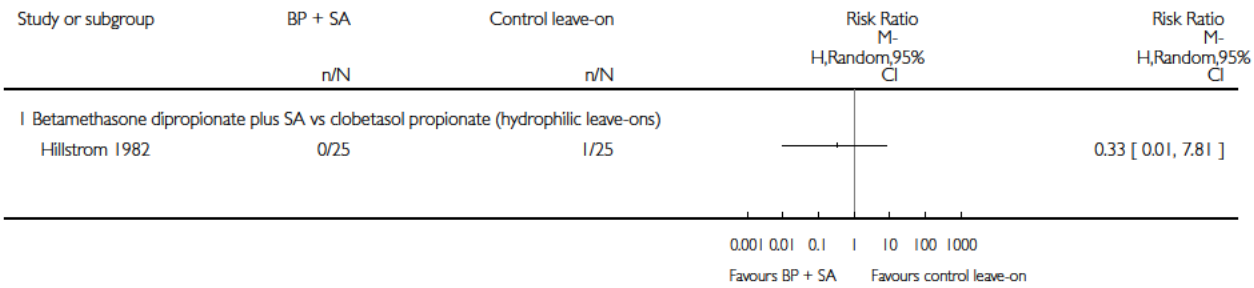


Analysis 14.3. Comparison 14 Other steroid plus salicylic acid comparisons, Outcome 3 Number of participants withdrawing due to adverse events.

Review: Topical treatments for scalp psoriasis

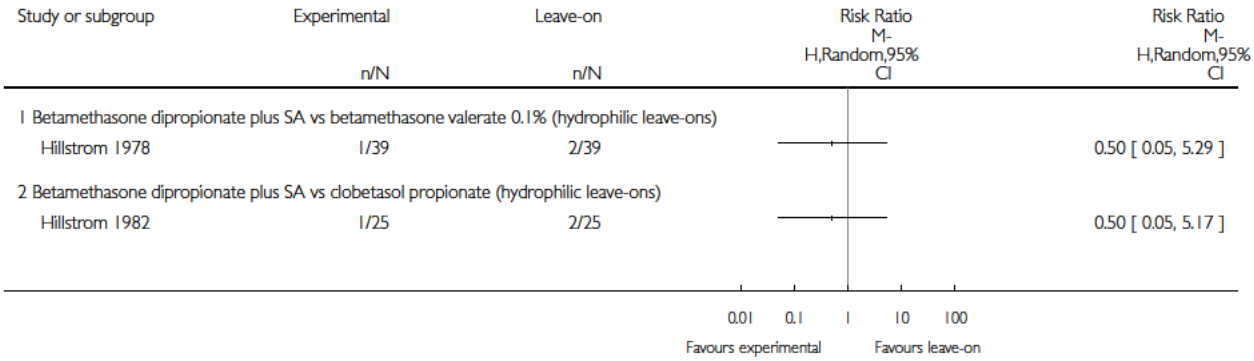
Comparison: 14 Other steroid plus salicylic acid comparisons

Outcome: 3 Number of participants withdrawing due to adverse events



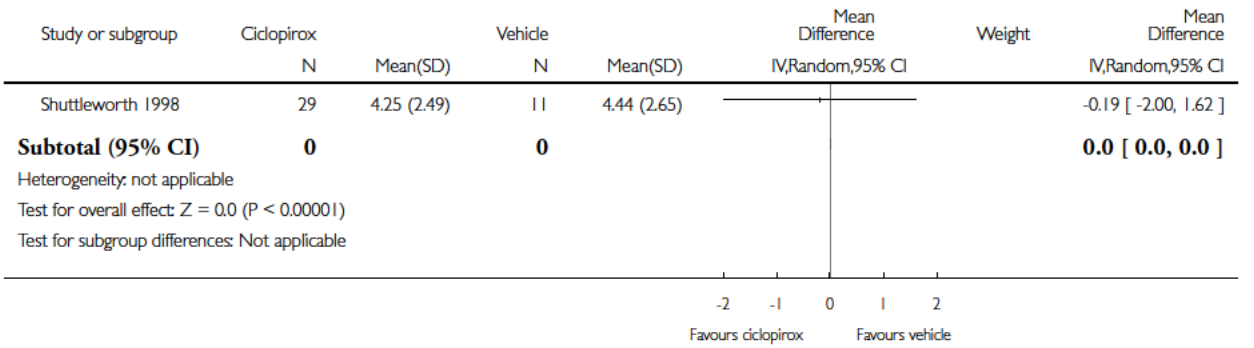
Analysis 14.4. Comparison 14 Other steroid plus salicylic acid comparisons, Outcome 4 Number of participants with at least one adverse event.

Review: Topical treatments for scalp psoriasis
Comparison: 14 Other steroid plus salicylic acid comparisons
Outcome: 4 Number of participants with at least one adverse event



Analysis 15.1. Comparison 15 Antifungals versus vehicle, Outcome 1 Mean score of the IGA.

Review: Topical treatments for scalp psoriasis
Comparison: 15 Antifungals versus vehicle
Outcome: 1 Mean score of the IGA

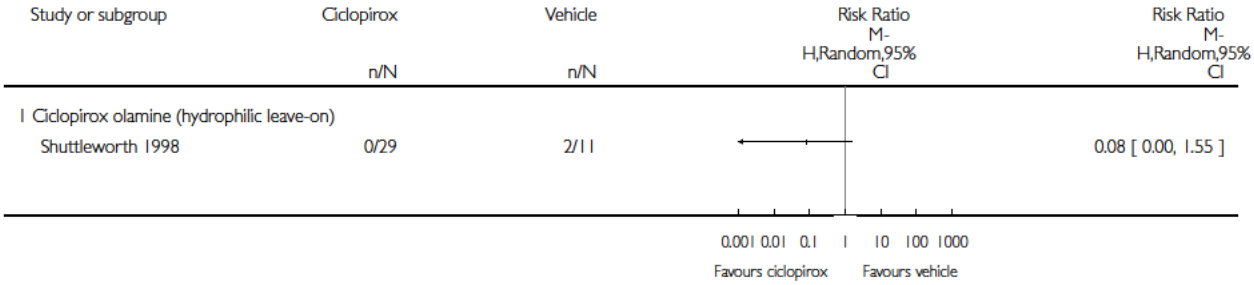


Analysis 15.2. Comparison 15 Antifungals versus vehicle, Outcome 2 Number of participants withdrawing due to adverse events.

Review: Topical treatments for scalp psoriasis

Comparison: 15 Antifungals versus vehicle

Outcome: 2 Number of participants withdrawing due to adverse events

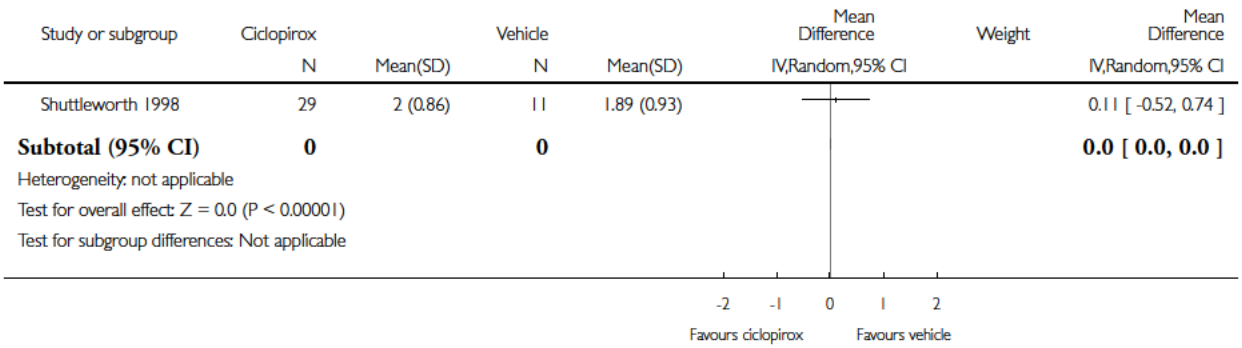


Analysis 15.3. Comparison 15 Antifungals versus vehicle, Outcome 3 Mean score of the PGA.

Review: Topical treatments for scalp psoriasis

Comparison: 15 Antifungals versus vehicle

Outcome: 3 Mean score of the PGA

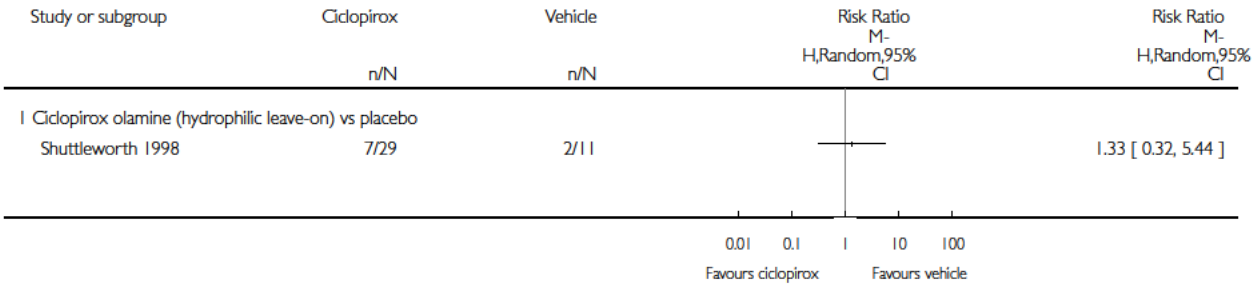


Analysis 15.4. Comparison 15 Antifungals versus vehicle, Outcome 4 Number of participants with at least one adverse event.

Review: Topical treatments for scalp psoriasis

Comparison: 15 Antifungals versus vehicle

Outcome: 4 Number of participants with at least one adverse event



ADDITIONAL TABLES

Table 1. Glossary of technical and medical terms

Medical terms	Explanation
Apoptosis	The process of programmed cell death, which is the natural developmental and maintenance process of the normal removal of cells
Immuno-suppressive	Specific property of certain medications (e.g. corticosteroids) that diminish the response or activation of the immune system
Hyperproliferation	An abnormality associated with a high rate of growth of cells by rapid division
Differentiation	The process by which a less specialised cell becomes a more specialised cell type
Erythematous	An abnormal redness of the skin caused by various agents, such as sunlight or drugs etc, which irritate and congest the blood capillaries
Plaque psoriasis	Patches with the well-defined characteristic of red, raised skin. They can appear on any skin surface, although the knees, elbows, scalp, trunk and nails are the most common locations
Keratolytic agents	A chemical or physical agent that causes peeling by the softening and shedding of the horny outer layer of the skin
Hypervascularisation	A local increase in the formation of blood vessels leading to a higher blood supply of the tissue mainly as a response to the action of the vascular endothelial growth factor (VEGF)
Pro-inflammatory	Provoking inflammation

Table 1. Glossary of technical and medical terms *(Continued)*

Anti-inflammatory	Inhibiting or reducing inflammation
Keratinocytes	Skin cells forming the superficial layer of the skin (epidermis)
Epigenetics	The interactions of specific proteins with the genome that influence the expression of certain genes without changing the genetic sequence
PUVA	A photochemotherapy of certain dermatological conditions with psoralen and ultra violet A light (UVA). Usually, psoralen is applied topically on the affected area to increase the sensibility to the UVA light
Rosacea	A chronic skin disease affecting mainly the cheeks, nose, forehead, scalp and ears. On the involved ruddy skin thin superficial blood vessels (teleangiectasia), papules and pustules may appear. In a certain type of rosacea, some facial areas (e.g. nose) enlarge and become bulbous (e.g. rhinophyma)
Cytoplasm	The watery fluid (cytosol) inside the cell in which the organelles and the skeleton of the cell are embedded

Table 2. Sensitivity analyses: summary table

Comparison	Outcome	Sensitivity analysis: ITT population[1]	Sensitivity analysis: allocation concealment[2]	Meta-analysis[3]
Steroid versus the vehicle	IGA: clearance	RR 11.67; 95% CI 4.88 to 27.90	RR 20.49; 95% CI 2.89 to 145.19	RR 14.58; 95% CI 7.28 to 29.17
	IGA: response	RR 7.67; 95% CI 4.24 to 13.89	RR 6.11; 95% CI 2.98 to 12.52	RR 5.24; 95% CI 3.83 to 7.17
	Withdrawal due to AE	RR 0.22; 95% CI 0.08 to 0.61	**RR 0.33; 95% CI 0.01 to 7.76**	RR 0.27; 95% CI 0.11 to 0.67
	Number of participants with at least 1 AE	RR 0.87; 95% CI 0.70 to 1.09	RR 1.56; 95% CI 0.56 to 4.37	RR 0.87; 95% CI 0.70 to 1.08
Steroid versus vitamin D	IGA: clearance	RR 1.81; 95% CI 1.47 to 2.24	Not applicable	RR 1.82; 95% CI 1.52 to 2.18
	Withdrawal due to AE	RR 0.22; 95% CI 0.08 to 0.57	Not applicable	RR 0.22; 95% CI 0.11 to 0.42
	PGA: clearance	RR 4.00; 95% CI 1.01 to 15.81	Not applicable	RR 2.22; 95% CI 1.47 to 3.35
Steroid plus vitamin D versus vitamin D	IGA: clearance	Not applicable	RR 3.55; 95% CI 1.84 to 6.85	RR 2.28; 95% CI 1.87 to 2.78
	IGA: response	Not applicable	RR 3.04; 95% CI 1.99 to 4.66	RR 2.31; 95% CI 1.75 to 3.04

Table 2. Sensitivity analyses: summary table *(Continued)*

	Withdrawal due to AE (short-term)	Not applicable	RR 0.11; 95% CI 0.02 to 0.51	RR 0.19; 95% CI 0.11 to 0.36
	Number of participants with at least 1 AE (short-term)	Not applicable	RR 0.61; 95% CI 0.47 to 0.78	RR 0.70; 95% CI 0.58 to 0.85

Bold text indicates a meaningful difference between effect estimates.
[1]Total effect estimate of all studies that provided sufficient information to ensure that ITT analysis was performed.
[2]Total effect estimate of all studies that provided sufficient information to ensure that allocation concealment was adequately performed.
[3]Total effect estimate of meta-analysis that included all relevant studies, regardless if ITT analysis or allocation concealment was performed or not.
AE: adverse event
CI: confidence interval
IGA: investigator's global assessment
ITT: intention-to-treat
PGA: patient global assessment
RR: risk ratio

APPENDICES

Appendix 1. CENTRAL (The Cochrane Library) search strategy

#1 MeSH descriptor Psoriasis explode all trees
#2 (psoria*)
#3 (#1 OR #2)
#4 MeSH descriptor Scalp explode all trees
#5 (scalp*)
#6 (#4 OR #5)
#7 (#3 AND #6)

Appendix 2. MEDLINE (Ovid) search strategy

1. exp Psoriasis/ or psoria$.mp.
2. exp Scalp/
3. scalp$.mp.
4. 2 or 3
5. randomized controlled trial.pt.
6. controlled clinical trial.pt.
7. randomized.ab.
8. placebo.ab.
9. clinical trials as topic.sh.
10. randomly.ab.
11. trial.ti.

12. 5 or 6 or 7 or 8 or 9 or 10 or 11
13. exp animals/ not humans.sh.
14. 12 not 13
15. 1 and 4 and 14
[Lines 5-14: Cochrane Highly Sensitive Search Strategy for identifying randomized trials in MEDLINE: sensitivity- and precision-maximizing version (2008 revision)]

Appendix 3. Embase (Ovid) search strategy

1. exp psoriasis/
2. psoria$.ti,ab.
3. 1 or 2
4. exp scalp/
5. scalp$.ti,ab.
6. 4 or 5
7. crossover procedure.sh.
8. double-blind procedure.sh.
9. single-blind procedure.sh.
10. (crossover$ or cross over$).tw.
11. placebo$.tw.
12. (doubl$ adj blind$).tw.
13. allocat$.tw.
14. trial.ti.
15. randomized controlled trial.sh.
16. random$.tw.
17. or/7-16
18. exp animal/ or exp invertebrate/ or animal experiment/ or animal model/ or animal tissue/ or animal cell/ or nonhuman/
19. human/ or normal human/
20. 18 and 19
21. 18 not 20
22. 17 not 21
23. 3 and 6 and 22

CONTRIBUTIONS OF AUTHORS

JGS was the contact person with the editorial base, co-ordinated contributions from the co-authors and wrote the final draft of the review.

JGS and SR screened papers against the eligibility criteria.

JGS and SR obtained data on ongoing and unpublished studies.

JGS and SR appraised the quality of papers.

JGS and SR extracted data for the review and sought additional information about papers.

JGS entered data into RevMan.

JGS, AN and AJ analysed and interpreted data.

JGS, AN, JS, RNW and AJ worked on the methods sections.

JGS, AN and RNW drafted the clinical sections of the background and responded to the clinical comments of the referees.

JGS, AJ, SR and JS responded to the methodology and statistics comments of the referees.

CS was the consumer co-author and checked the review for readability and clarity, as well as ensuring that outcomes are relevant to consumers.

Disclaimer

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

DECLARATIONS OF INTEREST

AN has received honoraria as a speaker in educational activities with direct or indirect sponsoring from Bayer, Pfizer, Novartis, Abbot and Biogen Idec. This has been in the last three years and is limited to the companies with an interest in psoriasis treatment.

The dEBM (JGS, SR, RNW and AJ) has received research grants from Pfizer, Biogen Idec, GSK and Merz.

JS received funding for investigator-initiated research from Novartis, MSD, Pfizer, Alk and Sanofi.

CS has no conflicts of interest to declare.

A clinical referee, who wishes to remain anonymous: "I received speaker's honoraria or fees as investigator of clinical trials from Leo Pharma and Galderma."

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Internal sources

- Universidade Federal de Sao Paulo, Brazil.
- Universidade Federal do Rio Grande do Norte, Brazil.

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

Only one author (AN) of the published protocol participated in the review process. However, we aimed to adhere closely to all methodological aspects and intentions that the previous authors described in the protocol.

We rewrote all sections of the 'Background' in order to be more precise and make the text easier to read. In this context, we divided the part 'Description of the condition' into the subsections 'Psoriasis in general', 'Scalp psoriasis' and 'Pathophysiology'. We also divided the part 'Description of the intervention' into the subsections 'Corticosteroids', 'Vitamin D analogues', 'Tar-based preparations', 'Calcineurin inhibitors', 'Anthralin (dithranol)', 'Salicylic acid' and 'Antifungals'.

Our outcomes are the same as planned in the protocol but we have defined them in more detail. See Results/Included studies/Outcomes section.

We did not run a separate search in MEDLINE for adverse events. Instead, we extracted data on adverse events that were reported in the included studies.

It was not possible to search for relevant trials in the Salford Database.

As mentioned in the protocol, we conducted available case analysis, if missing data could not be obtained from study authors or sponsors. For dichotomous efficacy outcomes, however, we intended to impute missing data as treatment failure and conducted ITT analysis, wherever treatment group affiliation of the drop-outs was replicable.

Given the high number of included interventions we did not create 'Summary of findings' tables for all comparisons. Instead, we created 'Summary of findings' tables only for three comparisons that we thought to be of major clinical interest.

We modified the 'Types of Interventions' section. It now contains all therapies that were assessed by the included studies. In this context, we also removed acupuncture from this section, as it is not considered as a topical treatment.

Lebenslauf

Mein Lebenslauf wird aus datenschutzrechtlichen Gründen in der elektronischen Version meiner Arbeit nicht veröffentlicht.

Komplette Publikationsliste

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Nicht zuletzt geht mein großer Dank an meine lieben Eltern, meine Brüder und an Virginia. Ihr Rückhalt und ihre mentale Unterstützung waren von unschätzbarem Wert für das Gelingen dieser Arbeit.