Seborrhoeic dermatitis of the scalp

Search date November 2013

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ABSTRACT

INTRODUCTION: Seborrhoeic dermatitis affects a variable proportion of the general population, ranging from 3% to 10%. Malassezia yeast species (previously referred to as Pityrosporum) are thought to be the responsible organisms, and cause inflammation by still poorly defined mechanisms. Seborrhoeic dermatitis tends to relapse after treatment. METHODS AND OUTCOMES: We conducted a systematic review and aimed to answer the following clinical question: What are the effects of topical treatments for seborrhoeic dermatitis of the scalp in adults? We searched: Medline, Embase, The Cochrane Library, and other important databases up to November 2013 (Clinical Evidence reviews are updated periodically; please check our website for the most up-to-date version of this review). We included harms alerts from relevant organisations such as the US Food and Drug Administration (FDA) and the UK Medicines and Healthcare products Regulatory Agency (MHRA). RESULTS: We found 14 studies that met our inclusion criteria. We performed a GRADE evaluation of the quality of evidence for interventions. CONCLUSIONS: In this systematic review we present information relating to the effectiveness and safety of the following interventions: bifonazole, ciclopirox, ketoconazole, pyrithione zinc, selenium sulfide, tar shampoo, terbinafine, and topical corticosteroids (betamethasone valerate, clobetasol propionate, clobetasone butyrate, hydrocortisone, mometasone furoate).

QUESTIONS

INTERVENTIONS

TOPICAL TREATMENTS FOR SEBORRHOEIC DERMATITIS OF SCALP

To be covered in future updates

Direct comparisons of topical treatments for seborrhoeic dermatitis of the scalp

Footnote

*Based on consensus.

Key points

- Seborrhoeic dermatitis affects at least 3% to 10% of the population and causes red patches with greasy scales on the face, chest, skin flexures, and scalp.

  The cause of seborrhoeic dermatitis is unknown. *Malassezia* yeast species are thought to have an important role.

  The inflammatory process may be mediated in susceptible people by fungal metabolites, namely free fatty acids, released from sebaceous triglycerides. The lipid layer of *Malassezia* can also modulate pro-inflammatory cytokine production by keratinocytes.

  Known risk factors include immunodeficiency, neurological or cardiac disease, and alcoholic pancreatitis. In this review, however, we deal with treatment in immunocompetent adults who have no known predisposing conditions.

  Seborrhoeic dermatitis tends to relapse after treatment.

- In adults with seborrhoeic dermatitis of the scalp, topical antifungal preparations containing ketoconazole seem to improve symptoms compared with placebo and are also useful as treatment in the maintenance phase.

  Ciclopirox seems to improve symptoms compared with placebo and may reduce relapse up to 12 weeks after initial treatment phase.

  Bifonazole and selenium sulfide are also likely to be effective, but we don't know whether terbinafine is beneficial as we found no RCTs.

  We found insufficient RCT evidence to fully assess the effectiveness of short courses of topical corticosteroids; however, there is consensus that topical corticosteroids are effective in treating seborrhoeic dermatitis of the scalp in adults. We found limited evidence that clobetasol propionate 0.05% may improve some symptoms of seborrhoeic dermatitis.

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Tar shampoo may reduce scalp dandruff and redness compared with placebo; however, nowadays it is rarely used.

Pyrithione zinc may be more effective than vehicle shampoo at reducing dandruff severity; however, the evidence is too weak and limited to draw conclusions about the effectiveness.

- Ketoconazole and ciclopirox have both been shown to be beneficial compared to placebo. In the next update of this review we will look for head-to-head comparisons of these.

Clinical context

GENERAL BACKGROUND

Seborrhoeic dermatitis is a chronic condition and one of the most common skin complaints. The scalp is one of the areas most frequently involved. Seborrhoeic dermatitis of the scalp can cause distress for patients in terms of itching and scaling, and also social embarrassment since the scalp is a visible area. The condition can have a major influence on a patient's life. Several treatment options are available.

FOCUS OF THE REVIEW

This review focuses on the topical treatment for seborrhoeic dermatitis of the scalp. It aims to discuss the suitable treatments in the acute phase as well as in the maintenance phase to try to prevent a relapse.

COMMENTS ON EVIDENCE

There is limited evidence available on the effectiveness of the different topical treatment agents for seborrhoeic dermatitis of the scalp. Only ketoconazole and ciclopirox have been studied in multiple RCTs. However, in several trials of ketoconazole, the focus is on dandruff rather than more specifically on seborrhoeic dermatitis. Moreover, long-term outcomes and prevention of relapse are scarcely studied and are areas for future research. This review deals with scalp treatment only. No RCTs are available on pimecrolimus or tacrolimus since no vehicle is available for the scalp.

SEARCH AND APPRAISAL SUMMARY

The update literature search for this review was carried out from the date of the last search, April 2010 to November 2013. Searches for new options added to the scope at this update were carried out from 1966 to November 2013. For more information on the electronic databases searched and criteria applied during assessment of studies for potential relevance to the review, please see the Methods section. Searching of electronic databases retrieved 75 studies. After deduplication and removal of conference abstracts, 59 records were screened for inclusion in the review. Appraisal of titles and abstracts led to the exclusion of 45 studies and the further review of 14 full publications. Of the 14 full articles evaluated, six RCTs were added at this update.

ADDITIONAL INFORMATION

In this version of the review we have only looked for effectiveness versus placebo to establish for which agents there is evidence of benefit. In the next update we will look for RCTs that compare the different active topical agents directly.

DEFINITION

Seborrhoeic dermatitis is one of the most common skin conditions. It occurs in areas of the skin with a rich supply of sebaceous glands and manifests as red, sharply marginated lesions with greasy-looking scales. The scalp is almost inevitably affected. Other areas commonly involved are the face and the chest; however, this review focuses on seborrhoeic dermatitis of the scalp. On the scalp it manifests as dry, flaking desquamation (dandruff) or yellow, greasy scaling with erythema. Dandruff is a lay term commonly used in the context of mild seborrhoeic dermatitis of the scalp. However, any scalp condition that produces scales could be labelled as dandruff. There is also an infantile variant, commonly affecting the scalp, flexures, and genital area, but this infantile variant seems to have a different pathogenesis from adult seborrhoeic dermatitis. Common differential diagnoses for seborrhoeic dermatitis of the scalp are psoriasis, eczema (see review on Atopic eczema), and tinea capitis (see table 1, p 29).

INCIDENCE/ PREVALENCE

Seborrhoeic dermatitis is estimated to affect from 3% to 10% of the general population. [1] The broad range in the prevalence depends on the age composition of the sample and the country analysed. The disease occurs more frequently in men than in women.

AETIOLOGY/ RISK FACTORS

The cause of seborrhoeic dermatitis is unknown and the disease seems to be multifactorial. *Malassezia* yeasts, a genus classified in 10 species, are considered to play an important role, especially *M globosa* and *M restricta*. They cause an inflammatory reaction that seems to be mediated by free fatty acids, released from sebaceous triglycerides by fungal enzymes such as lipases. The

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lipid layer of *Malassezia* can also modulate pro-inflammatory cytokine production by keratinocytes. Conditions that have been reported to predispose to seborrhoeic dermatitis include HIV, [2] neurological conditions such as Parkinson's disease, neuronal damage such as facial nerve palsy, [3] spinal injury, [4] ischaemic heart disease, [5] and alcoholic pancreatitis. [6] In this review, we deal with treatment in immunocompetent adults who have no known predisposing conditions.

PROGNOSIS Seborrhoeic dermatitis is a chronic condition that tends to flare and remit spontaneously, and is prone to recurrence after treatment. [1] [7]

AIMS OF INTERVENTION To reduce the symptoms and signs of seborrhoeic dermatitis with minimal adverse effects. Most therapeutic options aim to reduce colonisation with *Malassezia* yeast species and reduce inflammation, although they tend to palliate rather than cure.

OUTCOMES **Symptom severity**, including itching, scaling, and erythema; **adverse effects**.

METHODS *Clinical Evidence* search and appraisal November 2013. The following databases were used to identify studies for this systematic review: Medline 1966 to November 2013, Embase 1980 to November 2013, and The Cochrane Database of Systematic Reviews 2013, issue 11 (1966 to date of issue). Additional searches were carried out in the Database of Abstracts of Reviews of Effects (DARE) and the Health Technology Assessment (HTA) database. We also searched for retractions of studies included in the review. Titles and abstracts identified by the initial search, run by an information specialist, were first assessed against predefined criteria by an evidence scanner. Full texts for potentially relevant studies were then assessed against predefined criteria by an evidence analyst. Studies selected for inclusion were discussed with an expert contributor. All data relevant to the review were then extracted by an evidence analyst. Study design criteria for inclusion in this review were published RCTs and systematic reviews of RCTs in the English language, at least double-blinded, and containing at least 20 individuals, of whom at least 90% were followed up in trials of less than 4 weeks and 80% were followed up in trials of over 4 weeks. There was a minimum length of follow-up from start of treatment of 1 week. We excluded all studies described as 'single-blinded', 'open', 'open label', or not blinded. We included RCTs and systematic reviews of RCTs where harms of an included intervention were assessed, applying the same study design criteria for inclusion as we did for benefits. In addition, we use a regular surveillance protocol to capture harms alerts from organisations such as the FDA and the MHRA, which are added to the reviews as required. To aid readability of the numerical data in our reviews, we round many percentages to the nearest whole number. Readers should be aware of this when relating percentages to summary statistics such as relative risks (RRs) and odds ratios (ORs). We have performed a GRADE evaluation of the quality of evidence for interventions included in this review (see table, p 30). The categorisation of the quality of the evidence (high, moderate, low, or very low) reflects the quality of evidence available for our chosen outcomes in our defined populations of interest. These categorisations are not necessarily a reflection of the overall methodological quality of any individual study, because the Clinical Evidence population and outcome of choice may represent only a small subset of the total outcomes reported, and population included, in any individual trial. For further details of how we perform the GRADE evaluation and the scoring system we use, please see our website (www.clinicalevidence.com).

QUESTION What are the effects of topical treatments for seborrhoeic dermatitis of the scalp in adults?

OPTION KETOCONAZOLE SCALP PREPARATIONS VERSUS PLACEBO

- For GRADE evaluation of interventions for Seborrhoeic dermatitis of the scalp, see table, p 30 .
- In adults with seborrhoeic dermatitis of the scalp, antifungal preparations containing ketoconazole seem to improve symptoms compared with placebo.

Benefits and harms

Ketoconazole shampoo versus placebo:

We found no systematic review. We found seven RCTs. [8] [9] [10] [11] [12] [13] [14]

Symptom severity

Ketoconazole shampoo compared with placebo Ketoconazole shampoo seems more effective than placebo at improving scaling at up to 43 days and other scalp symptoms such as itching, redness, and dandruff at 4 weeks in people with seborrhoeic dermatitis of the scalp (moderate-quality evidence).

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Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Scalp scaling					
[8] RCT **Crossover design**	20 people (16 male, 4 female) with either dandruff or seborrhoeic dermatitis (no distinction made between these; proportion with seborrhoeic dermatitis not reported)	**Approximate median change in participant-rated scaling score , 4 weeks** –20 with ketoconazole (2% shampoo) +15 with placebo (shampoo base without ketoconazole) Absolute results reported graphically Scalp itching and scaling measured on a 100-mm visual analogue scale (VAS; 0 = none to 100 = 'worst ever') Median scores pre-crossover approximated from graphs	Significance not assessed		
[9] RCT	53 people with moderate to severe dandruff, 28 (53%) of whom had seborrhoeic dermatitis	**Mean change in adherent dandruff score (6 scalp areas assessed; 0 = no scaling to 10 = extremely severe scaling) , 15 days** –12 with ketoconazole (2% shampoo) –7 with placebo (shampoo base without ketoconazole)	P <0.05	○○○	ketoconazole
[9] RCT	53 people with moderate to severe dandruff, 28 (53%) of whom had seborrhoeic dermatitis	**Mean change in adherent dandruff score (6 scalp areas assessed; 0 = no scaling to 10 = extremely severe scaling) , 29 days** –19 with ketoconazole (2% shampoo) –13 with placebo (shampoo base without ketoconazole)	P <0.05	○○○	ketoconazole
[10] RCT **3-armed trial**	246 people with moderate to severe dandruff	**% reduction in mean adherent dandruff score (6 scalp areas assessed; 0 = none and 9 to 10 = severe/heavy) from baseline , 29 days** 73.0% with ketoconazole (2% shampoo) 44.5% with placebo (shampoo base without ketoconazole) Absolute numbers not reported 146 people in this analysis (97 in the ketoconazole 2% group, 49 in the placebo group) The remaining arm assessed the effects of selenium sulfide 2.5% shampoo	Significance not assessed		
[11] RCT **3-armed trial**	163 people with seborrhoeic dermatitis or dandruff	**Mean change in clinician-rated scaling score (0 = none to 4 = very severe) , 29 days** –1.2 with ketoconazole (2% shampoo) –0.3 with placebo (shampoo base without ketoconazole) 108 people in this analysis (54 in each arm)	P <0.01	○○○	ketoconazole

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Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
		The remaining arm assessed the effects of coal tar 4% plus ciclopirox olamine 1% shampoo			
[12] RCT **3-armed trial**	350 people with scalp seborrhoeic dermatitis (including people aged <16 years; see Further information on studies for details)	**Mean % change in participant-assessed scaling (scaling measured on a 100-mm VAS [0 = none to 100 = 'worst ever']) , 4 weeks** –51% with ketoconazole shampoo 2% –33% with placebo Absolute numbers not reported 200 people in this analysis (150 receiving ketoconazole, 50 receiving placebo) The remaining arm assessed ciclopirox olamine 1.5% shampoo	Significance not assessed		
[12] RCT **3-armed trial**	350 people with scalp seborrhoeic dermatitis (including people aged <16 years; see Further information on studies for details)	**Technician-assessed change in scaling (rated as cured or improved) , 4 weeks** 113/146 (77%) with ketoconazole shampoo 2% 35/49 (71%) with placebo 200 people in this analysis (150 receiving ketoconazole, 50 receiving placebo) 'Cure' defined as a value >0 at baseline and a value of 0 at day 29; 'improved' defined as a lower value at day 29 (but not 0) than at baseline (Mantel-Haenszel test for linear association) The remaining arm assessed ciclopirox olamine 1.5% shampoo	Significance not assessed		
[13] RCT **5-armed trial**	55 people with scalp seborrhoeic dermatitis	**Loose scaling , 4 weeks** with ketoconazole foaming gel 2% with vehicle shampoo (placebo) Absolute results reported graphically 22 people in this analysis The remaining 3 arms assessed clobetasol propionate shampoo 0.05% used for different durations See Further information on studies for details on differences between active treatment and placebo preparation	Reported as not significant	⟷	Not significant
[14] RCT **3-armed trial**	94 adults with seborrhoeic dermatitis (subgroup of larger cohort of 163 people with severe dandruff)	**Mean scores for scaling (assessed by technician using 5-point Likert scale (0 or 0.5 = none, 1 or 1.5 = slight, 2 or 2.5 = moderate, 3 or 3.5 = severe, 4 or 4.5 = very severe) , 43 days** with ketoconazole 2% (32 people) with vehicle (32 people) Absolute results reported graphically	P <0.01	○○○	ketoconazole

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Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
		Preparations were applied twice weekly for 4 weeks Assessments at days 8, 15, and 29 demonstrated non-significant between-group differences The remaining arm assessed ciclopirox olamine			
Scalp itching					
[8] RCT **Crossover design**	20 people (16 male, 4 female) with either dandruff or seborrhoeic dermatitis (no distinction made between these; proportion with seborrhoeic dermatitis not reported)	**Approximate median change in participant-rated itching score (measured on a 100-mm VAS [0 = none to 100 = 'worst ever']) , 4 weeks** –20 with ketoconazole (2% shampoo) +8 with placebo (shampoo base without ketoconazole) Absolute results reported graphically Median scores pre-crossover approximated from graphs	Significance not assessed		
[12] RCT	350 people with scalp dermatitis (including people aged <16 years; see Further information on studies for more details)	**Mean % change in participant-assessed itching (measured on a 100-mm VAS [0 = none to 100 = 'worst ever']) , 4 weeks** –49% with ketoconazole shampoo 2% –34% with placebo 200 people in this analysis (150 receiving ketoconazole, 50 receiving placebo) The remaining arm assessed ciclopirox olamine 1.5% shampoo	Significance not assessed		
[13] RCT **5-armed trial**	55 people with scalp seborrhoeic dermatitis	**Scalp itching , 4 weeks** with ketoconazole foaming gel 2% with vehicle shampoo (placebo) Absolute results reported graphically 22 people in this analysis The remaining 3 arms assessed clobetasol propionate shampoo 0.05% used for different durations See Further information on studies for details on differences between active treatment and placebo preparation	Reported as not significant	⟷	Not significant
[14] RCT **3-armed trial**	94 adults with seborrhoeic dermatitis (subgroup of larger cohort of 163 people with severe dandruff)	**Mean scores for itching (self-assessment using 8-point Likert scale [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]) , 43 days** with ketoconazole 2% (32 people) with vehicle (32 people)	Reported as not significant P values not reported	⟷	Not significant

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Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
		Absolute results reported graphically Preparations were applied twice weekly for 4 weeks Assessments at days 8, 15, and 29 demonstrated non-significant between-group differences The remaining arm assessed ciclopirox olamine			
Scalp redness (erythema)					
[11] RCT **3-armed trial**	163 people with seborrhoeic dermatitis or dandruff	**Mean change in clinician-rated redness score (0 = none to 4 = very severe) , 29 days** –1.3 with ketoconazole (2% shampoo) –0.5 with placebo (shampoo base without ketoconazole) 108 people in this analysis (54 in each arm) The remaining arm assessed coal tar 4% plus ciclopirox olamine 1% shampoo	P <0.001	○○○	ketoconazole
[12] RCT	350 people with scalp dermatitis (including people aged <16 years; see Further information on studies for more details)	**Technician's overall assessment of clinical changes in erythema (rated as cured, much improved, or improved) , 4 weeks** 90/146 (62%) with ketoconazole 22/49 (45%) with placebo 200 people in this assessment (150 receiving ketoconazole, 50 receiving placebo) 'Cure' defined as a value >0 at baseline and a value of 0 at day 29; 'improved' defined as a lower value at day 29 (but not 0) than at baseline (Mantel-Haenszel test for linear association) The remaining arm assessed ciclopirox olamine 1.5% shampoo	Significance not assessed		
[13] RCT **5-armed trial**	55 people with scalp seborrhoeic dermatitis	**Erythema, on a scale from 0 to 3 , 4 weeks** 0.1 with ketoconazole foaming gel 2% 0.7 with vehicle shampoo (placebo) 22 people in this analysis The remaining 3 arms assessed clobetasol propionate shampoo 0.05% used for different durations See Further information on studies for details on differences between active treatment and placebo preparation	P = 0.027	○○○	ketoconazole

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Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Global severity					
[9] RCT	53 people with moderate to severe dandruff, 28 (53%) of whom had seborrhoeic dermatitis	**Proportion of people responding to treatment (global evaluation of completely cleared, excellent, or good) , 29 days** 22/28 (79%) with ketoconazole (2% shampoo) 9/24 (38%) with placebo (shampoo base without ketoconazole)	P = 0.004	○○○	ketoconazole
[10] RCT **3-armed trial**	246 people with moderate to severe dandruff	**Proportion of people responding to treatment (global evaluation of completely cleared, excellent, or good) , 29 days** 65% with ketoconazole (2% shampoo) 29% with placebo (shampoo base without ketoconazole) Absolute numbers not reported 146 people in this analysis (97 with ketoconazole, 49 with placebo) The remaining arm assessed the effects of selenium sulfide 2.5% shampoo	P <0.001	○○○	ketoconazole
[11] RCT **3-armed trial**	163 people with seborrhoeic dermatitis or dandruff	**Area of scalp affected by seborrhoeic dermatitis , 29 days** with ketoconazole (2% shampoo) with placebo (shampoo base without ketoconazole) Absolute results not reported 108 people in this analysis (54 in each arm) The remaining arm assessed the effects of coal tar 4% plus ciclopirox olamine 1% shampoo	Reported as not significant P value not reported	⟷	Not significant
[12] RCT **3-armed trial**	350 people with scalp seborrhoeic dermatitis (including people aged <16 years; see Further information on studies for more details)	**Mean change from baseline in area of scalp seborrhoeic dermatitis (cm^2) , 4 weeks** –41.4 cm^2 with ketoconazole 2% shampoo –20.0 cm^2 with placebo 200 people in this analysis (150 receiving ketoconazole, 50 receiving placebo) The remaining arm assessed ciclopirox olamine 1.5% shampoo	Significance not assessed		
[13] RCT **5-armed trial**	55 people with scalp seborrhoeic dermatitis	**Total symptom severity, on a scale from 0 to 3 , 4 weeks** 0.7 with ketoconazole foaming gel 2% 2.6 with vehicle shampoo (placebo) Absolute results reported graphically 22 people in this analysis	P less than or equal to 0.02	○○○	ketoconazole

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Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
		The remaining 3 arms assessed clobetasol propionate shampoo 0.05% used for different durations See Further information on studies for details on differences between active treatment and placebo preparation			
[14] RCT **3-armed trial**	94 adults with seborrhoeic dermatitis (subgroup of larger cohort of 163 people with severe dandruff)	**Global evaluation of clinical change from baseline (assessed by technician using 5-point Likert scale [0 or 0.5 = none, 1 or 1.5 = slight, 2 or 2.5 = moderate, 3 or 3.5 = severe, 4 or 4.5 = very severe]) , 15 days** with ketoconazole 2% (32 people) with vehicle (32 people) Absolute results reported graphically Preparations were applied twice weekly for 4 weeks Assessment at day 8 demonstrated similar significant between-group differences The remaining arm assessed ciclopirox olamine	P <0.01	○○○	ketoconazole

Adverse effects

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Adverse effects					
[8] RCT **Crossover design**	20 people (16 male, 4 female) with either dandruff or seborrhoeic dermatitis (no distinction made between these; proportion with seborrhoeic dermatitis not reported)	**Adverse effects , 4 weeks** with ketoconazole (2% shampoo) with placebo (shampoo base without ketoconazole) Absolute results not reported The RCT reported that there were no adverse effects of treatment			
[9] RCT	53 people with moderate to severe dandruff, 28 (53%) of whom had seborrhoeic dermatitis	**Adverse effects , 29 days** with ketoconazole (2% shampoo) with placebo (shampoo base without ketoconazole) Absolute results not reported The RCT reported that there were no adverse effects of treatment			
[10] RCT **3-armed trial**	246 people with moderate to severe dandruff	**Adverse effects , 29 days** with ketoconazole (2% shampoo) with placebo (shampoo base without ketoconazole) Absolute numbers not reported The RCT reported that there were no adverse effects of treatment			

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Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
		146 people in this analysis (97 in ketoconazole arm, 49 in placebo arm) The remaining arm assessed the effects of selenium sulfide 2.5% shampoo			
[13] RCT **5-armed trial**	55 people with scalp seborrhoeic dermatitis	**Adverse effects , 4 weeks** with ketoconazole foaming gel 2% with vehicle shampoo (placebo) Absolute results not reported The RCT reported that there were no serious adverse events The remaining 3 arms assessed clobetasol propionate shampoo 0.05% used for different durations See Further information on studies for details on differences between active treatment and placebo preparation			
[14] RCT **3-armed trial**	163 people with severe dandruff	**Adverse effects , 43 days** with with ketoconazole 2% with vehicle Absolute results not reported No subgroup analysis was reported for the people with seborrhoeic dermatitis 30 adverse events reported by 24 subjects (intervention group not specified); for only 2 people (both receiving ketoconazole) was the adverse event (scalp irritation for both) considered as probably related to treatment The remaining arm assessed ciclopirox olamine			
Scalp tenderness					
[11] RCT **3-armed trial**	163 people with seborrhoeic dermatitis or dandruff	**Scalp tenderness , 29 days** with ketoconazole (2% shampoo) with placebo (shampoo base without ketoconazole) Absolute results not reported The RCT reported one instance of scalp tenderness that was probably related to ketoconazole treatment The remaining arm assessed the effects of coal tar 4% plus ciclopirox olamine 1% shampoo			
Eye stinging					
[12] RCT **3-armed trial**	350 people with scalp seborrhoeic dermatitis (including people aged <16 years; see Further information on studies for more details)	**Eye stinging , 29 days** 5/146 (3%) with ketoconazole 2% shampoo 2/49 (4%) with placebo Eye stinging was the most frequent adverse effect	Significance not assessed		

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Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
		200 people in this analysis (150 receiving ketoconazole, 50 receiving placebo) The remaining arm assessed ciclopirox olamine 1.5% shampoo (150 people)			

Further information on studies

[12] The RCT included some children aged between 12 and 16 years old, which is outside our population of interest. However, as the mean age of participants was about 43 years, the proportion of children in the trial was unlikely to be high.

[13] This five-arm RCT compared ketoconazole foaming gel 2%, clobetasol propionate shampoo 0.05% for 3 different durations, and a "clobetasol propionate vehicle" as the placebo treatment. The authors stated that, "Because of the different appearance of the shampoo and foaming gel preparations, blinding of the treatments' identity to the subjects was not possible. Blinding for investigators was maintained by using independent study personnel to dispense medication and collect returned medication". However, it is reasonable to assume that, in practice, participants were unaware of whether they were using an active treatment or the placebo.

Comment:

We found one large RCT (1162 people aged at least 12 years, mean age about 45 years) [15] that assessed the effects of ketoconazole cream 2% (210 people), ketoconazole foam 2% (427 people), vehicle cream (105 people), and vehicle foam (420 people) on seborrhoeic dermatitis of the scalp (62% of people in this RCT), face (33%), and body (5%).

The RCT did not carry out subgroup analyses for different body regions, and it included people aged under 16 years. We cannot, therefore, draw conclusions regarding our specific questions and population of interest, but have chosen to mention this RCT here as it is a large study that supports existing evidence that ketoconazole is beneficial in the treatment of seborrhoeic dermatitis of the scalp and body. The RCT found that ketoconazole foam significantly increased the proportion of people achieving treatment success (defined as Investigator's Static Global Assessment [ISGA] score of 0 or 1 [on a scale of 0–4] at week 4; people with a baseline score of 2 must have improved to a score of 0) compared with vehicle (placebo) foam (239/427 [56%] with ketoconazole foam *v* 176/420 [42%] with vehicle foam; P <0.0001), and that more people receiving ketoconazole cream achieved treatment success (56% with ketoconazole cream *v* 31% with vehicle cream; absolute numbers not reported; significance not assessed).

Clinical guide

In most of the RCTs there was a focus on dandruff instead of seborrhoeic dermatitis. Despite the fact that dandruff is a symptom of seborhoeic dermatitis, it might also include other diseases. Therefore, restrictions should be made to include only patients with seborrhoeic dermatitis in future research; that way a better evaluation of the precise effect of ketoconazole in seborrhoeic dermatitis can be achieved.

Ketoconazole 2% is the first-line treatment for seborrhoeic dermatitis of the scalp. [16] In clinical trials it has been shown to be effective for the clearance as well as the maintenance phase. The advice is to use ketoconazole twice a week during 4 weeks for clearance, followed by once every week or every other week for maintenance to prevent a relapse. The RCTs we reviewed showed mainly the results of ketoconazole shampoo 2%; more research should be performed to compare the different types of applications of ketoconazole. One advantage of topical ketoconazole is that it has not been found to have any severe side effects; in very few cases scalp irritation was reported. Moreover, it is cheaper than some of the other treatment options.

OPTION BIFONAZOLE SCALP PREPARATIONS VERSUS PLACEBO

- For GRADE evaluation of interventions for Seborrhoeic dermatitis of the scalp, see table, p 30 .

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- In adults with seborrhoeic dermatitis of the scalp, bifonazole may be more effective than placebo at treating symptoms.

Benefits and harms

Bifonazole shampoo versus placebo:

We found no systematic review. We found one RCT. [17]

Symptom severity

Bifonazole shampoo compared with placebo Bifonazole shampoo may be more effective at improving symptoms such as scaling and pruritus, and overall symptom severity at 6 weeks, in people with seborrhoea or seborrhoeic dermatitis of the scalp (low-quality evidence).

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Scalp scaling					
[17] RCT	51 people with seborrhoea or seborrhoeic dermatitis of the scalp	**Improvement in severity of scaling (graded by a clinician on a 4-point scale from 0 = none to 3 = severe) , 6 weeks** with bifonazole 1% shampoo with placebo Absolute results not reported	P = 0.01	○○○	bifonazole
Pruritus					
[17] RCT	51 people with seborrhoea or seborrhoeic dermatitis of the scalp	**Improvement in severity of pruritus (graded by a clinician on a 4-point scale from 0 = none to 3 = severe) , 6 weeks** with bifonazole 1% shampoo with placebo Absolute results not reported	P = 0.008	○○○	bifonazole
Global severity					
[17] RCT	51 people with seborrhoea or seborrhoeic dermatitis of the scalp	**Improvement in overall severity (graded by a clinician on a 4-point scale from 0 = none to 3 = severe) , 6 weeks** with bifonazole 1% shampoo with placebo Absolute results not reported	P = 0.012	○○○	bifonazole

Adverse effects

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Adverse effects					
[17] RCT	51 people with seborrhoea or seborrhoeic dermatitis of the scalp	**Adverse effects , 6 weeks** with bifonazole 1% shampoo with placebo Absolute results not reported The RCT reported "no major side effects"			

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Comment: Bifonazole shampoo is available for the treatment of seborrhoeic dermatitis of the scalp in Europe and Canada. However, it is not available in the US and, therefore, cannot be considered as a treatment option there.

Clinical guide
There is limited RCT evidence that bifonazole may be effective in the treatment of seborrhoeic dermatitis of the scalp. At the moment there is a preference for ketoconazole in clinical practice because it is a well-known treatment for seborrhoeic dermatitis. In the UK, bifonazole is not a prescription treatment for seborrhoeic dermatitis. Bifonazole is also more expensive than ketoconazole.

OPTION CICLOPIROX/CICLOPIROX OLAMINE SCALP PREPARATIONS VERSUS PLACEBO New

- For GRADE evaluation of interventions for Seborrhoeic dermatitis of the scalp, see table, p 30 .
- In adults with seborrhoeic dermatitis of the scalp, antifungal preparations containing ciclpirox seem to improve symptoms compared with placebo.
- There is some additional evidence that they may also reduce relapse up to 12 weeks after an initial treatment phase.

Benefits and harms

Ciclopirox/ciclopirox olamine versus placebo:

We found no systematic review. We found 5 RCTs. [14] [18] [19] [20] [21]

Symptom severity

Ciclopirox/ciclopirox olamine versus placebo Ciclopirox seems more effective than placebo at improving scalp symptoms such as scaling, itching, redness, and dandruff at 4 weeks in people with seborrhoeic dermatitis of the scalp, and may also reduce relapse rate up to a further 12 weeks (moderate-quality evidence).

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Total symptom severity					
[18] RCT	178 adults with moderate, stable or exacerbating seborrhoeic dermatitis of the scalp	**Mean change from baseline in sum score (erythema, scaling, pruritus, and burning assessed on a 4-point Likert scale, 0–3 of none to severe) , 4 weeks** with ciclopirox gel 0.77% with vehicle Absolute results reported graphically Preparations were applied to lesions twice daily for 28 consecutive days, with restriction from shampooing for at least 8 hours after application Significant improvement in favour of ciclopirox compared to vehicle was also observed at assessment time points day 15 (P = 0.01) and days 22 and 29 (P = 0.001) 160/178 (90%) completed the study Unclear if this analysis ITT or available case	P = 0.001	◌◌◌	ciclopirox
[19] RCT	203 adults with stable or exacerbating seborrhoeic	**Mean change from baseline in sum score (itching, scaling, and inflammation assessed on**	P = 0.6759 ciclopirox 0.1% *v* vehicle	◌◌◌	ciclopirox (1.0%)

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Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
4-armed trial	dermatitis of the scalp	**a 6-point Likert scale: 0 = none, 1 = slight, 2 = mild, 3 = moderate, 4 = pronounced, 5 = severe) , 4 weeks** –2.5 with ciclopirox 0.1% –3.2 with ciclopirox 0.3% –3.9 with ciclopirox 1.0% –2.9 with vehicle Preparations were applied twice per week for the first 4 weeks, then 2–3 times per week for a further 4 weeks	P = 0.4206 ciclopirox 0.3% *v* vehicle P = 0.0372 ciclopirox 1.0% *v* vehicle		
[20] RCT	499 people with mild to pronounced stable or exacerbating seborrhoeic dermatitis of the scalp	**Mean change from baseline in sum score (scaling, itching and erythema) , 4 weeks** –3.9 with ciclopirox 1% –2.6 with vehicle Preparations were applied twice weekly for 4 weeks Significant improvement in favour of ciclopirox compared to vehicle was observed at assessment time point week 2 (P = 0.0003; absolute values not reported)	P <0.0001		ciclopirox
Global severity					
[18] RCT	178 adults with moderate, stable or exacerbating seborrhoeic dermatitis of the scalp	**Global evaluation scores (scale of 0–5: 0 = 100% clearance, 1 = 75–<100% clearance, 2 = 50–<75% clearance, 3 = <50% clearance, 4 = no change from baseline, 5 = flare of treatment area) , up to 33 days** with ciclopirox gel 0.77% with vehicle Absolute results reported graphically	P = 0.01		ciclopirox
[20] RCT	499 people with mild to pronounced stable or exacerbating seborrhoeic dermatitis of the scalp	**Effective treatment (score = 0 [or 1 if >3 at baseline] for status, scaling, erythema, and itching) , at 4 weeks** 65/250 (26%) with ciclopirox 1% 32/249 (13%) with vehicle	OR 2.38 95% CI 1.49 to 3.80 P = 0.0001		ciclopirox
[20] RCT	499 people with mild to pronounced stable or exacerbating seborrhoeic dermatitis of the scalp	**Global evaluation 'status' of seborrhoeic dermatitis score, mean change from baseline to 4 weeks (6-point scale: 0 = none to 5 = severe)** 2.9 to 1.8 with ciclopirox 1% 2.9 to 2.3 with vehicle	Reported as not significant		Not significant
[21] RCT **3-armed trial**	942 adults with at least moderate stable or exacerbating seborrhoeic dermatitis of the scalp	**Proportion of patients effectively treated (efficacy parameters based on 6-point ordinal scales for status, scaling, and inflammation) , 4 weeks** 220/376 (58.5%) with ciclopirox 1% applied twice weekly with vehicle (190 people)	OR 3.06 95% CI 2.11 to 4.42 P <0.001		ciclopirox

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Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
		Preparations were applied for 4 weeks ITT analysis Absolute numbers for vehicle group were not reported Remaining arm assessed ciclopirox 1% applied once weekly			
[21] RCT **3-armed trial**	942 adults with at least moderate stable or exacerbating seborrhoeic dermatitis of the scalp	**Proportion of patients effectively treated (efficacy parameters based on 6-point ordinal scales for status, scaling, and inflammation) , 4 weeks** 171/376 (45.5%) with ciclopirox 1% applied once weekly with vehicle (190 people) Preparations were applied for 4 weeks ITT analysis Absolute numbers for vehicle group were not reported Remaining arm assessed ciclopirox 1% applied twice weekly	OR 1.81 95% CI 1.25 to 2.61 P <0.001 ciclopirox	●○○	ciclopirox
[21] RCT **3-armed trial**	428 adults with at least moderate stable or exacerbating seborrhoeic dermatitis of the scalp who previously responded positively to 4 weeks of ciclopirox 1% treatment (once or twice weekly)	**Relapse rate (defined as worsening of inflammation, scaling, itching by >2 points) , 12 weeks** 20/136 (14.7%) with ciclopirox 1% applied once weekly 32/145 (22.1%) with ciclopirox 1% applied twice weekly 50/141 (35.5%) with vehicle Preparations were applied for 12 weeks; see Further information on studies	P <0.001 both treatment groups combined (ciclopirox 1% once weekly and twice weekly) *v* vehicle	○○○	ciclopirox
[14] RCT **3-armed trial**	94 adults with seborrhoeic dermatitis (subgroup of larger cohort of 163 people with severe dandruff)	**Global evaluation, mean dandruff scores (reduction from baseline, assessed by technician) , 43 days** with ciclopirox olamine 1.5% (30 people) with vehicle (32 people) Absolute results reported graphically Preparations were applied twice weekly for 4 weeks Assessments at days 8, 15, and 29 demonstrated similar significant between-group differences	P <0.001	○○○	ciclopirox
Scalp itching					
[20] RCT	499 people with mild to pronounced stable or exacerbating seborrhoeic dermatitis of the scalp	**Itching, response rate (score = 0 [or 1 if >3 at baseline]) , at 4 weeks** 48% with ciclopirox 1% 30% with vehicle Absolute numbers not reported	P <0.0001	○○○	ciclopirox

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Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
[14] RCT **3-armed trial**	94 adults with seborrhoeic dermatitis (subgroup of larger cohort of 163 people with severe dandruff)	**Mean scores for itching (self-assessment using 8-point Likert scale: 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) , 43 days** with ciclopirox olamine 1.5% (30 people) with vehicle (32 people) Absolute results not reported Preparations were applied twice weekly for 4 weeks Assessments at Days 8, 15, and 29 demonstrated similar non-significant between-group differences The other arm evaluated ketoconazole 2%	No statistically significant difference was reported between ciclopirox 1.5% *v* vehicle P values not reported	⟷	Not significant
Scalp redness (erythema)					
[20]	499 people with mild to pronounced stable or exacerbating seborrhoeic dermatitis of the scalp	**Erythema, response rate (score = 0 [or 1 if >3 at baseline]) , at 4 weeks** 39% with ciclopirox 1% 21% with vehicle Absolute numbers not reported	P <0.0001	○○○	ciclopirox
Scalp scaling					
[20] RCT	499 people with mild to pronounced stable or exacerbating seborrhoeic dermatitis of the scalp	**Scaling, response rate (score = 0 [or 1 if >3 at baseline]) , at 4 weeks** 34% with ciclopirox 1% 20% with vehicle Absolute numbers not reported	P = 0.0002	○○○	ciclopirox

Adverse effects

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Adverse effects					
[20] RCT	499 people with stable or exacerbating seborrhoeic dermatitis of the scalp	**Serious adverse events , 4 weeks** 2/250 (0.8%) with ciclopirox 1% 0/249 (0%) with vehicle Preparations were applied twice weekly for 4 weeks Serious adverse events reported were myocardial infarction, angioplasty, dizziness, and heart block, all considered to be unrelated to ciclopirox treatment	Not reported		

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Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
[20] RCT	499 people with stable or exacerbating seborrhoeic dermatitis of the scalp	**Withdrawal due to adverse events** 2/250 (0.8%) with ciclopirox 1% 3/249 (1%) with vehicle Reasons for withdrawal in ciclopirox group were pruritus and dizziness. In the vehicle group it was due to worsening of seborrhoea, mild psoriasis, and gastroenteritis			
[21] RCT **3-armed trial**	942 adults with at least moderate stable or exacerbating seborrhoeic dermatitis of the scalp	**Serious adverse events** with ciclopirox 1% applied once weekly with ciclopirox 1% applied twice weekly with vehicle 3 serious adverse events were reported (shock, anxiety, and skin ulcer), but the groups that experienced these were not stated and the study reported that none of them was related to the study drug There were no serious adverse events in the subsequent 12-week prophylactic phase of the study (n = 428)			
[14] RCT **3-armed trial**	163 people with severe dandruff	**Adverse effects , 43 days** with ciclopirox with vehicle No subgroup analysis was reported for the people with seborrhoeic dermatitis 30 adverse events reported by 24 subjects (intervention group not specified); for only 2 people (both receiving ketoconazole) was the adverse event (scalp irritation for both) considered as probably related to treatment The remaining arm assessed ketoconazole			

Further information on studies

[21] The prophylaxis part of the study commenced immediately after the 4-week treatment section was completed, to assess the prophylactic efficacy of different application frequencies of ciclopirox shampoo. A total of 428 responders were again randomised (maintaining blinding) to three equal groups to use ciclopirox once every week, once every 2 weeks, or vehicle. The study was sponsored and conducted by Aventis Pharma.

Comment: The results of the available RCTs suggest that ciclopirox is effective in the treatment of seborrhoeic dermatitis of the scalp. In a single trial, ciclopirox also reduced the relapse rate in the subsequent 12 weeks after clearance when used once every week or other week. However, more research should be done to define the optimal treatment dosage of ciclopirox and to investigate the prevention of relapse. In this version of the review we have only looked for effectiveness versus placebo. In

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the next update of this review we will look for head-to-head comparisons, in particular ciclopirox versus ketoconazole, to determine the differences in treatment effect and adverse effects. While we did not search for head-to-head comparisons, we have included one three-armed RCT (163 people with severe dandruff, with a subgroup of 94 people with seborrhoeic dermatitis) comparing ciclopirox, ketoconazole, and placebo (results versus placebo reported above and in option on Ketoconazole, p 3). [14] It found no significant difference in mean dandruff scores between ciclopirox and ketoconazole on days 8, 15, or 29 (n = 108, P value not reported). However, at day 43, the mean change from baseline was significantly more with ketoconazole (41.3 to 7.2) compared with ciclopriox (40.7 to 14.6), P <0.01. For seborrhoeic dermatitis (n = 62, measured by technician assessment of scaling, redness, and area affected) there was no significant difference between ciclopirox and ketoconazole at any time point.

Clinical guide

In clinical practice, ciclopirox could be used for the treatment of seborrhoeic dermatitis of the scalp as an alternative to ketoconazole. The results of RCTs suggest that ciclopirox 1% twice a week would be a good alternative to ketoconazole for clearance and maintenance. It is not associated with severe adverse effects, aside from local irritation of the skin. The local costs of ciclopirox in comparison with ketoconazole should be considered when deciding about treatment. In the UK, ciclopirox shampoo is not presently a prescription treatment for seborrhoeic dermatitis.

OPTION PYRITHIONE ZINC SCALP PREPARATIONS VERSUS PLACEBO New

- For GRADE evaluation of interventions for Seborrhoeic dermatitis of the scalp, see table, p 30 .
- Pyrithione zinc may be more effective than vehicle shampoo at reducing mean dandruff severity at 1 week.
- However, the evidence is weak and limited to one small RCT in a mixed population of people with dandruff or mild to moderate seborrhoeic dermatitis.

Benefits and harms

Pyrithione zinc scalp preparations versus placebo:

We found one RCT comparing pyrithione zinc 0.5% and 1.0% with a vehicle shampoo for 4 weeks in people with dandruff or mild to moderate seborrhoeic dermatitis. [22]

Symptom severity

Pyrithione zinc scalp preparations versus placebo Zinc pyrithione may be more effective than vehicle shampoo at reducing mean dandruff severity at 1 week in people with mild to moderate seborrhoeic dermatitis of the scalp; however, we don't know how effective it is over longer treatment periods, and evidence is limited to one small study (very low-quality evidence).

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Total symptom severity					
[22] RCT **3-armed trial**	53 people with dandruff or mild to moderate seborrhoeic dermatitis of the scalp	**Mean dandruff severity (assessed using adherent scalp scaling score) , 1 week** 43.3 with zinc pyrithione 0.5% (18 people) 44.6 with zinc pyrithione 1.0% (20 people) 54.9 with vehicle (15 people) Preparations were applied for 4 weeks Significant improvement in favour of zinc pyrithione 0.5% compared to vehicle was observed until week 7, and up to week 10 with zinc pyrithione 1.0% compared to vehicle (P values not reported)	P <0.05 zinc pyrithione 0.5% or 1.0% *v* vehicle	○○○	zinc pyrithione

Adverse effects

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No data from the following reference on this outcome. [22]

Further information on studies

[22] The study included people with dandruff or mild to moderate seborrhoeic dermatitis. It was unclear how many of the 53 people randomised had a diagnosis of seborrhoeic dermatitis. People with severe seborrhoeic dermatitis were excluded. All participants completed a pre-randomisation phase where they were given a vehicle shampoo for 5 to 7 weeks. Only those with a Harding Scale Dandruff Severity Score greater than 28 at the end of this phase were randomised. The method of randomisation and allocation concealment were unclear. People were treated for 4 weeks and then all were given the vehicle shampoo for 6 weeks (regression phase). The study reported that the anti-dandruff efficacy of a zinc pyrithione-containing shampoo is highly dependent on the level of the active ingredient delivered to the scalp during the washing process.

Comment: There is very limited evidence available on pyrithione zinc. The results of the only available trial suggest that pyrithione zinc is effective in the treatment of seborrhoeic dermatitis by reducing dandruff. The long-term efficacy and possible adverse effects were not evaluated.

Clinical guide
Because there is only limited evidence for the use of pyrithione zinc in people with seborrhoeic dermatitis of the scalp, it should not be considered as a first-line treatment.

OPTION SELENIUM SULFIDE SCALP PREPARATIONS VERSUS PLACEBO

- For GRADE evaluation of interventions for Seborrhoeic dermatitis of the scalp, see table, p 30 .
- In adults with seborrhoeic dermatitis of the scalp, selenium sulfide may be more effective than placebo at treating symptoms.

Benefits and harms

Selenium sulfide shampoo versus placebo:
We found no systematic review. We found one RCT. [10]

Symptom severity

Selenium sulfide shampoo compared with placebo Selenium sulfide shampoo may be more effective at reducing dandruff, and at increasing response to treatment at 29 days, in people with moderate to severe dandruff (low-quality evidence).

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Scalp scaling					
[10] RCT **3-armed trial**	246 people with moderate to severe dandruff	**% reduction in mean adherent dandruff score from baseline (6 scalp areas were assessed; dandruff score ranged from 0 = none to 9–10 = severe/heavy) , 29 days** 67% with selenium sulfide 2.5% shampoo 45% with placebo (shampoo base without selenium sulfide) Absolute numbers not reported 149 people in this analysis	Reported as significant P value not reported	○○○	selenium sulfide

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Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
		The third arm assessed the effects of ketoconazole 2% shampoo Randomisation was in a 2:2:1 ratio: selenium sulfide 2.5% shampoo (100 people); ketoconazole 2.0% shampoo (97 people); and placebo (49 people)			
Global severity					
[10] RCT **3-armed trial**	246 people with moderate to severe dandruff	**Proportion of people responding to treatment (global evaluation of completely cleared, excellent, or good) , 29 days** 55% with selenium sulfide 2.5% shampoo 29% with placebo (shampoo base without selenium sulfide) Absolute numbers not reported 149 people in this analysis The third arm assessed the effects of ketoconazole 2% shampoo Randomisation was in a 2:2:1 ratio: selenium sulfide 2.5% shampoo (100 people); ketoconazole 2.0% shampoo (97 people); and placebo (49 people)	P = 0.004	○○○	selenium sulfide

Adverse effects

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Adverse effects					
[10] RCT **3-armed trial**	246 people with moderate to severe dandruff	**Adverse effects , 29 days** with selenium sulfide 2.5% shampoo with placebo (shampoo base without selenium sulfide) Absolute results not reported The RCT reported infrequent adverse events with selenium sulfide shampoo, including pruritus or burning sensation of the scalp (3 people), eruption near the hairline (1 person), psoriasis (1 person), lightening/bleaching of hair colour (2 people), orange staining of the scalp (1 person), and a chemical taste during shampooing (1 person) 149 people in this analysis The third arm assessed the effects of ketoconazole 2% shampoo Randomisation was in a 2:2:1 ratio: selenium sulfide 2.5% shampoo (100 people); ketoconazole 2.0% shampoo (97 people); and placebo (49 people)			

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Comment: None.

Clinical guide
Selenium sulfide seems to be effective in the treatment of seborrhoeic dermatitis of the scalp. However, there is limited evidence available. Selenium sulfide is associated with more side effects than ketoconazole. These are not frequent, but when they occur, burning sensations of the scalp and itching are most often reported. Therefore, selenium sulfide could not be considered as the first-choice treatment, but might be useful as an alternative when other treatments are not effective.

OPTION TAR SHAMPOO VERSUS PLACEBO

- For GRADE evaluation of interventions for Seborrhoeic dermatitis of the scalp, see table, p 30 .
- In adults with seborrhoeic dermatitis of the scalp, tar shampoo may reduce scalp dandruff and redness compared with placebo.

Benefits and harms

Tar shampoo versus placebo:

We found no systematic review. We found one RCT. [11]

Symptom severity

Tar shampoo compared with placebo Tar shampoo may be more effective than placebo at improving dandruff and redness at 29 days in people with seborrhoeic dermatitis or dandruff (low-quality evidence).

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Scalp scaling					
[11] RCT **3-armed trial**	163 people with seborrhoeic dermatitis or dandruff	**Mean change in dandruff score from baseline (assessed by a technician) , 29 days** –31 with coal tar 4% plus ciclopirox olamine 1% shampoo –19 with placebo (shampoo base without ketoconazole) 111 people in this analysis The third arm assessed the effects of ketoconazole (2% shampoo) See Further information on studies for details of calculation of dandruff score	P <0.01	○○○	tar shampoo
[11] RCT **3-armed trial**	163 people with seborrhoeic dermatitis or dandruff	**Scaling or area of seborrhoeic dermatitis , 29 days** with coal tar 4% plus ciclopirox olamine 1% shampoo with placebo (shampoo base without ketoconazole) Absolute results not reported 111 people in this analysis The third arm assessed the effects of ketoconazole (2% shampoo)	Reported as not significant	⟷	Not significant

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Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Scalp redness (erythema)					
[11] RCT **3-armed trial**	163 people with seborrhoeic dermatitis or dandruff	**Mean change in redness score (graded by a clinician on a 5-point scale from 0 = none to 4 = very severe) from baseline , 29 days** 1.2 with coal tar 4% plus ciclopirox olamine 1% shampoo 0.6 with placebo (shampoo base without ketoconazole) 111 people in this analysis The third arm assessed the effects of ketoconazole (2% shampoo)	P <0.05	○○○	tar shampoo
Global severity					
[11] RCT **3-armed trial**	163 people with seborrhoeic dermatitis or dandruff	**Area of scalp affected by seborrhoeic dermatitis , 29 days** with coal tar 4% plus ciclopirox olamine 1% shampoo with placebo (shampoo base without ketoconazole) Absolute results not reported 111 people in this analysis The third arm assessed the effects of ketoconazole (2% shampoo)	Reported as not significant P value not reported	⟷	Not significant

Adverse effects

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Adverse effects					
[11] RCT **3-armed trial**	163 people with seborrhoeic dermatitis or dandruff	**Adverse effects , 29 days** with coal tar 4% plus ciclopirox olamine 1% shampoo with placebo (shampoo base without ketoconazole) Absolute results not reported 111 people in this analysis The RCT reported no major adverse events The third arm assessed the effects of ketoconazole (2% shampoo)			

Further information on studies

[11] Dandruff score calculated by multiplying size of affected area by severity; size of affected area scored from 0 = 10% to 4 = more than 70%; severity scored from 1 = small flakes resembling a white powder to 5 = flakes adhering to the scalp as white or yellow plates.

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Comment: None.

Clinical guide
Tar shampoos are likely to be effective in seborrhoeic dermatitis of the scalp. However, they are not often used for this indication any more. Their distinct smell is unpleasant and may lead to a lack of compliance. Also, tar shampoo is associated with local skin irritation and a possible carcinogenic effect in long-term use. [23] [24] [25]

OPTION TERBINAFINE SCALP PREPARATIONS VERSUS PLACEBO

- For GRADE evaluation of interventions for Seborrhoeic dermatitis of the scalp, see table, p 30 .
- We don't know whether terbinafine is beneficial in adults with seborrhoeic dermatitis of the scalp as no studies have been found.
- We found no direct information from RCTs about whether terbinafine is better than no active treatment in adults with seborrhoeic dermatitis of the scalp.

Benefits and harms

Terbinafine versus placebo:

We found no systematic review or RCTs (see comment below).

Comment: Terbinafine is not manufactured as a scalp preparation in the UK and is not known to be available worldwide.

OPTION TOPICAL CORTICOSTEROIDS (HYDROCORTISONE, BETAMETHASONE VALERATE, CLOBETASONE BUTYRATE, MOMETASONE FUROATE, CLOBETASOL PROPIONATE) VERSUS PLACEBO

- For GRADE evaluation of interventions for Seborrhoeic dermatitis of the scalp, see table, p 30 .
- There is consensus that topical corticosteroids are effective in treating seborrhoeic dermatitis of the scalp in adults.
- We found limited evidence that clobetasol propionate 0.05% may improve some symptoms of scalp seborrhoeic dermatitis.
- We found no direct information from RCTs about whether topical corticosteroids other than clobetasol propionate shampoo 0.05% are better than no active treatment for seborrhoeic dermatitis of the scalp in adults.

Benefits and harms

Topical corticosteroids versus placebo:

We found no systematic review. We found one RCT. [13]

Symptom severity

Clobetasol propionate shampoo 0.05% compared with placebo Clobetasol propionate shampoo 0.05% applied twice weekly for 2.5, 5, or 10 minutes may be more effective at 4 weeks in improving total symptom severity scores. Clobetasol propionate shampoo 0.05% applied twice weekly for 5 minutes may be more effective at improving erythema and itching. Clobetasol propionate shampoo 0.05% applied twice weekly for 10 minutes may be more effective at improving scaling. We don't know whether clobetasol propionate used for other durations is more effective at improving symptoms (very low-quality evidence).

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Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Total symptom severity					
[13] RCT **5-armed trial**	55 people with scalp seborrhoeic dermatitis	**Total symptom severity on a scale of 0 to 3 (0 = no symptoms, 3 = most severe) , 4 weeks** 0.8 with clobetasol propionate shampoo 0.05% used for 2.5 minutes 2.6 with vehicle shampoo (placebo) 22 people in this analysis The remaining arms assessed clobetasol propionate 0.05% shampoo for 5 and 10 minutes, and ketoconazole 2.00% foaming gel	P less than or equal to 0.02	○○○	clobetasol propionate
[13] RCT **5-armed trial**	55 people with scalp seborrhoeic dermatitis	**Total symptom severity, on a scale of 0 to 3 (0 = no symptoms, 3 = most severe) , 4 weeks** 0.6 with clobetasol propionate shampoo 0.05% used for 5 minutes 2.6 with vehicle shampoo (placebo) 22 people in this analysis The remaining arms assessed clobetasol propionate 0.05% shampoo for 2.5 and 10 minutes, and ketoconazole 2.00% foaming gel	P less than or equal to 0.02	○○○	clobetasol propionate
[13] RCT **5-armed trial**	55 people with scalp seborrhoeic dermatitis	**Total symptom severity, on a scale of 0 to 3 (0 = no symptoms, 3 = most severe) , 4 weeks** 0.7 with clobetasol propionate shampoo 0.05% used for 10 minutes 2.6 with vehicle shampoo (placebo) 22 people in this analysis The remaining arms assessed clobetasol propionate 0.05% shampoo for 2.5 and 5 minutes, and ketoconazole 2.00% foaming gel	P less than or equal to 0.02	○○○	clobetasol propionate
Scalp scaling					
[13] RCT **5-armed trial**	55 people with scalp seborrhoeic dermatitis	**Loose scaling, on a scale from 0 to 3 (0 = clear, 3 = worst) , 4 weeks** with clobetasol propionate shampoo 0.05% for 2.5 minutes with vehicle shampoo (placebo) Absolute results not reported 22 people in this analysis The remaining arms assessed clobetasol propionate 0.05% shampoo for 5 and 10 minutes, and ketoconazole 2.00% foaming gel	Reported as not significant	⟷	Not significant

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Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
[13] RCT **5-armed trial**	55 people with scalp seborrhoeic dermatitis	**Loose scaling, on a scale from 0 to 3 (0 = clear, 3 = worst) , 4 weeks** 0.4 with clobetasol propionate shampoo 0.05% for 5 minutes 1.0 with vehicle shampoo (placebo) 22 people in this analysis The remaining arms assessed clobetasol propionate 0.05% shampoo for 2.5 and 10 minutes, and ketoconazole 2.00% foaming gel	P = 0.051	⟷	Not significant
[13] RCT **5-armed trial**	55 people with scalp seborrhoeic dermatitis	**Loose scaling, on a scale from 0 to 3 (0 = clear, 3 = worst) , 4 weeks** 0.3 with clobetasol propionate shampoo 0.05% for 10 minutes 1.0 with vehicle shampoo (placebo) 22 people in this analysis The remaining arms assessed clobetasol propionate 0.05% shampoo for 2.5 and 5 minutes, and ketoconazole 2.00% foaming gel	P = 0.027	○○○	clobetasol propionate
Scalp redness (erythema)					
[13] RCT **5-armed trial**	55 people with scalp seborrhoeic dermatitis	**Erythema, on a scale of 0 to 3 (0 = clear, 3 = worst) , 4 weeks** with clobetasol propionate shampoo 0.05% for 2.5 minutes with vehicle shampoo (placebo) Absolute numbers not reported 22 people in this analysis The remaining arms assessed clobetasol propionate 0.05% shampoo for 5 and 10 minutes, and ketoconazole 2.00% foaming gel	Reported as not significant	⟷	Not significant
[13] RCT **5-armed trial**	55 people with scalp seborrhoeic dermatitis	**Erythema, on a scale of 0 to 3 (0 = clear, 3 = worst) , 4 weeks** 0.1 with clobetasol propionate shampoo 0.05% for 5 minutes 0.7 with vehicle shampoo (placebo) 22 people in this analysis The remaining arms assessed clobetasol propionate 0.05% shampoo for 2.5 and 10 minutes, and ketoconazole 2.00% foaming gel	P = 0.024	○○○	clobetasol propionate
[13] RCT **Crossover design** **5-armed trial**	55 people with scalp seborrhoeic dermatitis	**Erythema, on a scale of 0 to 3 (0 = clear, 3 = worst) , 4 weeks** with clobetasol propionate shampoo 0.05% for 10 minutes with vehicle shampoo (placebo) Absolute results not reported	Reported as not significant	⟷	Not significant

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Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
		22 people in this analysis The remaining arms assessed clobetasol propionate 0.05% shampoo for 2.5 and 5 minutes, and ketoconazole 2.00% foaming gel			
Scalp itching					
[13] RCT **5-armed trial**	55 people with scalp seborrhoeic dermatitis	**Itching, measured on a 100-mm analogue scale (0 = no itching, 100 = worst) , 4 weeks** with clobetasol propionate shampoo 0.05% for 2.5 minutes with vehicle shampoo (placebo) Absolute results not reported 22 people in this analysis The remaining arms assessed clobetasol propionate 0.05% shampoo for 5 and 10 minutes, and ketoconazole 2.00% foaming gel	Reported as not significant	⟷	Not significant
[13] RCT **5-armed trial**	55 people with scalp seborrhoeic dermatitis	**Itching, measured on a 100-mm analogue scale (0 = no itching, 100 = worst) , 4 weeks** 4.8 mm with clobetasol propionate shampoo 0.05% for 5 minutes 34.0 mm with vehicle shampoo (placebo) 22 people in this analysis The remaining arms assessed clobetasol propionate 0.05% shampoo for 2.5 and 10 minutes, and ketoconazole 2.00% foaming gel	P = 0.007		
[13] RCT **5-armed trial**	55 people with scalp seborrhoeic dermatitis	**Itching, measured on a 100-mm analogue scale (0 = no itching, 100 = worst) , 4 weeks** with clobetasol propionate shampoo 0.05% for 10 minutes with vehicle shampoo (placebo) Absolute results not reported 22 people in this analysis The remaining arms assessed clobetasol propionate 0.05% shampoo for 2.5 and 5 minutes, and ketoconazole 2.00% foaming gel	Reported as not significant	⟷	Not significant

Adverse effects

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Folliculitis					
[13] RCT	55 people with seborrhoeic dermatitis of the scalp	**Folliculitis , 4 weeks**	Significance not assessed		

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Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
5-armed trial		1/11 with clobetasol propionate 0.05% shampoo for 5 minutes 0/11 with clobetasol propionate vehicle (placebo) The remaining arms assessed clobetasol propionate 0.05% shampoo for 2.5 and 10 minutes, and ketoconazole 2.00% foaming gel			
Dry skin					
[13] RCT **5-armed trial**	55 people with seborrhoeic dermatitis of the scalp	**Dry skin , 4 weeks** 1/11 with clobetasol propionate 0.05% shampoo for 10 minutes 0/11 with vehicle shampoo (placebo) The remaining arms assessed clobetasol propionate 0.05% shampoo for 2.5 and 5 minutes, and ketoconazole 2.00% foaming gel	Significance not assessed		

Comment: Although limited evidence is available from a single small RCT concerning clobetasol propionate shampoo 0.05%, there is consensus that topical corticosteroids are effective in treating seborrhoeic dermatitis of the scalp in adults.

Clinical guide
In clinical practice, topical corticosteroids are considered as a suitable treatment option in the clearance phase to reduce the acute state of seborrhoeic dermatitis of the scalp. However, they are not recommended as maintenance therapy because of their known adverse effects such as skin atrophy, striae, hypertrichosis, and folliculitis with long-term use.

GLOSSARY

Low-quality evidence Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.

Moderate-quality evidence Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.

Very low-quality evidence Any estimate of effect is very uncertain.

SUBSTANTIVE CHANGES

Ciclopirox/ciclopirox olamine scalp preparations versus placebo New option. Five RCTs added. [14] [18] [19] [20] [21] Categorised as 'beneficial'.

Pyrithione zinc scalp preparations versus placebo New option. One RCT added. [22] Categorised as 'unknown effectiveness'.

Ketoconazole scalp preparations versus placebo One RCT added. [14] Categorisation unchanged (beneficial).

Tar shampoo versus placebo Existing evidence re-evaluated. Categorisation unchanged (likely to be beneficial).

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Competing interests: LN has received fees for speaking from Johnson & Johnson and Wyeth and fees for consultancy from Johnson & Johnson and IBSA. JD declares that she has no competing interests.

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TABLE 1 **Differential diagnoses for seborrhoeic dermatitis of the scalp (see text).**

Diagnosis	Distinguishing features
Psoriasis	Prominent erythema Tendency for hair line involvement More prominent silver scale Presence of psoriasis elsewhere (skin, nails, joints)
Eczema (atopic and contact dermatitis)	Atopic dermatitis: • General skin examination • History Contact dermatitis: • Distribution of eczema • History
Tinea capitis	Microscopy Fungal culture of scalp scrapings

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GRADE **Evaluation of interventions for Seborrhoeic dermatitis of the scalp.**

Important outcomes					Symptom severity				
Studies (Participants)	Outcome	Comparison	Type of evidence	Quality	Consistency	Directness	Effect size	GRADE	Comment
What are the effects of topical treatments for seborrhoeic dermatitis of the scalp in adults?									
7 (851) [8] [9] [10] [11] [12] [13] [14]	Symptom severity	Ketoconazole shampoo versus placebo	4	–1	0	0	0	Moderate	Quality point deducted for incomplete reporting of results and methodological issues
1 (51) [17]	Symptom severity	Bifonazole shampoo versus placebo	4	–2	0	0	0	Low	Quality points deducted for sparse data and incomplete reporting of results
5 (at least 1706) [18] [19] [20] [21] [14]	Symptom severity	Ciclopirox/ciclopirox olamine versus placebo	4	–1	0	0	0	Moderate	Quality point deducted for incomplete reporting of results and methodological issues
1 (53) [22]	Symptom severity	Pyrithione zinc scalp preparations versus placebo	4	–2	0	–1	0	Very low	Quality points deducted for sparse data and weak methods; directness point deducted for mixed population of dandruff and mild to moderate seborrhoeic dermatitis
1 (149) [10]	Symptom severity	Selenium sulfide shampoo versus placebo	4	–2	0	0	0	Low	Quality points deducted for sparse data and incomplete reporting of results
1 (111) [11]	Symptom severity	Tar shampoo versus placebo	4	–2	0	0	0	Low	Quality points deducted for sparse data and incomplete reporting of results
1 (55) [13]	Symptom severity	Topical corticosteroids versus placebo	4	–3	–1	0	0	Very low	Quality points deducted for sparse data, incomplete blinding, and unclear randomisation methods; consistency point deducted for different results at different time points

We initially allocate 4 points to evidence from RCTs, and 2 points to evidence from observational studies. To attain the final GRADE score for a given comparison, points are deducted or added from this initial score based on preset criteria relating to the categories of quality, directness, consistency, and effect size. Quality: based on issues affecting methodological rigour (e.g., incomplete reporting of results, quasi-randomisation, sparse data [<200 people in the analysis]). Consistency: based on similarity of results across studies. Directness: based on generalisability of population or outcomes. Effect size: based on magnitude of effect as measured by statistics such as relative risk, odds ratio, or hazard ratio.

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