ClinicalEvidence

Athlete's foot

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ABSTRACT

INTRODUCTION: Around 15% to 25% of people are likely to have athlete's foot at any one time. The infection can spread to other parts of the body and to other people. METHODS AND OUTCOMES: We conducted a systematic review and aimed to answer the following clinical question: What are the effects of topical treatments for athlete's foot? We searched: Medline, Embase, The Cochrane Library, and other important databases up to July 2008 (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 systematic reviews, RCTs, or observational 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: improved foot hygiene, including socks and hosiery; topical allylamines (naftifine and terbinafine); topical azoles (bifonazole, clotrimazole, econazole nitrate, miconazole nitrate, sulconazole nitrate, and tioconazole); and topical ciclopirox olamine.

QUESTIONS

INTERVENTIONS

ATHLETE'S FOOT: TOPICAL AGENTS

Beneficial

Unknown effectiveness

To be covered in future updates

Oral allylamines
Oral azoles
Oral versus topical treatments
Topical griseofulvin
Topical tolnaftate
Topical undecanoic acid

Key points

- Fungal infection of the feet can cause white and soggy skin between the toes, dry and flaky soles, or reddening and blistering of the skin all over the foot.

  Around 15% to 25% of people are likely to have athlete's foot at any one time.

  The infection can spread to other parts of the body and to other people.
- Topical allylamines (naftifine and terbinafine), topical azoles (clotrimazole, miconazole nitrate, tioconazole, sulconazole nitrate, bifonazole, and econazole nitrate) and topical ciclopirox olamine are all more likely to cure fungal skin infections compared with placebo.

  Topical allylamines seem to have fewer treatment failures compared with topical azoles.

  We don't know if any one treatment is more effective than others.
- We don't know whether improving foot hygiene or changing footwear can help to cure athlete's foot.

DEFINITION

Athlete's foot is a cutaneous fungal infection caused by dermatophyte infection. It is characterised by itching, flaking, and fissuring of the skin. It may manifest in three ways: the skin between the toes may appear macerated (white) and soggy; the soles of the feet may become dry and scaly; and the skin all over the foot may become red, and vesicular eruptions may appear. [1] It is conventional in dermatology to refer to fungal skin infections as superficial in order to distinguish them from systemic fungal infections.

INCIDENCE/ PREVALENCE

Epidemiological studies have produced various estimates of the prevalence of athlete's foot. Studies are usually conducted in populations of people who attend dermatology clinics, sports centres, or swimming pools, or who are in the military. UK estimates suggest that athlete's foot is present in about 15% of the general population. [2] Studies conducted in dermatology clinics found prevalences of 25% in Italy (722 people) [3] and 27% in China (1014 people). [4] A population-based study conducted in 1148 children in Israel found the prevalence among children to be 30%. [5]

AETIOLOGY/ RISK FACTORS Swimming-pool users and industrial workers may be at increased risk of fungal foot infection. However, one survey identified fungal foot infection in only 9% of swimmers, with the highest prevalence (20%) being in men aged 16 years and older. [2]

PROGNOSIS Fungal infections of the foot are not life-threatening in people with normal immune status, but in some people they cause persistent itching and, ultimately, fissuring. Some people are apparently unaware of persistent infection. The infection can spread to other parts of the body and to other individuals.

AIMS OF INTERVENTION To control symptoms and prevent recurrence, with minimal adverse effects.

OUTCOMES **Mycological cure rates:** Rates of fungal eradication, shown by negative microscopy and culture, and resolution of clinical signs and symptoms at follow-up. We have chosen mycological cure as a primary outcome. This is because clinical cure is not reported consistently in superficial mycology trials. [6] The main systematic review identified by *Clinical Evidence* has expressed the outcome in terms of treatment failure rates. [7] Microscopy and culture results are the most frequently used efficacy outcomes in athlete's foot research. However, like many other diagnostic tests, microscopy and culture are not absolutely accurate. [8]

METHODS *Clinical Evidence* search and appraisal July 2008. The following databases were used to identify studies for this systematic review: Medline 1966 to July 2008, Embase 1980 to July 2008, and The Cochrane Database of Systematic Reviews and Cochrane Central Register of Controlled Clinical Trials 2008, Issue 2 (1966 to date of issue). An additional search was carried out of the NHS Centre for Reviews and Dissemination (CRD) — for Database of Abstracts of Reviews of Effects (DARE) and Health Technology Assessment (HTA). We also searched for retractions of studies included in the review. Abstracts of the studies retrieved from the initial search were assessed by an information specialist. Selected studies were then sent to the contributor for additional assessment, using pre-determined criteria to identify relevant studies. Study design criteria for inclusion in this review were: published systematic reviews and RCTs in any language, at least single blinded, and containing more than 20 individuals. Trials with any loss to follow-up were sent and there was no minimum length of follow-up required to include studies. We excluded all studies described as “open”, “open label”, or not blinded unless blinding was impossible. Where potentially relevant non-English language references were identified by searches, these have been translated and appraised for inclusion. Studies were not excluded based on high withdrawal rates, as this is a common problem for studies of athlete's foot. We included systematic reviews of RCTs, and RCTs where harms of an included intervention were studied 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 UK Medicines and Healthcare products Regulatory Agency (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 14). 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 athlete's foot?

OPTION NAFTIFINE, TERBINAFINE (TOPICAL ALLYLAMINES)

- For GRADE evaluation of interventions for Athlete's foot, see table, p 14 .
- Topical allylamines (naftifine and terbinafine) are all more likely to cure fungal skin infections compared with placebo.
- Topical allylamines seem to have fewer treatment failures compared with topical azoles, p 6 .
- We found no clinically important results from RCTs about topical allylamines compared with topical ciclopirox olamine in people with athlete's foot.

Benefits and harms

Topical allylamines versus placebo:

We found one systematic review (search date 2005) [7] and two subsequent RCTs [9] [10] assessing the effects of topical allylamines in athlete's foot.

Mycological cure rates

Topical allylamines compared with placebo Topical allylamines used for between 1 and 4 weeks are more effective at curing athlete's foot (defined as negative results on microscopy and no growth of dermatophytes in culture) at 2 to 6 weeks (moderate-quality evidence).

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Treatment failure rates					
[7] Systematic review	928 people Nine RCTs in this analysis	**Treatment failure rates , 2 weeks** 262/476 (55%) with allylamines 355/452 (79%) with placebo	RR 0.69 95% CI 0.56 to 0.87	●○○	allylamines
[7] Systematic review	1116 people 11 RCTs in this analysis	**Treatment failure rates , 6 weeks** 144/566 (25%) with allylamines 443/550 (81%) with placebo	RR 0.33 95% CI 0.24 to 0.44	●●○	allylamines
[7] Systematic review	612 people Five RCTs in this analysis	**Treatment failure rates , 2 weeks** 191/314 (61%) with naftifine 243/298 (82%) with placebo	RR 0.75 95% CI 0.60 to 0.93	●○○	naftifine
[7] Systematic review	607 people Five RCTs in this analysis	**Treatment failure rates , 6 weeks** 94/309 (30%) with naftifine 245/298 (82%) with placebo	RR 0.42 95% CI 0.30 to 0.59	●●○	naftifine
[7] Systematic review	316 people Four RCTs in this analysis	**Treatment failure rates , 2 weeks** 71/162 (44%) with terbinafine 112/154 (73%) with placebo	RR 0.58 95% CI 0.31 to 1.08	⟷	Not significant
[7] Systematic review	40 people Two RCTs in this analysis	**Treatment failure rates , 6 weeks** 2/18 (11%) with terbinafine 21/22 (95%) with placebo	RR 0.17 95% CI 0.05 to 0.57	●●●	terbinafine
[9] RCT	324 people with interdigital tinea pedis	**Treatment failure rates** 120/190 (63%) with terbinafine 14/83 (17%) with placebo Intention-to-treat analysis	P <0.0001	○○○	terbinafine
Mycological cure rates					
[10] RCT **3-armed trial**	84 people	**Mycological cure rates** 5/29 (17%) with terbinafine 1% 4/28 (14%) with terbinafine 3% 3/27 (12%) with placebo	Significance assessment between groups not reported		
[10] RCT	84 people	**Mycological cure rates , 4 weeks** 18/29 (69%) with terbinafine 1% 4/27 (16%) with placebo	P <0.0001	○○○	terbinafine

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
[10] RCT	84 people	**Mycological cure rates , 4 weeks** 18/28 (72%) with terbinafine 3% 4/27 (16%) with placebo	P <0.0001	○○○	terbinafine
[10] RCT	84 people	**Mycological cure rates , 6 weeks** 25/29 (86%) with terbinafine 1% 3/27 (11%) with placebo	P <0.0001	○○○	terbinafine
[10] RCT	84 people	**Mycological cure rates , 6 weeks** 9/28 (68%) with terbinafine 3% 3/27 (11%) with placebo	P <0.0001	○○○	terbinafine

Adverse effects

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Adverse effects					
[7] Systematic review	Unclear	**Serious adverse effects** with allylamines with placebo Absolute results not reported	Two RCTs included in the review reported an increase in liver enzymes with terbinafine cream 1% and with placebo, and one RCT reported neutropenia with placebo (results not reported). The adverse effects reported by RCTs in the review included burning, stinging, and itching sensations (further details not reported)		
[9] RCT	324 people with interdigital tinea pedis	**Adverse effects** with terbinafine with placebo Absolute results not reported	The RCT found no serious adverse effects associated with terbinafine 1% solution. Adverse effects reported included mild burning, moderate peripheral oedema, mild pain, and pruritus (further details not reported)		
[10] RCT	84 people	**Adverse effects** with terbinafine 1% or 3% with placebo	The RCT found no serious adverse effects associated with terbinafine 1% and 3% emulsion gel. Adverse effects reported included burning and stinging sensations, mild desquamation, erythema, and incrustation dryness (further details not reported)		

Topical allylamines versus each other:

The review identified one RCT (62 people) comparing naftifine versus terbinafine. [7] The review found no significant difference in treatment failure between naftifine and terbinafine at 2 and 6 weeks.

Mycological cure rates

Naftifine and terbinafine compared with each other Naftifine and terbinafine seem to be equally effective at curing athlete's foot (defined as negative results on microscopy and no growth of dermatophytes in culture) at 2 to 6 weeks (moderate-quality evidence).

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Treatment failure rates					
[7] Systematic review	62 people One RCT in this analysis	**Treatment failure rates , 2 weeks** 19/29 (66%) with naftifine 22/33 (67%) with terbinafine	RR 0.98 95% CI 0.69 to 1.41	⟷	Not significant
[7] Systematic review	62 people One RCT in this analysis	**Treatment failure rates , 6 weeks** 9/29 (31%) with naftifine 5/33 (15%) with terbinafine	RR 2.05 95% CI 0.77 to 5.42	⟷	Not significant

Adverse effects

No data from the following reference on this outcome. [7]

Topical allylamines versus topical azoles:

The review assessed treatment failure for short-term, medium-term, and long-term outcomes. [7]

Mycological cure rates

Topical allylamines compared with topical azoles Topical allylamines and topical azoles seem equally effective at curing athlete's foot (defined as negative results on microscopy and no growth of dermatophytes in culture) (moderate-quality evidence).

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Treatment failure rates					
[7] Systematic review	1519 people 10 RCTs in this analysis	**Treatment failure rates , 2 weeks** 272/809 (34%) with allylamines 243/710 (34%) with azoles	RR 0.86 95% CI 0.70 to 1.06	⟷	Not significant
[7] Systematic review	173 people Two RCTs in this analysis	**Treatment failure rates , 6 weeks** 21/102 (21%) with allylamines 40/71 (56%) with azoles	RR 0.34 95% CI 0.22 to 0.52	●●○	allylamines
[7] Systematic review	83 people One RCT in this analysis	**Treatment failure rates , 6 weeks** 7/40 (18%) with terbinafine 21/43 (49%) with clotrimazole	RR 0.36 95% CI 0.17 to 0.75	●●○	terbinafine
[7] Systematic review	962 people Five RCTs in this analysis	**Treatment failure rates , 6 weeks** 26/488 (5%) with allylamines 38/474 (8%) with azoles	RR 0.75 95% CI 0.33 to 1.72	⟷	Not significant
[7] Systematic review	1003 people Nine RCTs in this analysis	**Treatment failure rates , 6 weeks** 102/533 (19%) with allylamines 155/470 (33%) with azoles	RR 0.63 95% CI 0.42 to 0.94	●○○	allylamines

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
[7] Systematic review	141 people Two RCTs in this analysis	**Treatment failure rates , 12 weeks or above** 8/75 (11%) with allylamines 16/66 (24%) with azoles	RR 0.47 95% CI 0.22 to 1.02	⟷	Not significant

Adverse effects

No data from the following reference on this outcome. [7]

Topical allylamines versus topical ciclopirox:
We found no RCTs.

Further information on studies

[7] The review reported that there was significant statistical heterogeneity among RCTs included in the meta-analyses of all interventions at all time points (review set statistical heterogeneity as significant if P <0.05). The clinical heterogeneity among the RCTs included in the meta-analysis in language, healthcare systems, dosage, duration of treatment, and study quality may have led to the significant statistical heterogeneity reported by the review. [7]

[7] The systematic review included men and women of any age with a fungal infection of the skin of the foot identified by microscopy and growth of dermatophytes in culture. It calculated treatment failure rates from reported mycological results. Treatment success was defined as negative results on microscopy and no growth of dermatophytes in culture. The review excluded RCTs that did not subject skin samples to potassium hydroxide and culture. It reported outcomes at three different time points: short (2 weeks), medium (6 weeks), and long term (12 weeks or above).

Comment: None.

OPTION AZOLES (TOPICAL)

- For GRADE evaluation of interventions for Athlete's foot, see table, p 14 .
- Topical azoles (clotrimazole, miconazole nitrate, tioconazole, sulconazole nitrate, bifonazole, and econazole nitrate) are all more likely to cure fungal skin infections compared with placebo.

Benefits and harms

Topical azoles versus placebo:
We found one systematic review (search date 2005), [7] assessing the effects of topical azoles in athlete's foot.

Mycological cure rates

Topical azole creams compared with placebo Topical azole creams used for 4 to 6 weeks are more effective at curing athlete's foot (defined as negative results on microscopy and no growth of dermatophytes in culture) at 2 and 6 weeks (moderate-quality evidence).

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Treatment failure rates					
[7] Systematic review	329 people Five RCTs in this analysis	**Treatment failure rates , 2 weeks** 88/195 (45%) with azoles 95/134 (71%) with placebo	RR 0.59 95% CI 0.43 to 0.82	●○○	azoles
[7] Systematic review	1235 people 13 RCTs in this analysis	**Treatment failure rates , 6 weeks** 174/695 (25%) with azoles 349/540 (65%) with placebo	RR 0.40 95% CI 0.35 to 0.46	●●○	azoles
[7] Systematic review	176 people Four RCTs in this analysis	**Treatment failure rates , 4 to 6 weeks** 31/90 (34%) with bifonazole 62/86 (72%) with placebo Short-term follow-up (2 weeks)	RR 0.52 95% CI 0.37 to 0.73	●○○	bifonazole
[7] Systematic review	153 people One RCT in this analysis	**Treatment failure rates , 4 to 6 weeks** 57/105 (54%) with oxiconazole 33/48 (69%) with placebo Short-term follow-up (2 weeks)	RR 0.79 95% CI 0.61 to 1.02	⟷	Not significant
[7] Systematic review	182 people Four RCTs in this analysis	**Treatment failure rates , 4 to 6 weeks** 20/94 (21%) with bifonazole 55/88 (63%) with placebo Medium-term follow-up (6 weeks)	RR 0.36 95% CI 0.20 to 0.67	●●○	bifonazole
[7] Systematic review	371 people Three RCTs in this analysis	**Treatment failure rates , 4 to 6 weeks** 42/182 (23%) with clotrimazole 108/189 (57%) with placebo Medium-term follow-up (6 weeks)	RR 0.42 95% CI 0.27 to 0.64	●●○	clotrimazole
[7] Systematic review	54 people Two RCTs in this analysis	**Treatment failure rates , 4 to 6 weeks** 7/24 (29%) with miconazole 23/30 (77%) with placebo Medium-term follow-up (6 weeks)	RR 0.41 95% CI 0.14 to 1.14	⟷	Not significant
[7] Systematic review	451 people Two RCTs in this analysis	**Treatment failure rates , 4-6 weeks** 78/311 (25%) with oxiconazole 95/140 (68%) with placebo Medium-term follow-up (6 weeks)	RR 0.37 95% CI 0.30 to 0.46	●●○	oxiconazole
[7] Systematic review	58 people One RCT in this analysis	**Treatment failure rates , 4 to 6 weeks** 17/54 (31%) with sulconazole 41/63 (65%) with placebo Medium-term follow-up (6 weeks)	RR 0.48 95% CI 0.31 to 0.75	●●○	sulconazole
[7] Systematic review	60 people One RCT in this analysis	**Treatment failure rates , 4 to 6 weeks** 10/30 (33%) with tioconazole	RR 0.37 95% CI 0.22 to 0.62	●●○	tioconazole

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
		27/30 (90%) with placebo Medium-term follow-up (6 weeks)			

Adverse effects

No data from the following reference on this outcome. [7]

Topical azoles versus each other:

The review identified nine RCTs (1287 people) comparing different azoles versus each other and reported short-term (2 weeks) and medium-term (6 weeks) outcomes. [7]

Mycological cure rates

Topical azoles compared with each other Bifonazole, clotrimazole, econazole, miconazole, tioconazole, and sulconazole seem equally effective at curing athlete's foot (defined as negative results on microscopy and no growth of dermatophytes in culture) at 2 and 6 weeks (moderate-quality evidence).

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Treatment failure rates					
[7] Systematic review	497 people Two RCTs in this analysis	**Treatment failure rates , 2 weeks (short term)** 73/176 (41%) with clotrimazole 103/321 (32%) with econazole	RR 1.13 95% CI 0.92 to 1.39	⟷	Not significant
[7] Systematic review	41 people One RCT in this analysis	**Treatment failure rates , 2 weeks (short term)** 6/20 (30%) with miconazole 1/21 (5%) with sulconazole	RR 6.30 95% CI 0.83 to 47.80 The wide CI suggests that the RCT was likely to have been underpowered to detect a clinically important difference between groups	⟷	Not significant
[7] Systematic review	105 people One RCT in this analysis	**Treatment failure rates , 6 weeks** 0/17 (0%) with bifonazole 0/19 (0%) with croconazole	RR not estimable		
[7] Systematic review	264 people One RCT in this analysis	**Treatment failure rates , 6 weeks** 23/131 (18%) with bifonazole 111/133 (83%) with flutrimazole	RR 0.21 95% CI 0.14 to 0.31	●●○	bifonazole
[7] Systematic review	28 people One RCT in this analysis	**Treatment failure rates , 6 weeks** 4/14 (29%) with bifonazole 5/14 (36%) with miconazole	RR 0.80 95% CI 0.27 to 2.37	⟷	Not significant
[7] Systematic review	497 people Two RCTs in this analysis	**Treatment failure rates , 6 weeks** 64/176 (36%) with clotrimazole 85/321 (26%) with econazole	RR 0.95 95% CI 0.31 to 2.88	⟷	Not significant

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
[7] Systematic review	100 people One RCT in this analysis	**Treatment failure rates , 6 weeks** 19/50 (38%) with clotrimazole 18/50 (36%) with ketoconazole	RR 1.06 95% CI 0.63 to 1.76	⟷	Not significant
[7] Systematic review	220 people One RCT in this analysis	**Treatment failure rates , 6 weeks** 21/57 (37%) with miconazole 18/63 (29%) with tioconazole	RR 1.29 95% CI 0.77 to 2.16	⟷	Not significant

Adverse effects

No data from the following reference on this outcome. [7]

Topical azoles versus topical allylamines:

See options on topical allylamines, p 2 .

Adverse effects

No data from the following reference on this outcome. [7]

Topical azoles versus ciclopirox olamine:

The systematic review identified one RCT. [7]

Mycological cure rates

Clotrimazole compared with ciclopirox olamine Clotrimazole and ciclopirox olamine seem equally effective at curing athlete's foot (defined as negative results on microscopy and no growth of dermatophytes in culture) at 2 weeks and 4 to 6 weeks (moderate-quality evidence).

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Treatment failure rates					
[7] Systematic review	87 people One RCT in this analysis	**Treatment failure rates , 2 weeks** 13/44 (30%) with clotrimazole 9/43 (21%) with ciclopirox olamine	RR 1.41 95% CI 0.67 to 2.95	⟷	Not significant
[7] Systematic review	87 people One RCT in this analysis	**Treatment failure rates , 4 weeks** 7/44 (16%) with clotrimazole 4/43 (9%) with ciclopirox olamine	RR 1.71 95% CI 0.54 to 5.42	⟷	Not significant
[7] Systematic review	87 people One RCT in this analysis	**Treatment failure rates , 6 weeks** 8/37 (22%) with clotrimazole	RR 1.78 95% CI 0.59 to 5.38	⟷	Not significant

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
		4/33 (12%) with ciclopirox olamine			

Adverse effects

No data from the following reference on this outcome. [7]

Further information on studies

Comment: None.

OPTION CICLOPIROX OLAMINE (TOPICAL)

- For GRADE evaluation of interventions for Athlete's foot, see table, p 14 .
- Topical ciclopirox olamine is more likely to cure fungal skin infections compared with placebo.
- We found no clinically important results from RCTs about ciclopirox olamine compared with topical allylamines in people with athlete's foot.

Benefits and harms

Topical ciclopirox olamine versus placebo:

We found one systematic review (search date 2005; 2 RCTs, 485 people), [7] and one additional RCT [11] comparing ciclopirox olamine versus placebo.

Mycological cure rates

Compared with placebo Topical ciclopirox olamine (0.77% or 1%) is more effective at curing athlete's foot (defined as negative results on microscopy and no growth of dermatophytes in culture) at 2 and 6 weeks (moderate-quality evidence).

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Treatment failure rates					
[7] Systematic review	168 people One RCT in this analysis	**Treatment failure rates , 2 weeks** 18/85 (21%) with ciclopirox olamine 41/83 (49%) with placebo	RR 0.43 95% CI 0.27 to 0.68	●●○	ciclopirox olamine
[7] Systematic review	461 people Two RCTs in this analysis	**Treatment failure rates , 4 weeks** 38/231 (16%) with ciclopirox olamine 164/230 (71%) with placebo	RR 0.27 95% CI 0.11 to 0.66	●●○	ciclopirox olamine
Mycological cure rates					
[11] RCT	100 people with interdigital tinea pedis	**Mycological cure rates , 4 weeks**	P = 0.007 for ciclopirox olamine once daily *v* placebo		

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
3-armed trial		82% with ciclopirox olamine once daily 80% with ciclopirox olamine twice daily 43% with placebo Absolute numbers not reported	P = 0.013 for ciclopirox olamine twice daily *v* placebo		

Adverse effects

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Adverse effects					
[11] RCT	100 people with interdigital tinea pedis	**Adverse effects , 4 weeks** 58% with ciclopirox olamine 0.77% once daily 65% with ciclopirox olamine 0.77% twice daily 70% with placebo Absolute numbers not reported The most common adverse effects reported were burning and itching, and most adverse effects were of mild-to-moderate severity	Reported as not significant	⟷	Not significant

No data from the following reference on this outcome. [7]

Topical ciclopirox olamine versus topical azoles:
See options on topical azoles, p 6 .

Topical ciclopirox olamine versus topical allylamines:
See options on topical allylamines, p 2 .

Further information on studies

[7] The review gave no information on adverse effects associated with ciclopirox olamine. However, the RCTs included in the review reported burning, stinging, and itching sensations (no further details reported).

Comment: None.

OPTION **SOCKS, STOCKINGS, FOOT HYGIENE**

- For GRADE evaluation of interventions for Athlete's foot, see table, p 14 .
- We don't know whether improving foot hygiene or changing footwear can help to cure athlete's foot.

Benefits and harms

Socks, stocking, foot hygiene:

We found no direct information from RCTs on the effects of foot hygiene and hosiery in the treatment of athlete's foot.

Further information on studies

Comment: Evidence from the placebo arms of RCTs suggests that improved foot hygiene can achieve mycological cure in some people. [12]

GLOSSARY

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.

SUBSTANTIVE CHANGES

Topical allylamines (naftifine, terbinafine): One already reported systematic review updated [7] and two RCTs added. [9] [10] The updated review confirmed previous conclusions, and found that naftifine and terbinafine were more effective at curing athlete's foot (defined as negative results on microscopy and no growth of dermatophytes in culture) compared with placebo, but not significantly different compared with each other. It found that the results for cure rates between allylamines and azoles were inconclusive. [7] The RCTs found that topical allylamines were more effective than placebo at curing fungal skin infections. [9] [10] Categorisation unchanged (Beneficial).

Topical azoles: One already reported systematic review updated, [7] which confirmed previous conclusions. The updated review found that azole preparations were more effective at 4 to 6 weeks at curing athlete's foot (defined as negative results on microscopy and no growth of dermatophytes in culture) compared with placebo. It found that the results for cure rates between allylamines and azoles were inconclusive. The review found insufficient evidence of a difference in cure rates between different azoles at 2 to 6 weeks. It also found no significant difference in cure rates between clotrimazole and ciclopirox olamine. Categorisation unchanged (Beneficial).

Topical ciclopirox olamine: One already reported systematic review updated, [7] which confirmed previous conclusions. It found that ciclopirox olamine was more effective at curing athlete's foot (defined as negative results on microscopy and no growth of dermatophytes in culture) at 2 and 4 weeks compared with placebo, but found no significant difference between clotrimazole and ciclopirox olamine. Categorisation unchanged (Beneficial).

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GRADE **Evaluation of interventions for Athlete's foot.**

Important outcomes			Adverse effects, Mycological cure rates						
Studies (Participants)	Outcome	Comparison	Type of evidence	Quality	Consistency	Directness	Effect size	GRADE	Comment
What are the effects of topical treatments for athlete's foot?									
13 (1524) [7] [9] [10]	Mycological cure rates	Topical allylamines versus placebo	4	0	–1	0	0	Moderate	Consistency point deducted for heterogeneity among RCTs
1 (68) [7]	Mycological cure rates	Topical allylamines versus each other	4	–1	0	0	0	Moderate	Quality point deducted for sparse data
15 (2042) [7]	Mycological cure rates	Topical allylamines versus topical azoles	4	0	–1	0	0	Moderate	Consistency point deducted for heterogeneity among RCTs
13 (1259) [7]	Mycological cure rates	Topical azoles versus placebo	4	0	–1	0	0	Moderate	Consistency point deducted for conflicting results
9 (1287) [7]	Mycological cure rates	Topical azoles versus each other	4	0	–1	0	0	Moderate	Consistency point deducted for conflicting results
1 (87) [7]	Mycological cure rates	Topical azoles versus ciclopirox olamine	4	–1	0	0	0	Moderate	Quality point deducted for sparse data
3 (618) [7] [11]	Mycological cure rates	Topical ciclopirox olamine versus placebo	4	0	–1	0	0	Moderate	Consistency point deducted for heterogeneity among RCTs

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.