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Topical antifungal treatments for tinea cruris and tinea corporis (Review)

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[Intervention Review]

Topical antifungal treatments for tinea cruris and tinea corporis

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ABSTRACT

Background

Tinea infections are fungal infections of the skin caused by dermatophytes. It is estimated that 10% to 20% of the world population is affected by fungal skin infections. Sites of infection vary according to geographical location, the organism involved, and environmental and cultural differences. Both tinea corporis, also referred to as 'ringworm' and tinea cruris or 'jock itch' are conditions frequently seen by primary care doctors and dermatologists. The diagnosis can be made on clinical appearance and can be confirmed by microscopy or culture. A wide range of topical antifungal drugs are used to treat these superficial dermatomycoses, but it is unclear which are the most effective.

Objectives

To assess the effects of topical antifungal treatments in tinea cruris and tinea corporis.

Search methods

We searched the following databases up to 13th August 2013: the Cochrane Skin Group Specialised Register, CENTRAL in *The Cochrane Library* (2013, Issue 7), MEDLINE (from 1946), EMBASE (from 1974), and LILACS (from 1982). We also searched five trials registers, and checked the reference lists of included and excluded studies for further references to relevant randomised controlled trials. We handsearched the journal Mycoses from 1957 to 1990.

Selection criteria

Randomised controlled trials in people with proven dermatophyte infection of the body (tinea corporis) or groin (tinea cruris).

Data collection and analysis

Two review authors independently carried out study selection, data extraction, assessment of risk of bias, and analyses.

Main results

Of the 364 records identified, 129 studies with 18,086 participants met the inclusion criteria. Half of the studies were judged at high risk of bias with the remainder judged at unclear risk. A wide range of different comparisons were evaluated across the 129 studies, 92 in total, with azoles accounting for the majority of the interventions. Treatment duration varied from one week to two months, but in most studies this was two to four weeks. The length of follow-up varied from one week to six months. Sixty-three studies contained no usable or retrievable data mainly due to the lack of separate data for different tinea infections. Mycological and clinical cure were assessed in the majority of

studies, along with adverse effects. Less than half of the studies assessed disease relapse, and hardly any of them assessed duration until clinical cure, or participant-judged cure. The quality of the body of evidence was rated as low to very low for the different outcomes.

Data for several outcomes for two individual treatments were pooled. Across five studies, significantly higher clinical cure rates were seen in participants treated with terbinafine compared to placebo (risk ratio (RR) 4.51, 95% confidence interval (CI) 3.10 to 6.56, number needed to treat (NNT) 3, 95% CI 2 to 4). The quality of evidence for this outcome was rated as low. Data for mycological cure for terbinafine could not be pooled due to substantial heterogeneity.

Mycological cure rates favoured naftifine 1% compared to placebo across three studies (RR 2.38, 95% CI 1.80 to 3.14, NNT 3, 95% CI 2 to 4) with the quality of evidence rated as low. In one study, naftifine 1% was more effective than placebo in achieving clinical cure (RR 2.42, 95% CI 1.41 to 4.16, NNT 3, 95% CI 2 to 5) with the quality of evidence rated as low.

Across two studies, mycological cure rates favoured clotrimazole 1% compared to placebo (RR 2.87, 95% CI 2.28 to 3.62, NNT 2, 95% CI 2 to 3).

Data for several outcomes were pooled for three comparisons between different classes of treatment. There was no difference in mycological cure between azoles and benzylamines (RR 1.01, 95% CI 0.94 to 1.07). The quality of the evidence was rated as low for this comparison. Substantial heterogeneity precluded the pooling of data for mycological and clinical cure when comparing azoles and allylamines. Azoles were slightly less effective in achieving clinical cure compared to azole and steroid combination creams immediately at the end of treatment (RR 0.67, 95% CI 0.53 to 0.84, NNT 6, 95% CI 5 to 13), but there was no difference in mycological cure rate (RR 0.99, 95% CI 0.93 to 1.05). The quality of evidence for these two outcomes was rated as low for mycological cure and very low for clinical cure.

All of the treatments that were examined appeared to be effective, but most comparisons were evaluated in single studies. There was no evidence for a difference in cure rates between tinea cruris and tinea corporis. Adverse effects were minimal - mainly irritation and burning; results were generally imprecise between active interventions and placebo, and between different classes of treatment.

Authors' conclusions

The pooled data suggest that the individual treatments terbinafine and naftifine are effective. Adverse effects were generally mild and reported infrequently. A substantial number of the studies were more than 20 years old and of unclear or high risk of bias; there is however, some evidence that other topical antifungal treatments also provide similar clinical and mycological cure rates, particularly azoles although most were evaluated in single studies.There is insufficient evidence to determine if Whitfield’s ointment, a widely used agent is effective.

Although combinations of topical steroids and antifungals are not currently recommended in any clinical guidelines, relevant studies included in this review reported higher clinical cure rates with similar mycological cure rates at the end of treatment, but the quality of evidence for these outcomes was rated very low due to imprecision, indirectness and risk of bias. There was insufficient evidence to confidently assess relapse rates in the individual or combination treatments.

Although there was little difference between different classes of treatment in achieving cure, some interventions may be more appealing as they require fewer applications and a shorter duration of treatment. Further, high quality, adequately powered trials focusing on patient-centred outcomes, such as patient satisfaction with treatment should be considered.

PLAIN LANGUAGE SUMMARY

Treatments applied to the skin for fungal infections of the groin and body

Background
Up to 20% of the world's population is affected by fungal skin infections of the groin ('jock' itch, or tinea cruris) or of the body (ringworm, or tinea corporis), which generally appear as red and itchy areas on the skin. Many topical (directly applied to the skin) treatments are available.

Review question
Which topical treatments work best for 'jock' itch and ringworm?

Study characteristics
We included 129 studies published up to August 2013 which examined 18,086 people. Participants included men and women of any age, although most were between 18 to 70 years old. There was considerable variation in the reporting quality of the studies. A quarter were partially funded by pharmaceutical companies, and it was unclear what impact this may have had on reporting of the results.

Most studies appeared to be conducted within dermatology outpatient clinics. A range of treatments were evaluated, mostly in single studies. Most treatments were applied once or twice daily for between two and four weeks. Mycological cure (disappearance of fungal infection); and clinical cure (absence of symptoms such as redness and itchiness); were assessed in the majority of studies, along with side effects. Less than half of the studies assessed disease recurrence and hardly any assessed the time to achieve clinical cure, or whether study participants considered they had been cured.

Key results
Almost all treatments were effective at achieving both mycological and clinical cure, compared with placebo.

We combined data for several outcomes in two individual treatments: terbinafine against placebo and naftifine against placebo. Both were shown to be effective treatments.

We combined data on different groups of treatments. There was no difference in rate of mycological cure between azoles and benzylamines. Combinations of antifungal treatment with a topical corticosteroid achieved higher clinical cure rates, probably because the skin redness disappears sooner due to the effect of the corticosteroid. There was no evidence of any difference in the speed of resolution of fungal infection with these combination treatments.

Quality of the evidence
The overall quality of the evidence for the different outcomes was rated as low to very low. There is currently insufficient evidence to be able to decide if one particular treatment is better than any of the others. All the treatments we evaluated reported low rates of mild side effects.

This review highlights the need for better quality studies on treatments for fungal skin infections. Despite the limitations of our main findings, it appears that most active treatments are effective and further research should concentrate on comparing active treatments, rather than comparisons with a placebo. Topical treatments that need to be used only once a day over a short period of time may be more appealing in practice. Some of the treatments examined in our review may not be readily available in-low income countries.

Summary of findings for the main comparison. Terbinafine 1% cream/gel compared with placebo cream/gel for tinea cruris and tinea corporis

Terbinafine 1% cream/gel compared with placebo cream/gel for tinea cruris and tinea corporis

Patient or population: patients with tinea cruris and tinea corporis
Settings: hospital and primary care clinics
Intervention: terbinafine 1% cream/gel
Comparison: placebo cream/gel

Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	No of Participants (studies)	Quality of the evidence (GRADE)	Comments
	Assumed risk	Corresponding risk				
	Placebo cream/gel	Terbinafine 1% cream/gel				
Mycological cure Negative KOH microscopy, or culture, or both. Treatment duration 1-2 weeks	See comment	See comment	Not estimable	330 (7 studies)	⊕⊕⊝⊝ **low** [1,2]	Unexplained statistical heterogeneity, data not pooled
Clinical cure Resolution of clinical signs and symptoms. Treatment duration 1-2 weeks Follow-up: 2-4 weeks	**Study population**		**RR 4.51** (3.1 to 6.56)	273 (5 studies)	⊕⊕⊝⊝ **low** [3,4,5]	
	165 per 1000	**746 per 1000** (513 to 1000)				
	Moderate					
	133 per 1000	**600 per 1000** (412 to 872)				
Adverse effects Reported by investigators 'and' or 'or' participants Follow-up: 0-8 weeks	**Study population**		**RR 0.43** (0.2 to 0.92)	469 (7 studies)	⊕⊝⊝⊝ **very low** [1,6]	Contact dermatitis type symptoms, no systemic adverse effects reported
	97 per 1000	**42 per 1000** (19 to 89)				
	Moderate					
	29 per 1000	**12 per 1000** (6 to 27)				
Relapse or recurrence	See comment	See comment	Not estimable	168 (3 studies)	⊕⊕⊝⊝ **low** [7,8]	Only Budimulja 1998 allowed an accurate

Evidence of clinical or mycological infection in previously cured participants Follow-up: 1-8 weeks						assessment of relapse - none were seen in either group (n = 101)
Participant-judged cure Judgement of treatment as 'good' or 'very good'	**Study population**		**RR 4.46** (3.16 to 6.31)	253 (2 studies)	⊕⊕⊝⊝ **low** [9,10,11]	
	198 per 1000	**885 per 1000** (627 to 1000)				
	Moderate					
Duration of treatment until clinical cure Not assessed	**Study population**		Not estimable	0 (0)	See comment	Outcome not assessed by study authors
	See comment	See comment				
	Moderate					

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

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

[1] Random sequence generation, allocation concealment and blinding at unclear risk of bias across studies, with 2 studies (Lebwohl 2001 and Millikan 1990) judged overall at high risk of bias. In both of these studies, there was a high drop-out rate (20% to 25%) in already underpowered studies
[2] Substantial unexplained heterogeneity
[3] Three studies (Lebwohl 2001; Millikan 1990 and Zaias 1993) judged at high risk of bias overall
[4] Small sample size, optimal information size would be 2790 participants
[5] Although there is a large effect (RR 4.51, in all studies RR > 4.00), there are threats to validity, see risk of bias
[6] CI includes the threshold for appreciable benefit (0.75) and nearly no effect (1.0), very low number of events, low sample size (optimal information size would be 4238 participants)
[7] Millikan 1990 judged at high risk of bias overall - high drop-out rate in an underpowered study; sequence generation, allocation concealment and blinding judged at unclear risk of bias in remaining studies
[8] Low number of events, sample size is lower than optimal information size
[9] Blinding for both studies judged at unclear risk of bias, and Zaias 1993 judged overall at high risk of bias - details on total number of randomised participants not given
[10] Number of events < 300 and optimal information size would be 2210 participants

[11] Although there is a large effect (RR > 2), there are threats to validity, see risk of bias

Summary of findings 2. Naftifine 1% cream once or twice daily compared with placebo cream once or twice daily for tinea cruris and tinea corporis

Naftifine 1% cream once or twice daily compared with placebo cream once or twice daily for tinea cruris and tinea corporis

Patient or population: patients with tinea cruris and tinea corporis
Settings: outpatient clinics
Intervention: naftifine 1% cream once or twice daily
Comparison: placebo cream once or twice daily

Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	No of Participants (studies)	Quality of the evidence (GRADE)	Comments
	Assumed risk	Corresponding risk				
	Placebo cream once or twice daily	Naftifine 1% cream once or twice daily				
Mycological cure Negative KOH microscopy and culture. Treatment duration 2-4 weeks	**Study population**		**RR 2.38** (1.8 to 3.14)	187 (3 studies)	⊕⊕⊝⊝ **low** [1,2,3]	
	359 per 1000	**854 per 1000** (646 to 1000)				
	Moderate					
	321 per 1000	**764 per 1000** (578 to 1000)				
Clinical cure Resolution of clinical signs and symptoms at least 2 weeks from start of treatment Follow-up: 6 weeks	**Study population**		**RR 2.42** (1.41 to 4.16)	63 (1 study)	⊕⊕⊝⊝ **low** [4,5]	
	323 per 1000	**781 per 1000** (455 to 1000)				
	Moderate					
Adverse effects Reported by investigators 'and' or 'or' participants Follow-up: 0-6 weeks	**Study population**		**RR 0.44** (0.13 to 1.57)	195 (3 studies)	⊕⊝⊝⊝ **very low** [1,6]	Contact dermatitis type symptoms. No systemic adverse effects reported
	73 per 1000	**32 per 1000** (9 to 114)				

	Moderate					
	54 per 1000	**24 per 1000** (7 to 85)				
Relapse or recurrence Evidence of clinical or mycological infection in previously cured participants Follow-up: 6 weeks	**Study population**		**RR 0.07** (0 to 1.25)	44 (1 study)	⊕⊕⊖⊖ **low** [7]	Based on participants who had negative culture at the end of the 2-week treatment period
	214 per 1000	**15 per 1000** (0 to 268)				
	Moderate					
Participant-judged cure Not assessed	**Study population**		Not estimable	0 (0)	See comment	Outcome not assessed by study authors
	See comment	See comment				
	Moderate					
Duration of treatment until clinical cure Not assessed	**Study population**		Not estimable	0 (0)	See comment	Outcome not assessed by study authors
	See comment	See comment				
	Moderate					

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

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

[1] Dobson 1991 judged at high risk of bias overall - high drop-out rate (27%) in an already underpowered study. Numbers of participants in each group after randomisation unclear
[2] Low sample size, optimal information size would be 938
[3] Although large treatment effect (RR > 2), there were threats to validity, see risk of bias

[4] Very low total number of participants, optimal information size would be 1114, and wide CI
[5] Although large treatment effect (RR > 2), there were threats to validity, see imprecision
[6] CI includes appreciable harm, no effect and appreciable benefit. Furthermore, low number of events and small sample size (optimal information size would be 5804 participants)
[7] CI includes appreciable harm, no effect and appreciable benefit. Furthermore, low sample size (optimal information size would be 1608 participants)

Summary of findings 3. Azoles compared with allylamines for tinea cruris and tinea corporis

Azoles compared with allylamines for tinea cruris and tinea corporis

Patient or population: patients with tinea cruris and tinea corporis
Settings: outpatient clinics
Intervention: azoles
Comparison: allylamines

Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	No of Participants (studies)	Quality of the evidence (GRADE)	Comments
	Assumed risk	Corresponding risk				
	Allylamines	Azoles				
Mycological cure Negative KOH microscopy and culture. Treatment duration 1-7 weeks	See comment	See comment	Not estimable	638 (7 studies)	⊕⊖⊖⊖ **very low** [1,2,3]	[4] Substantial heterogeneity, data not pooled
Clinical cure Resolution of clinical signs and symptoms at least 2 weeks from the start of treatment. Treatment duration 1-7 weeks	See comment	See comment	Not estimable	605 (6 studies)	⊕⊖⊖⊖ **very low** [2,3,5]	Substantial heterogeneity, data not pooled
Adverse effects Reported by investigators 'and' or 'or' participants Follow-up: 0-8 weeks	**Study population**		**RR 0.7** (0.18 to 2.68)	386 (5 studies)	⊕⊖⊖⊖ **very low** [1,6]	Contact dermatitis type symptoms. No systemic adverse effects reported
	21 per 1000	**15 per 1000** (4 to 57)				
	Moderate					
	22 per 1000	**15 per 1000** (4 to 59)				

Relapse or recurrence Evidence of clinical and mycological relapse after the end of treatment. Assessed in 3 studies Follow-up: 2-4 weeks	**Moderate**		**RR 2.33** (0.21 to 26.23)	105 (3 studies[7])	⊕⊖⊖⊖ **very low** [1,8]	Only 1 study (Hantschke 1980) reported relapses (1/3 in azole group, 1/7 in allylamine group)[9]
Participant-judged cure Not assessed	**Study population**		Not estimable	0 (0)	See comment	Outcome not assessed by study authors
	See comment	See comment				
	Moderate					
Duration of treatment until clinical cure Scale from: 21 to 77	The mean duration of treatment until clinical cure in the control groups was **54.6 days**	The mean duration of treatment until clinical cure in the intervention groups was **33.60 lower** (46.91 to 20.29 lower)		7 (1 study)	⊕⊖⊖⊖ **very low** [10,11]	Hantschke 1980 - 3 weeks in azole group (n = 2) and 6-11 weeks in allylamine group (n = 5)

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

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

[1] Haroon 1996 and Jerajani 2013 were both open trials and blinding was therefore judged at high risk of bias. In addition, the attrition rate was also high in both studies (20% and 25% respectively). Sequence generation, allocation concealment and blinding all judged at an unclear risk of bias in remaining studies
[2] Substantial heterogeneity (I^2 = 75%)
[3] Six different azole creams used across the studies. Allylamine treatment regimens different across all studies
[4] Jerajani 2013 - only KOH microscopy assessed
[5] Jerajani 2013 judged at high risk of bias due to lack of blinding and high attrition rate. Sequence generation, allocation concealment and blinding for the remaining studies all judged at an unclear risk of bias
[6] Low number of events, CI is wide, including appreciable harm, no effect and appreciable benefit, small sample size (optimal information size would be 20,382 participants)
[7] Hantschke 1980; Haroon 1996; Jerajani 2013
[8] Low total number of participants and wide CI including no effect and appreciable harm

[9] Haroon 1996, no relapses reported in 18 participants in azole group and no relapses in 15 participants in allylamine group. Jerajani 2013, no relapses in 40 participants in azole group nor in 22 participants in allylamine group

[10] Sequence generation, allocation concealment and blinding all judged at unclear risk of bias

[11] Only 9 participants in total

Summary of findings 4. Azoles compared with moderate-potent corticosteroid/azole combinations for tinea cruris and tinea corporis

Azoles compared with moderate-potent corticosteroid/azole combinations for tinea cruris and tinea corporis

Patient or population: patients with tinea cruris and tinea corporis
Settings: outpatient clinics
Intervention: azoles
Comparison: moderate-potent corticosteroid/azole combinations

Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	No of Participants (studies)	Quality of the evidence (GRADE)	Comments
	Assumed risk	Corresponding risk				
	Moderate-potent corticosteroid/azole combinations	Azoles				
Mycological cure Negative KOH microscopy and culture. Treatment duration 2-3 weeks	**Study population**		**RR 0.99** (0.93 to 1.05)	625 (6 studies)	⊕⊕⊖⊖ **low** [1,2]	
	795 per 1000	**787 per 1000** (739 to 835)				
	Moderate					
	881 per 1000	**872 per 1000** (819 to 925)				
Clinical cure (immediately at end of treatment) Resolution of clinical signs and symptoms at least 2 weeks from the start of treatment	**Study population**		**RR 0.67** (0.53 to 0.84)	353 (4 studies)	⊕⊖⊖⊖ **very low** [1,2,3]	
	773 per 1000	**518 per 1000** (410 to 650)				
	Moderate					
	836 per 1000	**560 per 1000** (443 to 702)				
Adverse effects	**Study population**		**RR 1.36** (0.68 to 2.69)	668 (5 studies)	⊕⊖⊖⊖	Although different individual azoles and

Reported by investigators 'and' or 'or' participants Follow-up: 0-4 weeks	**39 per 1000**	**53 per 1000** (27 to 105)			**very low** [1,4]	combination creams were assessed, the total number of adverse effects was low, mainly contact dermatitis-like symptoms
	Moderate					
	18 per 1000	**24 per 1000** (12 to 48)				
Relapse or recurrence Not assessed	**Study population**		Not estimable	0 (0)	See comment	Outcome not assessed by study authors
	See comment	See comment				
	Moderate					
Participant-judged cure 4-point symptom score scale	**Study population**		Not estimable	0 (1 study)	⊕⊕⊖⊖ **low** [5]	Minimal data reported[6]
	See comment	See comment				
	Moderate					
Duration of treatment until clinical cure Not assessed	**Study population**		Not estimable	0 (0)	See comment	Outcome not assessed by study authors
	See comment	See comment				
	Moderate					

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

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

[1] Sequence generation, allocation concealment and blinding at unclear risk of bias across all studies. Pariser 1995 judged overall at high risk of bias

[2] Four different azole creams and two different corticosteroid/azole creams assessed in these studies
[3] Low sample size, optimal sample size would be 500, CI includes threshold 0.75 (appreciable benefit)
[4] CI includes appreciable harm, no effect and appreciable benefit. Furthermore, low number of events and very small sample size (optimal sample size would be 10,840)
[5] Blinding judged at unclear risk of bias, and minimal data were reported on patient-judged cure
[6] No data were provided. The authors stated: 'Patient-rated symptom severity scores were not statistically significant, but they favoured the clotrimazole/betamethasone dipropionate group over the ketoconazole group'

Summary of findings 5. Azoles compared with benzylamines for tinea cruris and tinea corporis

Azoles compared with benzylamines for tinea cruris and tinea corporis

Patient or population: patients with tinea cruris and tinea corporis
Settings: dermatology outpatient clinics
Intervention: azoles
Comparison: benzylamines

Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	No of Participants (studies)	Quality of the evidence (GRADE)	Comments
	Assumed risk	Corresponding risk				
	Benzylamines	Azoles				
Mycological cure Negative KOH microscopy and culture. Treatment duration 2-4 weeks	**Study population**		**RR 1.01** (0.94 to 1.07)	219 (3 studies)	⊕⊕⊖⊖ **low** [1,2]	
	944 per 1000	**953 per 1000** (887 to 1000)				
	Moderate					
	931 per 1000	**940 per 1000** (875 to 996)				
Clinical cure Resolution of clinical signs and symptoms at least 2 weeks from the start of treatment	See comment	See comment	Not estimable	169 (2 studies)	⊕⊕⊖⊖ **low** [3,4]	Total numbers cured - 47/84 azoles compared to 45/85 benzylamines. Not pooled due to substantial unexplained heterogeneity
Adverse effects Reported by investigators 'and' or 'or' participants Follow-up: 0-8 weeks	**Study population**		**RR 0.85** (0.41 to 1.76)	263 (3 studies)	⊕⊖⊖⊖ **very low** [1,5]	Contact dermatitis type symptoms. No systemic adverse effects reported
	106 per 1000	**90 per 1000**				

		(43 to 187)				
	Moderate					
	103 per 1000	**88 per 1000** (42 to 181)				
Relapse or recurrence Evidence of clinical or mycological disease after successful treatment Follow-up: 4-8 weeks	**Study population**		**RR 1.84** (0.35 to 9.6)	215 (3 studies[6])	⊕⊖⊖⊖ **very low** [1,2,7]	In total 4 participants relapsed in the azole group and 2 in the benzylamine group
	19 per 1000	**35 per 1000** (7 to 183)				
	Moderate					
Participant-judged cure Not assessed	**Study population**		Not estimable	0 (0)	See comment	Outcome not assessed by study authors
	See comment	See comment				
	Moderate					
Duration of treatment until clinical cure Not assessed	**Study population**		Not estimable	0 (0)	See comment	Outcome not assessed by study authors
	See comment	See comment				
	Moderate					

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

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

[1] Ramam 2003 judged at high risk of bias overall - high attrition rate and study funded by industry supplying both interventions
[2] Different azoles assessed in the studies

[3] Substantial heterogeneity
[4] Low total number of participants
[5] Low sample size (optimal information size would be 3760), and confidence interval includes both no effect and appreciable harm
[6] Li 2006; Ramam 2003; Singal 2005
[7] Very wide confidence interval, low event rate, small sample size

Summary of findings 6. Azoles versus placebo for tinea cruris and tinea corporis

Azoles versus placebo for tinea cruris and tinea corporis

Patient or population: patients with tinea cruris and tinea corporis
Settings: hospital and community clinics
Intervention: azoles
Comparison: placebo

Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	No of Participants (studies)	Quality of the evidence (GRADE)	Comments
	Assumed risk	Corresponding risk				
	Placebo	Azoles				
Mycological cure Negative KOH microscopy and culture. Treatment duration 2-4 weeks	See comment	See comment	Not estimable	490 (4 studies[1])	⊕⊖⊖⊖ **very low** [2,3,4]	Clinical heterogeneity, data not pooled
Clinical cure Resolution of clinical signs and symptoms. Treatment duration 2-4 weeks	See comment	See comment	Not estimable	336 (3 studies[1])	⊕⊖⊖⊖ **very low** [3,4,5]	Clinical heterogeneity, data not pooled
Adverse effects Reported by investigators 'and' or 'or' participants Follow-up: 0-5 weeks	**Study population**		**RR 0.25** (0.06 to 0.99)	266 (3 studies[1,6])	⊕⊖⊖⊖ **very low** [5,7]	Contact dermatitis symptoms such as burning and erythema
	82 per 1000	**21 per 1000** (5 to 81)				
	Moderate					
Relapse or recurrence Not assessed	**Study population**		Not estimable	0 (0)	See comment	Outcome not assessed by study authors
	See comment	See comment				

	Moderate				
Participant-judged cure Not assessed	**Study population**	Not estimable	0 (0)	See comment	Outcome not assessed by study authors
	See comment See comment				
	Moderate				
Duration of treatment until clinical cure Not assessed	**Study population**	Not estimable	0 (0)	See comment	Outcome not assessed by study authors
	See comment See comment				
	Moderate				

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

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

[1] Miura 1979 - 2 comparisons (econazole versus placebo and clotrimazole versus placebo)
[2] Spiekermann 1976 judged at high risk of bias overall due to high attrition rate (33%) and industry-funded study. Sequence generation, allocation concealment and blinding all judged at unclear risk of bias across remaining studies
[3] Substantial heterogeneity
[4] 4 different azoles
[5] Sequence generation, allocation concealment and blinding all judged at unclear risk of bias across all studies
[6] Bagatell 1986; Miura 1979; Tanenbaum 1989
[7] Wide confidence interval including appreciable harm and low sample size (optimal information size would be 4724)

BACKGROUND

Description of the condition

Tinea infections are fungal infections of the skin, and they are amongst the most common skin conditions worldwide (Gupta 2003). These infections can often be severe and recurrent (Gupta 2004). They are caused by dermatophytes, a group of closely-related fungi that consist of the genera *Epidermophyton, Microsporum,* and *Trichophyton* (Weitzman 1995). The infection is seen throughout the world, and evidence supports a greater prevalence in warmer and more humid conditions (Aly 1994). It is estimated that 10% to 20% of the world population is affected by fungal skin infections (including other forms of tinea, e.g. tinea pedis, also known as athlete's foot) (Drake 1996). Anatomical patterns of infection vary according to geographical location, the organism involved, and environmental and cultural differences (Havlickova 2008). For instance, wearing occlusive clothing, particularly in tropical climates, is associated with a higher frequency of infection (Macura 1993). A variety of other factors are at play in determining if infection will take hold, e.g. the age and sex of the affected individual or 'host', immune status, and genetic factors (Brasch 2010).

The dermatophytes can be subdivided into three groups - anthropophilic (confined to humans), zoophilic (animals), and geophilic (live in soil). The most common dermatophyte causing tinea cruris and tinea corporis worldwide is *Trichophyton rubrum*, an anthropophilic dermatophyte (Ameen 2010; Seebacher 2008).

Tinea corporis, commonly referred to as 'ringworm', can be caused by any of the dermatophytes. It is a superficial skin infection that is unable to affect deeper tissues and organs in people with normally-functioning immune systems, or 'immunocompetent hosts' (Smijs 2011). Tinea corporis refers to such a fungal infection anywhere on the body apart from the scalp, beard area, feet, or hands. It presents clinically as a well-demarcated annular plaque (or raised area) with a scaly and advancing border. Lesions may show concentric rings with red plaques in the centre; these may clear as the lesion spreads, leaving an area of central hypopigmentation (loss of skin colour) (Weinstein 2002).

Tinea cruris, otherwise known as 'jock itch', is an infection in the groin, perineal, and perianal area, usually affecting adult men. It can present unilaterally or bilaterally with a red, raised, and active border. Small vesicles, papules, and scaling may be present (Aridogan 2005). It typically spares the penis and scrotum, and this may be helpful in distinguishing it from other rashes in the area (Hainer 2003). The type of dermatophyte causing tinea cruris varies according to geographical location; common organisms include *Trichophtyon rubrum* and *Epidermophyton floccosum* (Bassiri-Jahromi 2009; Weitzman 1995).

In both of these conditions, the severity of the lesions ranges from mild to severe, with itch being the predominant complaint. Those affected can be in some discomfort and are often embarrassed at the need to keep scratching. These conditions are frequently seen by primary care doctors and dermatologists. The infection can be transmitted from one person to another mainly via direct skin-to-skin contact, although the shedding of infected dead skin cells on clothing, bedding, and towels provides other sources of transmission. Less commonly, infection from animals and soil with zoophilic and geophilic dermatophytes, respectively, can occur (Noble 1998). Although people from all socioeconomic groups can be affected, the condition tends to be seen in those with low socioeconomic status. Crowded living conditions, poor levels of hygiene, and close proximity to animals can aid the transmission of infection (Havlickova 2008). In addition, those suffering with particular co morbidities, e.g. diabetes mellitus, are at an increased risk of infection, particularly chronic infection (Balci 2008). Tinea infections, as mentioned here, are unable to affect deeper organs; therefore, internal fungal infection of immunocompromised hosts (people with an affected immune system) is only very rarely caused by dermatophytes (Jain 2010).

The diagnosis in practice is usually based on clinical appearance, although scrapings can be taken and analysed using microscopy or Wood's lamp examination (Andrews 2008). Culturing of the organism can also be performed, although this is a lengthy process, but it may be important in determining the species causing infection and thus the likely source. Occasionally, the condition is misdiagnosed by patients and healthcare professionals, and treatments for other skin rashes, particularly steroids, are given inappropriately (Wacker 2004). This can alter the appearance of the infection leading to a condition known as 'tinea incognito', adding further diagnostic uncertainty.

Description of the intervention

An array of topical (externally applied) treatments exist for this problem. As the dermatophytes causing this infection are limited to the superficial keratinised tissue, topical treatments are the most appropriate to use, providing the infection is not widespread. The two main groups of antifungal drugs are the azoles and the allylamines. Newer drugs tend to be within one or other of these groups (Gupta 2008). Other antifungal drugs used for tinea infections include the benzylamines and hydroxypyridones (Havlickova 2008a). There are different strength preparations of the same active compound and different dosing regimens suggested. There are other less widely-used topical treatments, such as oil of bitter orange and *Eucalyptus pauciflora.* Some treatments also contain antibacterial and corticosteroid components alongside the antifungal agent. In many countries, topical antifungal treatments are available directly to the public without the need for a medical consultation.

The ideal topical treatment is one that possesses a high cure rate, a low relapse rate, has a short duration of action, and causes minimal adverse effects (Crawford 2007). In addition, it is important to find a treatment regimen that is satisfactory to the person with the condition to ensure compliance. Most topical treatments require application once or twice a day, for periods of commonly between one and three weeks. Topical antifungal treatments are normally well-tolerated and tend not to cause adverse effects. Similar topical treatments are sometimes used for other forms of tinea, e.g. tinea pedis, but oral therapy is also used. For evidence of the effectiveness of these treatments, please see previous reviews in *The Cochrane Library* (Bell-Syer 2002; Crawford 2007; Gonzalez 2007).

How the intervention might work

All commonly used topical antifungal treatments seek to disrupt ergosterol synthesis, which is a vital component of fungal cell membranes. Changes in the cell membrane cause inhibition of fungal growth. Ergosterol synthesis is a complex process

involving the formation of several intermediate stages; different treatments affect different parts of the pathway. Azole antifungals, such as miconazole, possess mainly fungistatic (inhibit fungal cell growth) activity; at high concentrations they may also be fungicidal (kill fungal cells) (Ghannoum 1999; Gupta 2008; Havlickova 2008a). Their principal effect is selective inhibition of the fungal Cytochrome P450 (CYP450) 14 α-demethylase enzyme. This prevents conversion of lanosterol to ergosterol, thus, disrupting membrane integrity and preventing growth (Grudzien 2009). Terbinafine, an allylamine, acts by blocking the conversion of squalene into squalene-2,3-epoxide, a precursor of ergosterol formation. This exerts both a fungistatic effect by prevention of cell growth as well as a fungicidal effect via the accumulation of squalene (Darkes 2003).

Other treatments are involved in the disruption of the fungal cell membrane by other means. Treatments that include a corticosteroid component are used in people troubled by itch in the hope of rapidly reducing the inflammatory response (Rosen 1995). Absorption of topical corticosteroids into the blood and lymphatic systems is negligible meaning that serious side effects are extremely unlikely; however, prolonged use of these corticosteroid-containing treatments have been reported to cause problems, such as striae, papule formation, and scarring (Barkey 1987; Greenberg 2002; Reynolds 1991).

Why it is important to do this review

This common infection is seen by primary care physicians, dermatologists, paediatricians, and other health professionals, and it is successfully treated using topical medication in the majority of cases. Although untreated or partially treated infection is not associated with overwhelming serious internal infection, it may result in chronic, difficult-to-treat cases, necessitating the use of more toxic oral therapy. In addition, complications such as bacterial superinfection, lichenification, and maceration are more likely to occur in chronic infection (Gupta 2003). Therefore, prompt, effective treatment, particularly in people with other conditions such as diabetes, is required.

There is evidence to suggest that non-dermatologists e.g. primary care physicians, prescribe far more corticosteroids and antifungal combination treatments for tinea infections than dermatologists, and there is continuing doubt whether this treatment is any more effective than a topical antifungal alone (Erbagci 2004; Greenberg 2002; Smith 1998).

In view of the prevalence of this condition, a systematic review is necessary to ascertain if there is any clinical benefit to the combination approach, particularly as these combination treatments are generally more costly. There are also many different drug and treatment regimens, which is another reason for a systematic assessment of the effectiveness of these regimens.

The plans for this review were published as a protocol '*Topical antifungal treatments for tinea cruris and tinea corporis*' (El-Gohary 2012).

OBJECTIVES

To assess the effects of topical antifungal treatments (and whether combination products, e.g. those containing topical corticosteroids plus antifungals, are any more effective than topical antifungals alone) for treating tinea corporis and tinea cruris infections in men and women.

METHODS

Criteria for considering studies for this review

Types of studies

Randomised controlled trials.

Types of participants

Men and women of any age with a proven dermatophyte infection of the body (tinea corporis), excluding head, hands, and feet or a proven dermatophyte infection of the groin (tinea cruris). Diagnosis of infection, confirmed by detection of dermatophytes using either microscopy, growth of dermatophytes in culture, or both. We included studies involving participants with a mix of fungal infection sites, e.g. tinea cruris, tinea corporis, and tinea pedis. However, we only considered data relating to tinea cruris and tinea corporis.

We excluded trials involving participants with other fungal skin infections, e.g. *Candida* or *Malassezia furfur* and trials involving participants with an immunocompromising illness or if they were on immunosuppressant medication.

Types of interventions

Any regimen of topical treatments for tinea corporis or tinea cruris either used alone or in combination with other treatments, e.g. those containing topical corticosteroids plus antifungals compared with other topical treatment, no treatment, or placebo. Trials using combinations of topical agents with photodynamic therapy were excluded.

Types of outcome measures

Primary outcomes

1. Rate of mycological cure - defined as the follow-up reporting of negative mycological testing at least two weeks from the start of treatment in each trial participant (negative microscopy findings, the absence of any growth of the dermatophytes in culture, or both).
2. Clinical cure - defined as the resolution of clinical signs and symptoms suggestive of dermatophyte infection, as judged by study investigators with trial participants. This was measured at least two weeks from the start of treatment.

Secondary outcomes

1. Relapse or recurrence - defined as the recurrence of either clinically or mycologically proven infection in participants having previously been documented as cured. We used the last mycology and clinical assessment of the trial participants in the studies if this was measured after the cessation of treatment. Relapse was considered to have taken place if the problem recurred at the same site after four weeks and up to six months from the initiation of treatment.
2. Adverse effects - the measurement of reported side effects in each included study thought to be related to the intervention, e.g. skin sensitisation, irritation.
3. Duration of treatment - the length of treatment in days until clinical cure was obtained.

4. Participant-judged cure.

Search methods for identification of studies

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

Electronic searches

We searched the following databases up to 13th August 2013:

- the Cochrane Skin Group Specialised Register using the following terms: ringworm or "crotch itch" or "crotch rot" or "jock itch" or "dhobie itch" or "gym itch" or "eczema marginatum" or (tinea and (cruris or corporis or glabrosa or circinata or body));
- the Cochrane Central Register of Controlled Trials (CENTRAL) 2013, Issue 7, in *The Cochrane Library* using the search strategy in Appendix 1;
- MEDLINE via OVID (from 1946) using the strategy in Appendix 2;
- EMBASE via OVID (from 1974) using the strategy in Appendix 3; and
- LILACS (Latin American and Caribbean Health Science Information database, from 1982) using the strategy in Appendix 4.

A final prepublication search for this review was undertaken on 21 May 2014. Although it has not been possible to incorporate RCTs identified through this search within this review, relevant references are listed under Studies awaiting classification. They will be incorporated into the next update of the review.

Searching other resources

Trials registers

We (MEG and EvZ) searched the following trials registers up to 1 June 2014 with the following search terms: tinea, tinea cruris, tinea corporis, dermatophyte.

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

Handsearching

The journal *Mycoses* was handsearched (MEG) from its inception in 1957 to 1990 on 16 August 2013. Later editions of the journal are indexed in MEDLINE and EMBASE.

References from published studies

A single author (MEG) checked the bibliographies of included and excluded studies for further references to relevant trials.

Adverse effects

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

Data collection and analysis

Some parts of the methods section of this review uses text that was originally published in other Cochrane reviews co-authored by ZF and EVZ (predominantly van Zuuren 2012).

Selection of studies

Two review authors (EvZ and ZF) independently screened all titles and abstracts of identified studies to assess whether or not the study was eligible for inclusion. In the event of a disagreement between these two authors, we retrieved the full text of the study in question for further assessment. If there was still no agreement, we referred the full text to a third review author. For all abstracts deemed eligible for inclusion, we retrieved the corresponding full texts. In the event of identifying a suitable study written in an alternative language, we made realistic attempts to obtain an accurate English language translation. We listed in the excluded studies tables of the review studies that were initially thought to meet the eligibility criteria but were subsequently excluded.

Data extraction and management

Review authors MEG, EvZ, ZF, HB and ED independently extracted data from the included studies, using a data collection form, which was pilot tested. The authors resolved any differences that arose in the data collected through discussion and consultation to reach a consensus.

The review authors extracted the following details.

1. Trial methods
   a. sequence generation
   b. method of concealment of allocation
   c. masking of participants, trialists and outcome assessors
   d. exclusion of participants after randomisation and proportion and reasons for losses at follow-up
2. Participants
   a. country of origin and study setting
   b. sample size
   c. age
   d. gender
   e. inclusion and exclusion criteria
3. Intervention group
   a. type
   b. dose and frequency
   c. duration of intervention and follow-up
4. Control group
   a. type
   b. dose and frequency
   c. duration of intervention and follow-up
5. Outcomes: primary and secondary outcomes mentioned in the 'Types of outcome measures' section of this review .

If stated in the trial reports, the review authors recorded the sources of funding of all included studies and used this information to help

in the assessment of the clinical heterogeneity and external validity of all included trials.

Trial investigators were contacted and were asked to provide missing data or to clarify study details (see Table 1)

Assessment of risk of bias in included studies

Two review authors (EvZ and ZF) independently assessed the risk of bias in the included studies following the domain-based evaluation described in Chapter 8 of the*Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011). The evaluations were compared, and any inconsistencies between the review authors were discussed and resolved using a third review author (MEG) if required.

The following domains were rated separately for each of the included studies as 'low risk of bias', 'high risk of bias', and 'unclear' if the risk of bias was uncertain or unknown:

1. the allocation sequence was adequately generated ('sequence generation');
2. the allocation was adequately concealed ('allocation concealment');
3. knowledge of the allocated interventions was adequately prevented during the study ('blinding');
4. incomplete outcome data were adequately addressed;
5. reports of the study were free of suggestion of selective outcome reporting;
6. the study was apparently free of other sources of bias that could put it at high risk of bias, e.g. potential conflicts of interest, pharmaceutical funding, or support, or both (Lexchin 2003).

These assessments are reported in the 'Risk of bias' table for each individual study in the 'Characteristics of included studies' section of the review.

We also categorised and reported the overall risk of bias of each of the included studies according to the following:

- low risk of bias (plausible bias unlikely to seriously alter the results) if all criteria were met;
- unclear risk of bias (plausible bias that raises some doubt about the results) if one or more criteria were assessed as unclear; or
- high risk of bias (plausible bias that seriously weakens confidence in the results) if one or more criteria were not met.

These assessments are reported in the 'Risk of bias in included studies' section of this review.

Measures of treatment effect

We have reported the risk ratios (RR) for dichotomous data with their associated 95% confidence intervals (CI) and where appropriate, the number needed to treat (NNT) with the 95% CI and the baseline risk to which it applies, NNTs were calculated on the advice provided in Sections 12.5.4.1 and 12.5.4.2 of the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011). Duration of treatment was described narratively if data were available.

Unit of analysis issues

Cross-over studies

Unit of analysis issues can arise in studies where participants have been randomised to multiple treatments in multiple periods or where there has been an inadequate wash-out period. There were no cross-over trials with usable data identified in this review.

Within-patient studies

Only one within-patient trial with usable data was identified in this review. If further trials are identified in future updates, as the analysis of paired data is not possible with Review Manager, all data from within-patient studies will be entered into tables and summarised. Where possible, a conditional odds ratio (based on the discordant cases only) will be calculated and reported in the text (Curtin 2002).

Cluster randomised trials

We did not identify any cluster randomised trials for inclusion in this review. If in future updates cluster randomised trials, i.e. groups of individuals randomised to intervention or control, are identified in the searches, these will be checked for unit of analysis errors based on the advice provided in Section 16.3.4 of the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011).

Multiple treatment arms

Where studies had multiple treatment arms, data were taken from relevant intervention groups and combined with other studies if appropriate, following advice as presented in Chapter 16.5.4 of the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011).

Dealing with missing data

If data were missing from trials that were less than 10 years old, attempts were made to contact the investigators or sponsors of these studies wherever possible. We were successful in contacting the investigators in a number of the trials, to clarify inconsistencies and to obtain some of the missing data. For further details see Table 1.

The methods that we used to deal with unavailable missing data are based on the advice that is provided in Chapter 16.1 of the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011). Two types of missing data were identified; late exclusion and ineligibility of participants post randomisation due to negative mycology and, losses of participants at follow-up. In all instances we checked for any imbalance in the total number of exclusions and missing participants between treatment arms, and used this information to aid in our assessment of the potential risk of attrition bias within each individual trial. See ICH Expert Working Group 1998.

Although the retrospective exclusion of participants after randomisation is likely to create uncertainty with the overall treatment effect in these trials, this may more accurately reflect the real life clinical situation where a confirmed diagnosis may be delayed pending receipt of laboratory results (Fergusson 2002). Ideally, these trials should have included an intention-to-treat (ITT) analysis which included all randomised participants in addition to conducting sensitivity analyses investigating the impact of missing data, associated with ineligible participants, on the effect estimate. Inconsistency and incompleteness of data reporting in many of the older studies did not allow us to confidently undertake other than

an available case analysis for efficacy related to cure, whereas for adverse effects wherever possible we re-analysed and reported the data according to the ITT principle.
See 'Differences between protocol and review'.

Assessment of heterogeneity

We assessed clinical heterogeneity by examining the characteristics of the studies, the similarity between the types of participants, and the interventions. The degree of heterogeneity between the studies was assessed using the I^2 statistic. We reported heterogeneity as important if it was at least moderate to substantial by an I^2 statistic > 50% (Higgins 2011). If this could be explained by clinical reasoning and a coherent argument could be made for combining the studies, these were entered into a meta-analysis. In cases where the heterogeneity could not be adequately explained, the data were not pooled.

The clinical diversity between the studies included in this review as well as the limited number of studies that could be combined for each intervention only allowed us to make assessments of heterogeneity between the studies for a limited number of the comparisons.

Assessment of reporting biases

The low number of studies that evaluated similar interventions did not permit an assessment of publication bias.

Data synthesis

Four authors (MEG, EvZ, ZF and BS) analysed the data in RevMan and reported them in accordance with the advice in Chapter 9 in the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011). We combined data as appropriate from individual studies in a meta-analysis, using a random-effects model, if heterogeneity as measured by I^2 statistic was ≤ 50%. We presented a narrative synthesis for most of the treatment comparisons.

Subgroup analysis and investigation of heterogeneity

We pre-specified the following subgroup analyses in the protocol for this review, however these were not undertaken due to a paucity of studies examining similar interventions and comparisons.

- site of infection - tinea cruris or tinea corporis;
- means of mycological diagnosis - potassium hydroxide (KOH) microscopy, alternative microscopy, or growth of organism in culture;
- location of study - geographical factors, such as climate; and
- length of treatment - < two weeks or > two weeks.

Sensitivity analysis

In several of the studies with high levels of missing data we undertook sensitivity analyses to examine the impact of missing data, due to attritional losses, on the overall treatment effect. The potential impact of missing data on the findings of the review are considered further in the 'Discussion'.

RESULTS

Description of studies

See 'Characteristics of included studies' and 'Characteristics of excluded studies'.

Results of the search

We retrieved the following references:

- Searches of databases: 279 (five were duplicates)
- Searches of trials registers: seven
- Handsearches of the journal Mycoses (315 issues): 19 (of which 15 were included, one excluded (Wiedey 1982), and two await further assessment (Binet 1994; Kuokkanen 1982); one study Meinicke 1987 was a duplicate publication of an earlier paper but contained more data).
- Handsearches of the references to our included and excluded studies: 68 (of which 44 were included; 15 were excluded (Arreaza de Arreaza 1984; Baran 1979; el Darouti 1990; Hay 1985; Kagawa 1989; Kamalam 1980; László 1991; Nada 1994; No authors listed 1992; Sartani 1988; Scherwitz 1977; Szarmach 1984; Török 1993; Tulli 1988; Tulli 1988a); six await assessment (Alomar 1995; el Darouti 1989; Fredriksson 1974; Gooskens 1994; Male 1981; Nolting 1995); and three were duplicates (Nolting 1987 was a duplicate of Nolting 1985; Zaun 1987 was a duplicate of Zaun 1984; and Nolting 1988 was a duplicate of Nolting 1992).

The total number of references retrieved from all sources before de-duplication was 373. Following removal of duplicates we had 364 records. After examination of the titles and abstracts 191 of these were not relevant to this review. Full texts of the remaining 173 records were obtained and subjected to further evaluation.

We excluded a further 24 records, see Characteristics of excluded studies. Of the remaining 149 records, 12 were added to studies awaiting classification assessment (see the 'Characteristics of studies awaiting classification' section). Seven ongoing studies (see the 'Characteristics of ongoing studies' section) were identified which, if assessed as eligible, will be included in future updates of this review. One study, Banerjee 2012, was a further report of Banerjee 2011 providing additional data.

Finally, 129 studies were included. For further details see the 'Study Flow Diagram' Figure 1.

Figure 1. Study flow diagram.

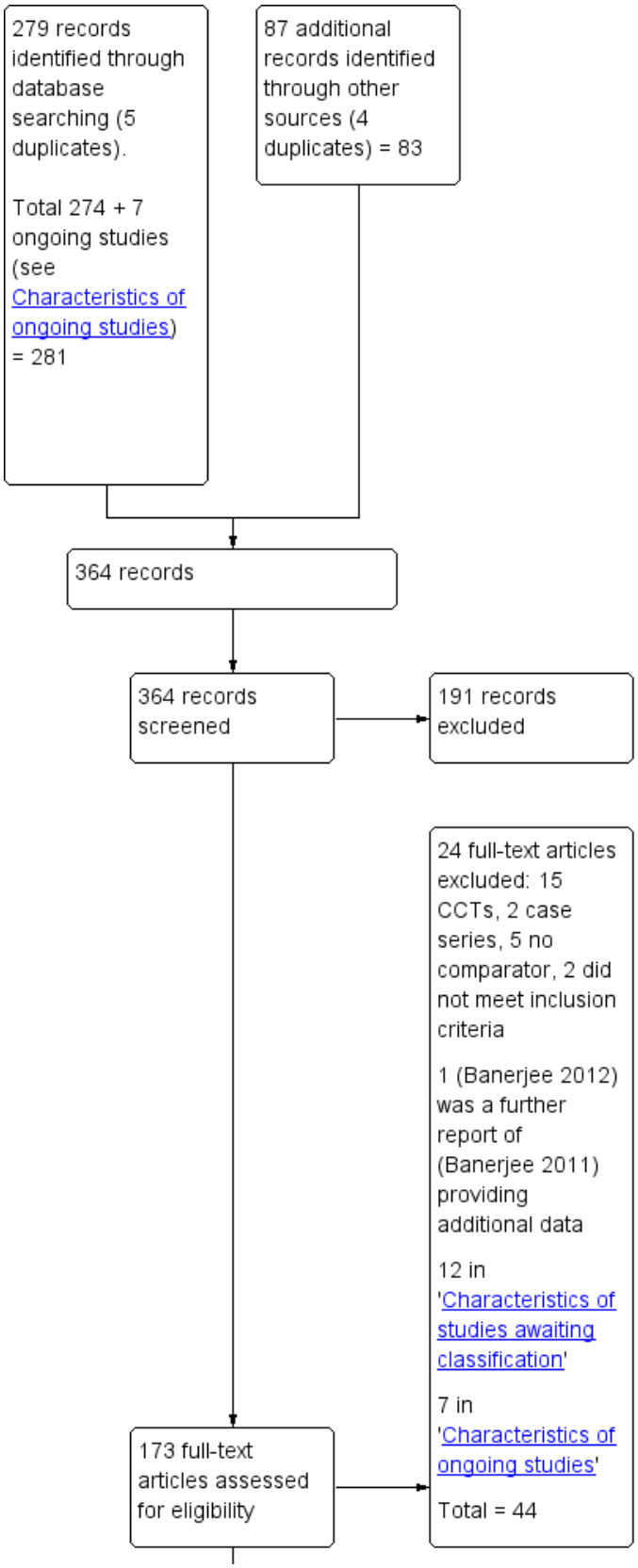
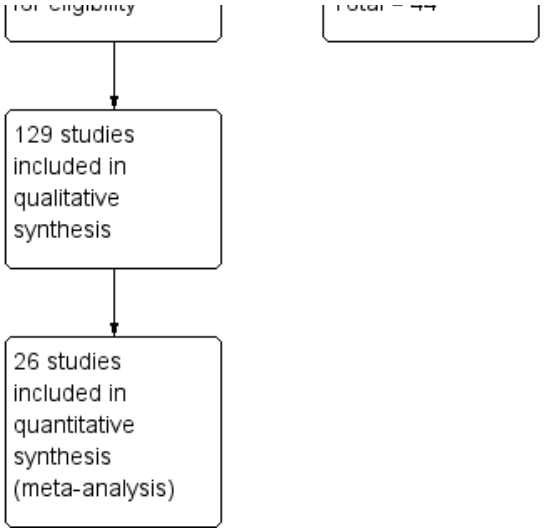


Figure 1. (Continued)



Included studies

The review included 129 studies comprising 18,086 participants (see the 'Characteristics of included studies' section).

Characteristics of the trial setting and methods

All of the studies were randomised controlled trials, 27 had a placebo arm, 98 an active control treatment arm and four studies included both an active arm (or arms) and placebo arm. Most (118) of the studies were conducted prior to the year 2000. More than half (72) studies were single-centre studies, 51 were multi-centre studies and in six studies it was unclear. Most studies appeared to be conducted within dermatology outpatient clinics. The studies were conducted in Europe (62), in the USA (21), in Mid and South-America (7), in Asia (30), in Africa (4) and one remained unclear and four on two different continents.

Characteristics of the participants

Although the total number of participants was 18,086, incomplete reporting of demographic details in 20 of the studies only allowed us to confirm that 8029 of the total were male and 3836 were female and for 6221 the gender was not clearly reported. Ten studies included only male participants and the remaining studies were mixed, both men and women, but with a preponderance of men. The majority of participants were in the age range of 18 to 70 years although there were a small number of studies with participants outside this range, and the median age across the studies was 40 years. In one-third of the studies the infections were confined to tinea cruris, tinea corporis or both, and these were combined with other dermatophyte infections, yeasts infections (Candida or pityriasis versicolor) or erythrasma in the remaining studies.

Characteristics of the interventions

A wide range of interventions were evaluated, which can be categorised into six groups: azoles, allylamines, benzylamines, hydroxy pyridones, thiocarbamates and others (see Table 2). However, there was a clear over-representation of the azole group among the interventions that were evaluated. The 129 studies covered 92 comparisons, most of which included an active control arm and of these comparisons, a total of 37, which had been evaluated in 63 studies, did not report any usable data (see Table 3). Study duration varied from one week to two months, but in the majority of studies this was between two and four weeks. Interventions were normally applied once daily or twice daily, in some cases three or four times daily.

Characteristics of the outcome measures

Our primary outcomes were in part addressed in most of the studies although hardly any of them directly assessed duration of treatment until clinical- or participant-judged cure had been achieved. However, although not listed as a specific outcome in any of the studies, in some of them it was possible to retrieve data, which enabled calculation of the duration of treatment until clinical cure.

Excluded studies

Twenty-four studies were excluded, and the reasons for their exclusion are reported in the 'Characteristics of excluded studies' tables. All of these studies were excluded only after assessment of the full text of the report. The most frequent reason for their exclusion was that they were non-randomised trials.

Risk of bias in included studies

We assessed each of the included studies for risk of bias and reported the judgements for the individual domains in the 'Risk of bias' table associated with each study. We have also presented these in the 'Risk of bias' graph in Figure 2 and the 'Risk of bias' summary in Figure 3.

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

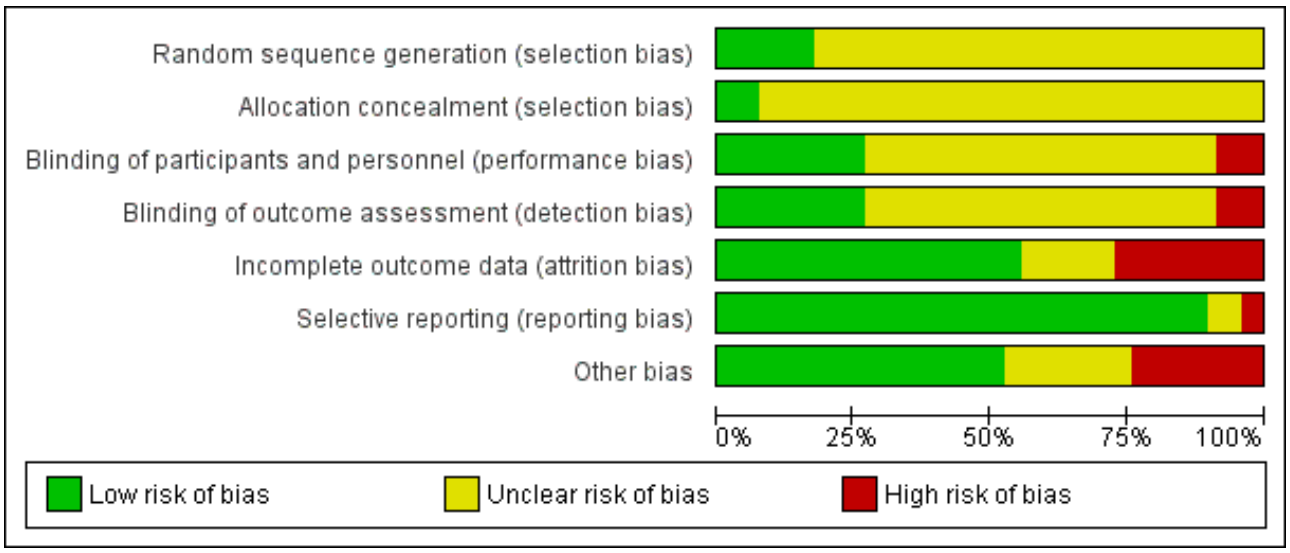


Figure 3. 'Risk of bias' summary: review authors' judgements about each risk of bias item for each included study.

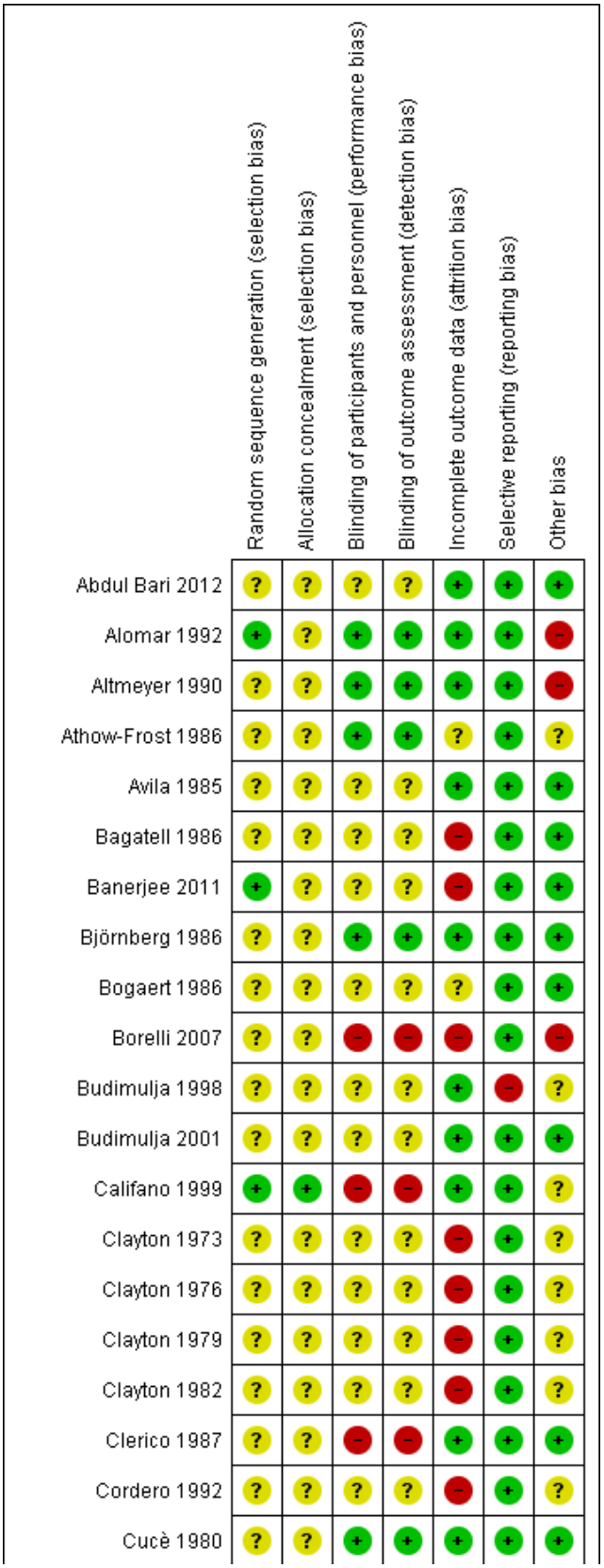


Figure 3. (Continued)

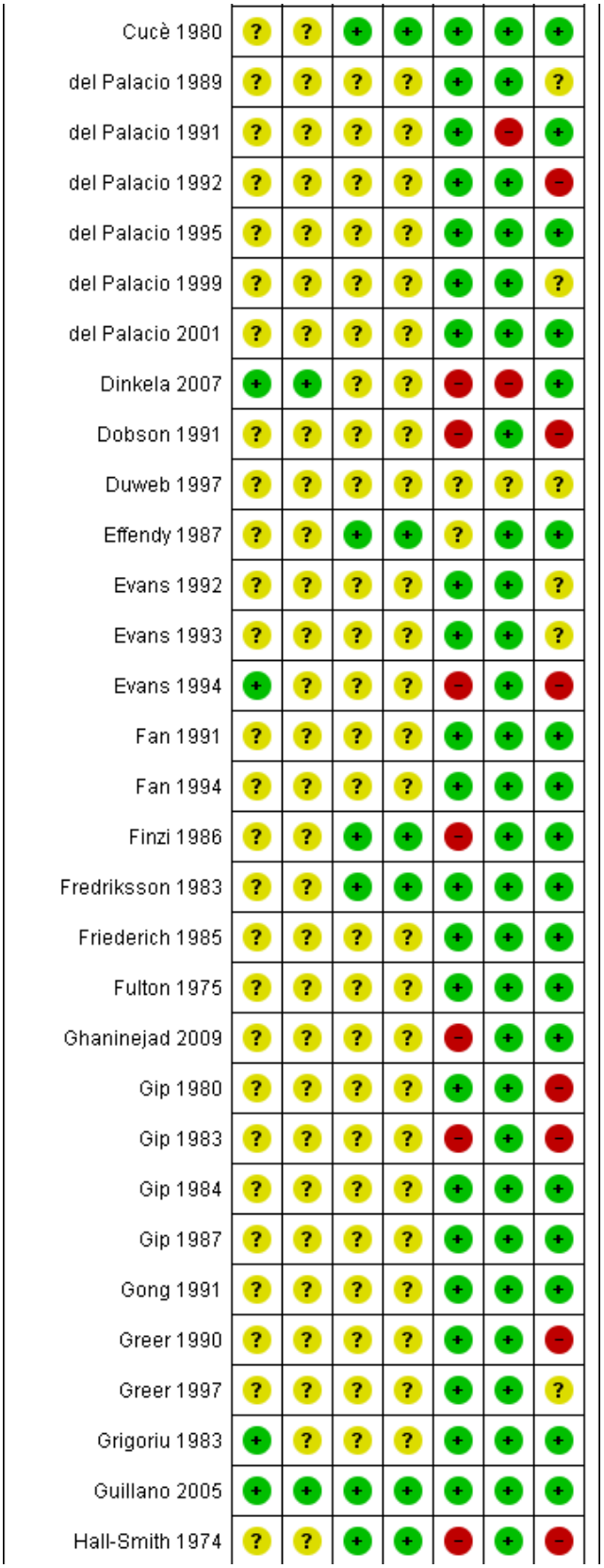


Figure 3. (Continued)

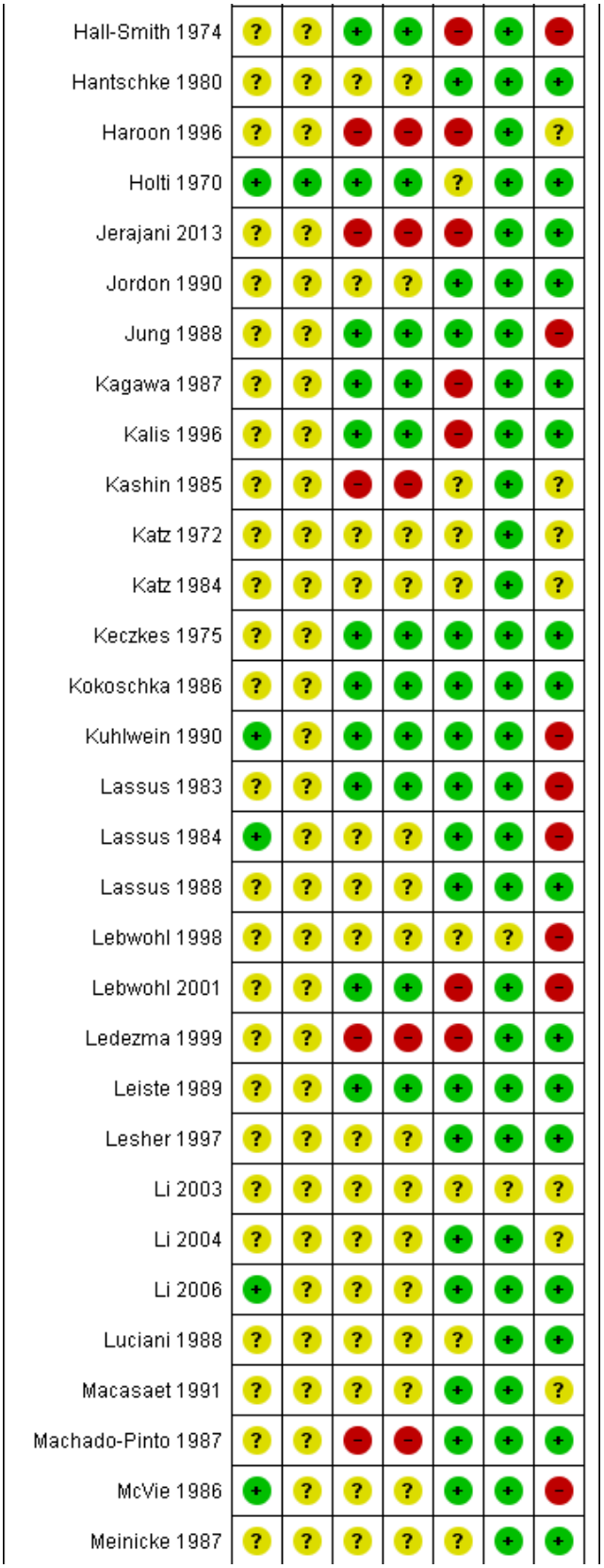


Figure 3. (Continued)

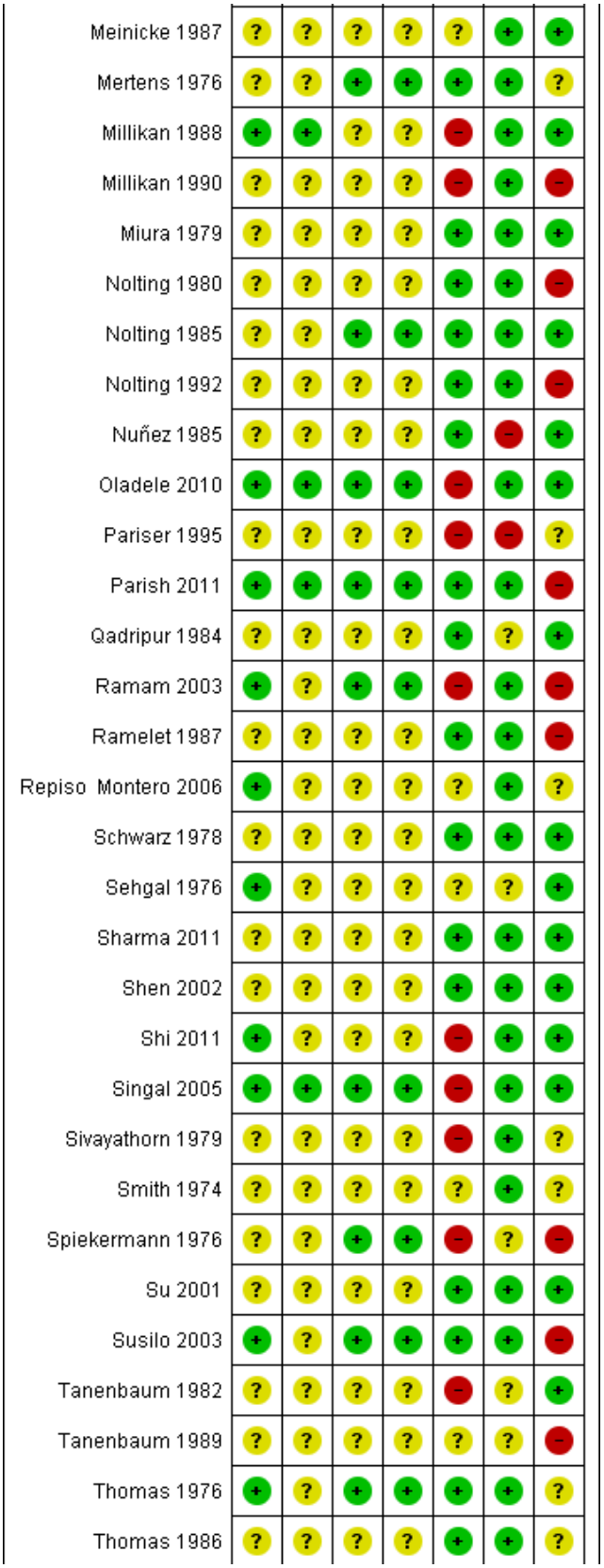
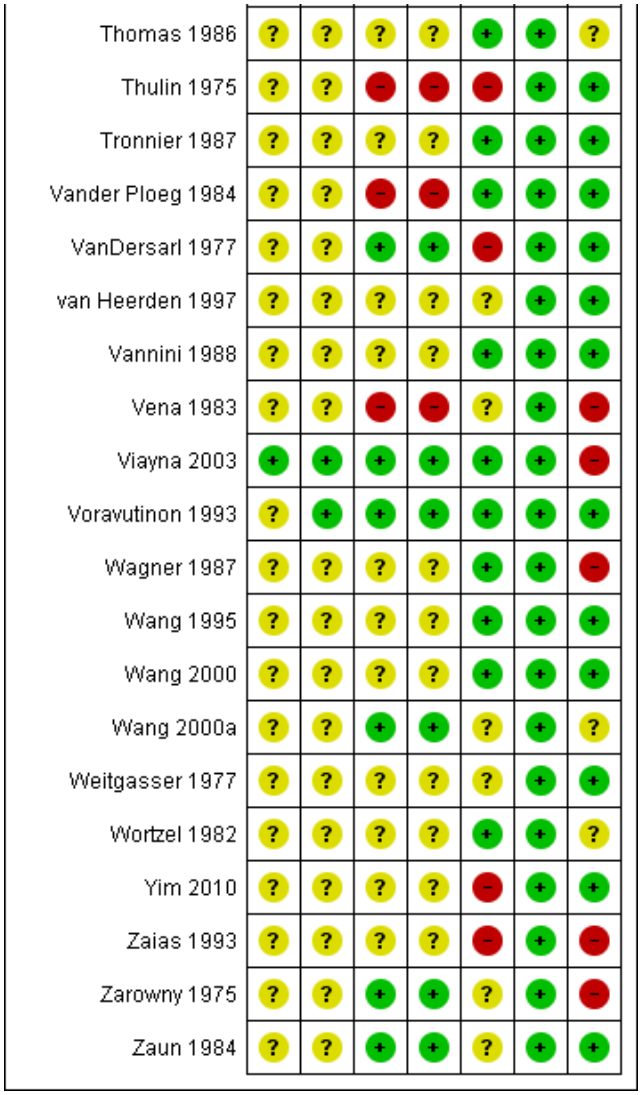


Figure 3. (Continued)



The overall risk of bias was assessed for each study, and 64 were categorised as high risk of bias (plausible bias that seriously weakens confidence in the results) because one or more domains received a judgement of high risk. The remaining 65 studies were rated as unclear risk of bias (plausible bias that raises some doubt about the result) because one or more criteria were assessed as unclear.

Some of these assessments were, to a certain extent, based on the inadequate reporting of the criteria that are a prerequisite in the evaluation of methodological rigour, in terms of trial design and conduct. Concealment of the allocation sequence and blinding are key domains in the assessment of risk of bias, and a number of the studies in this review provided insufficient detail to enable accurate judgements to be made. Protocol deviation, losses to follow-up with incomplete data, and subsequent available case analyses were other important sources of potential bias in a number of the included studies. We were able to amend the judgements for a number of the domains after contacting several of the trial investigators. For these and further details, see the 'Risk of bias' tables in the 'Characteristics of included studies' section.

Allocation

The methods used to generate the allocation sequence and how the sequence was concealed, such that participants and investigators enrolling participants could not foresee the upcoming assignment, are the most important and sensitive indicators that bias has been minimised in a clinical trial (Schulz 1995).

Sequence generation

In 18 of the studies the method used to generate the allocation sequence was described in sufficient detail to allow an assessment of whether it should produce comparable groups (Alomar 1992; Califano 1999; Evans 1994; Grigoriu 1983; Guillano 2005; Holti 1970; Kuhlwein 1990; Lassus 1984; Li 2006; McVie 1986; Millikan 1988; Ramam 2003; Repiso Montero 2006; Sehgal 1976; Shi 2011; Susilo 2003; Thomas 1976; Viayna 2003). All of these studies were judged as low risk of bias for this domain. After email communication with trial investigators we were able to confirm adequate sequence generation in five additional studies (Banerjee 2011; Dinkela 2007; Oladele 2010; Parish 2011; Singal 2005) and therefore, this domain

was judged as low risk of bias for 23 of the studies. The remaining studies were judged as unclear risk of bias.

Allocation concealment

Only eight of the studies provided adequate reassurance that the intervention allocations could not have been foreseen in advance of, or during, enrolment and were therefore judged low risk of bias for this domain (Califano 1999; Dinkela 2007; Guillano 2005; Holti 1970; Millikan 1988; Oladele 2010; Singal 2005; Voravutinon 1993). After email contact with the investigators, we were able to confirm low risk of bias for this domain in two further studies (Parish 2011; Viayna 2003). In the remainder of the studies the method used to conceal the allocation sequence was not reported and they received a judgment of unclear risk of bias for this domain.

Blinding

The majority of studies were reported to be 'double-blind', and five as 'single blind' (Fan 1991; Fredriksson 1983; Li 2003; Pariser 1995; Thomas 1986). Blinding was achieved largely through the use of either identical pre-labelled bottles or tubes or with the use of similar packaging. The measures used to blind study participants and personnel from knowledge of which intervention a participant received as well as blinding of outcomes assessors were described in sufficient detail in only 35 of the studies.

Seven studies (Borelli 2007; Califano 1999; Clerico 1987; Haroon 1996; Jerajani 2013; Kashin 1985; Thulin 1975) were described as open-label, and therefore the outcome or outcome measurement was likely to be influenced by lack of blinding and thus, this domain was judged as high risk of bias. A further four trials were assessed as high risk of bias for this domain because of a total lack of reporting or because inadequate measures were used to blind participants or trialists to the allocated intervention (Ledezma 1999; Machado-Pinto 1987; Vander Ploeg 1984; Vena 1983).

See 'Risk of bias in included studies'.

Incomplete outcome data

In slightly more than half (72) of the studies, incomplete outcome data appear to have been adequately addressed and the losses were reasonably well-balanced across intervention groups, with similar reasons for missing data across the groups. However, a judgement of high risk of bias was given for 35 studies, mainly due to substantial (> 20%) drop-out rates and subsequent available case data analysis. We judged the risk of bias in the remaining 22 studies unclear for this domain.

Selective reporting

The protocols were not available for any of the included studies. Based on the information in the methods section of the reports, 116 of the 129 studies appear to have reported all prespecified outcomes and were therefore judged to be free of selective reporting. The 13 remaining studies were judged to be unclear (8), and high risk (5) of bias.Three of these studies (Duweb 1997; Lebwohl 1998; Li 2003) were abstracts to conference proceedings, which provided insufficient information to make a clear judgement for this domain.

Other potential sources of bias

Half of the included studies were free of other potential sources of bias, but for 31 studies this domain was assessed at high risk of bias, largely because the investigators were employed by the pharmaceutical company conducting the study and a few studies suffered from baseline imbalance. The remainder (30) were judged as at unclear risk of bias.

Effects of interventions

See: **Summary of findings for the main comparison** Terbinafine 1% cream/gel compared with placebo cream/gel for tinea cruris and tinea corporis; **Summary of findings 2** Naftifine 1% cream once or twice daily compared with placebo cream once or twice daily for tinea cruris and tinea corporis; **Summary of findings 3** Azoles compared with allylamines for tinea cruris and tinea corporis; **Summary of findings 4** Azoles compared with moderate-potent corticosteroid/azole combinations for tinea cruris and tinea corporis; **Summary of findings 5** Azoles compared with benzylamines for tinea cruris and tinea corporis; **Summary of findings 6** Azoles versus placebo for tinea cruris and tinea corporis

We have addressed our prespecified outcomes under the following intervention headings

1. Azoles

1.1 Azoles versus placebo (comparisons 1-4)
1.2 Comparisons of different azoles (comparisons 5-14)
1.3 Comparisons of same azole with different dosing regimens (comparisons 15-16)

2. Allylamines

2.1 Allylamines versus placebo (comparisons 17-19)
2.2 Comparisons of same allylamines with different dosing regimens (comparison 20)

3. Azoles versus allylamines

3.1 Comparisons of azoles and terbinafine (comparisons 21-23)
3.2 Comparisons of azoles and naftifine (comparisons 24-26)

4. Corticosteroid combined therapies - studies combining topical antifungals with topical corticosteroids

4.1 Azoles versus corticosteroid and azole combination (comparisons 27-32)

5. Other topical antifungals

5.1 Comparisons of azoles and other topical antifungals (comparisons 33-42)
5.2 Comparisons of azoles and benzylamines (comparisons 43-45)
5.3 Comparisons of other antifungals and placebo (comparisons 46-49)
5.4 Comparisons of all other antifungals (comparisons 50-55)

Pooling of outcome data across studies to provide a summary estimate of effect was only possible for several outcomes in six interventions and comparisons. Three of these investigated the effects of an individual intervention versus placebo: clotrimazole 1% cream versus placebo, topical terbinafine versus placebo and naftifine 1% versus placebo. The other three compared different classes of interventions: azoles versus moderate to potent corticosteroid and azole combination therapy, azoles versus

allylamines and azoles versus benzylamines. It was only possible to pool data for mycological cure, clinical cure and adverse effects for these comparisons, with the exception of studies evaluating naftifine versus placebo and azoles versus benzylamines which reported insufficient clinical cure data to enable pooling. See Summary of findings for the main comparison; Summary of findings 2; Summary of findings 3; Summary of findings 4; Summary of findings 5; Summary of findings 6.

Outcome data for mycological and clinical cure were collected at the end of the prescribed length of treatment, or at the follow-up visit closest to this time point, and at least two weeks after the start of treatment. Where negative microscopy and negative culture data were separately available to calculate mycological cure, data on culture were used in the relevant meta-analyses, unless the majority of studies in any one meta-analysis only assessed microscopy. Relapse, length of treatment until clinical cure and patient satisfaction were not assessed in the majority of studies. We report data for all outcomes based on an available case analysis, with the exception of adverse events data. For further details see Dealing with missing data, and Characteristics of included studies. Where studies had multiple treatment arms, data were split into pair-wise comparison groups as far as possible.

Of the 129 included studies, almost half (63), covering 37 comparisons provided no usable or retrievable data and did not contribute further to the results of this review. The main reasons why data could not be used were: the absence of separate data for different tinea infections, or due to the very limited data available in abstracts to conference proceedings. See Table 3.
In addition, a substantial number of the studies included in this review were categorised as 'unclear' or 'high' risk of bias (see Figure 2; Figure 3) and therefore caution is advised in interpretation of their results and in the extrapolation of the effects of these interventions.

1 Azoles

1.1 Azoles versus placebo

Four studies provided usable data comparing a topical azole against a placebo (Bagatell 1986; Miura 1979; Spiekermann 1976; Tanenbaum 1989). In all studies with the exception of Bagatell 1986, both mycological and clinical cure significantly favoured azoles. Data were not pooled as different comparisons were carried out in these studies.

(1) Clotrimazole (1%) solution/cream versus vehicle solution/ cream each applied twice daily

Two trials within Spiekermann 1976, which were assessed as high risk of bias, reported some usable outcome data for these comparisons. The impact of the high attrition rate, in both trials, and subsequent available case analysis is likely to have inflated the effect estimate and raises concerns about the possible reliability of the data and conclusions. Outcome data for participants with tinea cruris and tinea corporis were not reported separately. A second three-armed study (Miura 1979) also provided data for this comparison (see also comparison 2 and 5).

Primary outcomes

Rate of mycological cure

Both trials in Spiekermann 1976 were combined for mycological cure:

Potassium hydroxide (KOH) microscopy-assessed cure was achieved in 103/111 of the participants in the clotrimazole group compared to 42/102 in the vehicle group (risk ratio (RR) 2.25, 95% confidence interval (CI) 1.78 to 2.86; P < 0.00001; NNT 2, 95% CI 2 to 3). Cure based on negative culture was achieved in 99/111 of the participants in the clotrimazole group versus (30/102) in the vehicle group (RR 3.03, 95% CI 2.23 to 4.12; P < 0.00001; NNT 2, 95% CI 2 to 3).

In Miura 1979, KOH-assessed cure in tinea corporis was more effective in the clotrimazole group (28/31 cured) compared to placebo (12/29 cured) (RR 2.18, 95% CI 1.39 to 3.42; P = 0.0006; NNT 3, 95% CI 2 to 4). Similarly, in tinea cruris, clotrimazole was also more effective, with 30/34 cured compared to 10/37 in the placebo group (RR 3.26, 95% CI 1.90 to 5.62; P < 0.0001; NNT 2, 95% CI 2 to 3).

When pooling data from Miura 1979 and Spiekermann 1976 for mycological cure, clotrimazole remains more effective compared to placebo (RR 2.87, 95% CI 2.28 to 3.62; P < 0.00001; NNT 2, 95% CI 2 to 3, I^2 = 0%), see Analysis 1.1.

Clinical cure

The overall evaluation of improvement in signs and symptoms was reported in both trials in Spiekermann 1976, but this did not include any data on clinical cure rates.

In Miura 1979, clinical cure favoured clotrimazole over placebo in both tinea corporis: 28/39 cured at two weeks compared to 8/45 in the placebo group (RR 4.04, 95% CI 2.09 to 7.80, P < 0.0001; NNT 2, 95% CI 2 to 3), and tinea cruris: 30/43 cured at two weeks in the clotrimazole group compared to 11/40 in the placebo group (RR 2.54, 95% CI 1.48 to 4.35, P = 0.0007; NNT 3, 95% 2 to 5)

Secondary outcomes

Relapse or recurrence

Not assessed.

Adverse effects

Data from the 699 participants in Spiekermann 1976 who received clotrimazole solution or cream were combined, and the overall incidence of adverse events that were possibly drug-related was 2.7%. These consisted mainly of irritation, stinging or burning and led to the discontinuation of treatment in just 0.6% of the participants. The incidence of possibly drug-related adverse events in participants receiving the vehicles was 3% and urticaria was reported in two participants who had received the vehicle solution.

In Miura 1979, there was no difference between the clotrimazole and placebo groups, with 3/82 participants in the clotrimazole group reporting an adverse effect compared to 6/85 in the placebo group (RR 0.52, 95% CI 0.13 to 2.00). These adverse effects consisted of smarting, burning, redness and itching and an acne like rash was reported in the placebo group.

Duration of treatment until clinical cure

Not assessed.

Participant-judged cure

Not assessed.

(2) Econazole cream versus placebo cream each applied twice daily

A single three-armed study compared these interventions and reported usable data (Miura 1979) (see also comparison 1 and 5). Primary outcome data for participants with tinea cruris and tinea corporis were reported separately.

Primary outcomes

Rate of mycological cure

Tinea corporis: After two weeks of treatment, 32/34 of the participants in the econazole group had negative microscopy compared to 12/29 in the placebo group (RR 2.27, 95% CI 1.46 to 3.54; P = 0.0003; NNT 2, 95% CI 2 to 4) significantly favouring econazole.

Tinea cruris: 28/34 of the econazole group had negative microscopy compared to 10/37 in the placebo group (RR 3.05, 95% CI 1.75 to 5.29; P < 0.0001; NNT 2, 95% CI 2 to 3) also favouring econazole.

Clinical cure

Tinea corporis: after two weeks, 26/41 of the participants in the econazole group were assessed as clinically cured compared to 8/45 in the placebo group (RR 3.57, 95% CI 1.83 to 6.97; P = 0.0002; NNT 3, 95% CI 2 to 4) favouring econazole.

Tinea cruris: 26/43 in the econazole group were cured compared to 11/40 in the placebo group (RR 2.20, 95% CI 1.26 to 3.84; P = 0.006; NNT 4, 95% CI 2 to 9).

Secondary outcomes

Relapse or recurrence

Not assessed.

Adverse effects

There was no difference in the adverse effects reported between these groups with 2/84 in the econazole group having an adverse effect compared to 6/85 in the placebo group (RR 0.34, 95% CI 0.07 to 1.62). These adverse effects consisted of smarting, burning, redness and itching and an acne like rash was reported in the placebo group.

Duration of treatment until clinical cure

Not assessed.

Participant-judged cure

Not assessed.

(3) Bifonazole (1%) cream versus vehicle each applied once a day

One study rated as high risk of bias evaluated this intervention. Outcome data for participants with tinea cruris and tinea corporis were not reported separately (Bagatell 1986).

Primary outcomes

Rate of mycological cure

At the end of the treatment period of thee weeks, KOH-assessed cure rates were 89% (17/19) in the bifonazole group compared to 71% (10/14) in the vehicle group (RR 1.25, 95% CI 0.87 to 1.81). Cure rates based on negative cultures were 100% (19/19) in the bifonazole group compared to 71% (10/14) in the vehicle group (RR 1.39, 95% CI 0.99 to 1.95).

Clinical cure

At the end of three weeks, clinical cure, which was defined as having very mild symptoms, was reported in 18/19 participants in the bifonazole group compared to 13/14 in the vehicle group (RR 1.02, 95% CI 0.85 to 1.22).

Secondary outcomes

Relapse or recurrence

Although this was not assessed there appeared to have been a number of relapses in the vehicle group, but it was not possible to accurately confirm these in view of the large number of withdrawals.

Adverse effects

No adverse events were reported in either group.

Duration of treatment until clinical cure

Not assessed.

Participant-judged cure

Not assessed.

(4) Sulconazole (1%) cream versus vehicle each applied twice daily

Only one study provided usable data for these interventions Tanenbaum 1989 (second study). Outcome data for participants with tinea cruris and tinea corporis were not reported separately.

Primary outcomes

Rate of mycological cure

After three weeks of treatment, 26/26 participants in the sulconazole group had negative KOH microscopy compared to 10/23 in the vehicle group (RR 2.24, 95% CI 1.42 to 3.54; P = 0.0005; NNT 2, 95% CI 2 to 3). Similarly, in participants with a positive culture at baseline, after three weeks of treatment 21/21 in the sulconazole group had negative cultures compared to 10/24 in the vehicle group (RR 2.33, 95% CI 1.46 to 3.70; P = 0.0004; NNT 2; 95% CI 2 to 3).

Clinical cure

After three weeks of treatment, 25/26 of participants in the sulconazole group were assessed as clinically cured, as determined by complete clearance of lesions, compared to 2/26 in the vehicle group (RR 12.50, 95% CI 3.29 to 47.44; P = 0.0002; NNT 2, 95% CI 2 to 2).

Secondary outcomes

Relapse or recurrence

Not assessed.

Adverse effects

None of the 28 participants in the sulconazole group experienced an adverse event compared to 5/29 in the vehicle group who reported erosions and burning reactions (RR 0.09, 95% CI 0.01 to 1.63).

Duration of treatment until clinical cure

Not assessed.

Participant-judged cure

Not assessed.

1.2 Comparisons of different azoles

(5) Clotrimazole (1%) cream versus econazole (1%) cream each applied twice daily

A single three-armed study compared these interventions and reported usable data (Miura 1979) (see also comparison 1 and 2). Primary outcome data for participants with tinea cruris and tinea corporis were reported separately.

Primary outcomes

Rate of mycological cure

Tinea corporis: After two weeks of treatment, 32/34 of the participants in the econazole group had negative microscopy compared to 28/31 in the clotrimazole group (RR 1.04, 95% CI 0.90 to 1.20).

Tinea cruris: 28/34 of the econazole group had negative microscopy compared to 30/34 in the clotrimazole group (RR 0.93, 95% CI 0.77 to 1.14).

Clinical cure

Tinea corporis: after two weeks, 26/41 of the participants in the econazole group were assessed as clinically cured compared to 28/39 in the clotrimazole group (RR 0.88, 95% CI 0.65 to 1.20).
Tinea cruris: 26/43 in the econazole group were cured compared to 30/43 in the placebo group (RR 0.87, 95% CI 0.63 to 1.18).

Secondary outcomes

Relapse or recurrence

Not assessed.

Adverse effects

There was no difference in the adverse effects reported between these groups with 2/84 in the econazole group having an adverse effect compared to 3/82 in the clotrimazole group (RR 0.65, 95% CI 0.11 to 3.79).

Duration of treatment until clinical cure

Not assessed.

Participant-judged cure

Not assessed.

(6) Clotrimazole (1%) cream versus fluconazole (0.5%) gel each applied twice daily

One study compared these interventions in participants with tinea corporis (Banerjee 2011). The same data for participants in the clotrimazole group was published in an earlier paper (see comparison 33).

Primary outcomes

Rate of mycological cure

After four weeks of treatment, 32/42 participants in the clotrimazole group had negative KOH microscopy compared to 33/41 in the fluconazole group (RR 0.95, 95% CI 0.75 to 1.19).

Clinical cure

Clinical cure based on physician's assessment of efficacy rated 'good' or 'excellent' was achieved in 40/42 participants in the clotrimazole group, compared to 37/41 in the fluconazole group after four weeks of treatment (RR 1.06, 95% CI 0.93 to 1.19).

Secondary outcomes

Relapse or recurrence

Only three participants in the clotrimazole group and four participants in the fluconazole group attended the follow-up visit four weeks after the end of treatment. There was no sign of clinical or mycological relapse in any of these participants.

Adverse effects

One participant in each group reported increased erythema at the application site which persisted throughout treatment.

Duration of treatment until clinical cure

Not assessed.

Participant-judged cure

Participant assessment of efficacy was reported as 'excellent' or 'good' by 38/42 in the clotrimazole group compared to 36/41 in the fluconazole group (RR 1.03, 95% CI 0.89 to 1.20).

(7) Miconazole (2%) cream versus clotrimazole (1%) cream each applied twice daily to three times daily

One study, with more than 40% losses to follow-up and assessed as high risk of bias, compared these two interventions and provided some usable outcome data (Clayton 1976), however, the results should be viewed in the context of the significant losses to follow-up. Data were reported for participants with tinea cruris only. Treatment was applied twice daily.

A further four-armed study compared these two interventions amongst two others (Sivayathorn 1979) (see also comparison 35, 37, 38, 45 and 55). Treatment was applied three times a day.

Primary outcomes

Rate of mycological cure

In Clayton 1976, at the end of the study, 14/15 participants in the miconazole group were cured, based on a negative culture, compared to 10/11 in the clotrimazole group (RR 1.03, 95% CI 0.82 to 1.29).

In Sivayathorn 1979, after two weeks, 21/27 of the participants in the miconazole group were cured compared to 16/27 in the clotrimazole group (RR 1.31, 95% CI 0.90 to 1.90).

Data from the two studies were not pooled as statistical heterogeneity was substantial (I^2 = 65%).

Clinical cure

Not assessed in Clayton 1976.

In Sivayathorn 1979, clinical cure was achieved in 22/27 participants in the miconazole group compared to 21/27 in the clotrimazole group (RR 1.05, 95% CI 0.80 to 1.37).

Secondary outcomes

Relapse or recurrence

In Clayton 1976, in the miconazole group 1/14 relapsed after four weeks of therapy compared to 2/10 in the clotrimazole group (RR 0.36, 95% CI 0.04 to 3.42).

This outcome was not assessed in Sivayathorn 1979.

Adverse effects

The report of Clayton 1976 did not provide separate data for participants with tinea cruris, however, only three participants in total experienced adverse effects, which were transient burning and irritation, and did not require discontinuation of treatment. No adverse effects were reported in the participants in Sivayathorn 1979.

Duration of treatment until clinical cure

Not assessed.

Participant-judged cure

Not assessed.

(8) Sertaconazole nitrate (2%) cream versus miconazole (2%) cream each applied twice daily

A single study provided data for these interventions (Sharma 2011). Outcome data for participants with tinea cruris and tinea corporis were not reported separately.

Primary outcomes

Rate of mycological cure

At the end of week two, 76/122 participants in the sertaconazole group were cured based on a negative culture compared to 57/128 in the miconazole group (RR 1.40, 95% CI 1.10 to 1.77; P = 0.006; NNT 6, 95% CI 4 to 19).

Clinical cure

The rates for clinical and mycological cure were identical.

Secondary outcomes

Relapse or recurrence

Not assessed.

Adverse effects

In the sertaconazole group 5/128 participants experienced an adverse event compared to 9/132 in the miconazole group (RR 0.53, 95% CI 0.18 to 1.54). The adverse events were reported to be mild, transient and included dry skin, itching, burning, erythema and irritation.

Duration of treatment until clinical cure

Not assessed.

Participant-judged cure

Not assessed.

(9) Fenticonazole (2%) cream versus miconazole (2%) cream each applied twice daily

Only one study with a small sample size, consisting of one participant with tinea cruris and three with tinea corporis, provided very limited data for this comparison (Clerico 1987).

Primary outcomes

Rate of mycological cure

Insufficient separate data were reported for the three participants with tinea corporis.

Clinical cure

The single participant with tinea cruris in the fenticonazole group and two of the three participants with tinea corporis in the miconazole group, were considered to be cured at the completion of the study.

Secondary outcomes

Relapse or recurrence

Not assessed.

Adverse effects

No adverse events were reported in either group.

Duration of treatment until clinical cure

Not assessed.

Participant-judged cure

Not assessed.

(10) Bifonazole (1%) cream once a day versus miconazole (2%) cream twice daily

A single within-patient study of participants with tinea cruris, which was assessed as high risk of bias, compared these two interventions (Vena 1983). Access to original data to enable an accurate within-patient analysis was unobtainable.

Primary outcomes

Rate of mycological cure

After two weeks of treatment, all (30/30) of the sites treated with bifonazole 1% had negative KOH microscopy and culture results, compared to 23/30 in the miconazole group (RR 1.30, 95% CI 1.06 to 1.59; P = 0.01; NNT 5, 95% CI 3 to 10).

Clinical cure

At two weeks after completion of treatment, all sites treated with bifonazole were reported to be completely cured, whereas some symptoms persisted in sites treated with miconazole.

Secondary outcomes

Relapse or recurrence

At four weeks after completion of treatment, no recurrence of symptoms or mycological evidence of infection was reported in either treatment group.

Adverse effects

No adverse effects were reported in either group.

Duration of treatment until clinical cure

Not assessed.

Participant-judged cure

Not assessed.

(11) Tioconazole (1%) cream versus miconazole (2%) cream each applied twice daily

One study, which included participants with tinea cruris, tinea corporis and other fungal infections compared these interventions (Vander Ploeg 1984).

Primary outcomes

Rate of mycological cure

At 28 days, mycological cure as assessed by negative KOH microscopy and culture was achieved in 9/10 of the tioconazole group compared to 6/6 of the miconazole group in those participants with tinea corporis (RR 0.93, 95% CI 0.68 to 1.27).

In those with tinea cruris, all participants in both groups were cured at 28 days (7/7 in the tioconazole group and 10/10 in the miconazole group).

Clinical cure

Clinical cure data were combined with mycological cure data, therefore cannot be reported accurately.

Secondary outcomes

Relapse or recurrence

At four weeks follow-up, no relapses were seen in either group.

Adverse effects

No separate data were provided for tinea cruris and tinea corporis, but the authors report five patients who experienced adverse effects, one in the miconazole group and four in the tioconazole group.

Duration of treatment until clinical cure

Not assessed.

Participant-judged cure

Not assessed.

(12) Bifonazole (1%) gel once a day versus sulconazole (1%) cream twice daily

One study, which included participants with tinea pedis (two sites) and tinea cruris (one site), compared these interventions and reported data (Thomas 1986).

Primary outcomes

Rate of mycological cure

After three weeks of treatment, the only participant with mycologically proven tinea cruris in the bifonazole group and a solitary participant in the sulconazole group were assessed cured based on negative KOH microscopy and culture.

Clinical cure

After three weeks of treatment, both participants were considered clinically cured.

Secondary outcomes

Relapse or recurrence

Four weeks after the end of treatment there was no evidence of relapse in the participant in the bifonazole group and the participant in the sulconazole group failed to attend for follow-up

Adverse effects

No adverse events were reported in either group.

Duration of treatment until clinical cure

Not assessed.

Participant-judged cure

Not assessed.

(13) Sulconazole (1%) cream once a day versus clotrimazole (1%) cream twice daily

Only one study provided usable data for these interventions Tanenbaum 1989 (first study). Outcome data for participants with tinea cruris and tinea corporis were not reported separately.

Primary outcomes

Rate of mycological cure

All of the participants in both intervention groups, (29/29 sulconazole; 26/26 clotrimazole) with positive KOH microscopy at baseline had negative cultures after three weeks of treatment. Similarly, all participants (27/27 sulconazole; 25/25 clotrimazole) with positive cultures at baseline had negative cultures at three weeks.

Clinical cure

After three weeks of treatment, clinical cure as determined by complete clearing of lesions, was achieved in all of the participants in the sulconazole group (29/29) as well as the clotrimazole group (26/26).

Secondary outcomes

Relapse or recurrence

Not assessed.

Adverse effects

No adverse effects were reported in the sulconazole group whereas 4/30 participants in the clotrimazole group reported side effects consisting of severe irritation (3) and one participant with fissuring and erythema (RR 0.11, 95% CI 0.01 to 1.98).

Duration of treatment until clinical cure

Not assessed.

Participant-judged cure

Not assessed.

(14) Oxiconazole (1%) cream versus ketoconazole (2%) cream each applied once a day

Only one study, which included participants with tinea cruris, compared these interventions and reported some usable data (Kalis 1996).

Primary outcomes

Rate of mycological cure

No separate data for mycological cure were reported at day 14 (cure rate combined with clinical cure). At day 21, no mycological cure data were reported.

Clinical cure

At day 21, 35/36 of the oxiconazole group were considered clinically cured, compared to 26/30 of the ketoconazole group (RR 1.12, 95% CI 0.96 to 1.30).

Secondary outcomes

Relapse or recurrence

Not assessed.

Adverse effects

No adverse effects were reported in the 42 participants in the oxiconazole group whereas 9/37 participants in the ketoconazole group experienced irritant dermatitis (6) which necessitated the discontinuation of treatment in one participant, and contact dermatitis in three requiring the cessation of treatment (RR 0.05, 95% CI 0.00 to 0.77; P = 0.08; NNT 5, 95% CI 3 to 8).

Duration of treatment until clinical cure

Not assessed.

Participant-judged cure

In the oxiconazole group, all (42/42) of the participants rated the treatment as 'excellent' or 'good' compared to 31/36 in the ketoconazole group (RR 1.16, 95% CI 1.01 to 1.33; P = 0.03; NNT 8, 95% CI 4 to 21).

1.3 Comparisons of same azole with different dosing regimens

(15) Eberconazole cream (1%) once a day versus eberconazole cream (1%) twice daily versus eberconazole cream (2%) once a day versus eberconazole cream (2%) twice daily

Only one study compared and provided data for these comparisons (del Palacio 1995). Outcome data for participants with tinea cruris and tinea corporis were not reported separately.

Primary outcomes

Rate of mycological cure

After four weeks of treatment, all participants in the four intervention groups had negative KOH microscopy:

- Eberconazole 1% once a day (15/15); eberconazole 1% twice a day (13/13); eberconazole 2% once a day (13/13) eberconazole 2% twice a day (14/14)

The number of negative cultures at four weeks:

- 10/15 eberconazole 1% once a day
- 12/13 eberconazole 1% twice a day
- 11/13 eberconazole 2% once a day
- 10/14 of eberconazole 2% twice a day

Combined KOH/culture results were reported for each group.

The data were combined to allow a comparison between once daily and twice-daily regimens. This showed no difference between groups (RR 0.92, 95% CI 0.70 to 1.22).

Clinical cure

At the end of the treatment period, clinical cure was achieved by:

- 10/15 eberconazole 1% once a day
- 12/15 eberconazole 1% twice a day
- 8/15 eberconazole 2% once a day
- 8/15 eberconazole 2% twice a day

There was no difference between once daily and twice-daily regimens in achieving clinical cure (RR 0.90, 95% CI 0.61 to 1.32).

Secondary outcomes

Relapse or recurrence

The authors reported at least three relapses but it was not clear in which groups these occurred.

Adverse effects

- 0/15 participants in the eberconazole 1% once a day group
- 2/15 of the eberconazole 1% twice a day group; mild burning and itching
- 2/15 of the eberconazole 2% once a day group; intense burning and itching and discontinued treatment
- 2/15 of the eberconazole 2% twice a day; burning and itching did not discontinue treatment

There was no difference between once daily and twice-daily regimens with respect to the reporting of adverse effects (RR 0.50, 95% CI 0.10 to 2.53).

Duration of treatment until clinical cure

The mean time until clinical cure was reported as:

- 30 days eberconazole 1% once a day
- 27 days eberconazole 1% twice a day
- 23 days eberconazole 2% once a day
- 27 days eberconazole 2% twice a day

Participant-judged cure

Not assessed.

(16) Oxiconazole (1%) cream once a day versus oxiconazole (1%) cream twice daily

One study provided data for these comparisons Ramelet 1987. Data were reported separately for tinea cruris and tinea corporis.

Primary outcomes

Rate of mycological cure

Data on mycological cure could not be extracted from the report as only the cure rates for each organism were provided and not for each site of infection.

Clinical cure

At the final clinical evaluation:
Tinea cruris: all (19/19) of the participants in the oxiconazole once a day group were considered to be cured compared to 22/23 in the oxiconazole twice a day group (RR 1.04, 95% CI 0.92 to 1.18).
Tinea corporis: 9/13 participants in the once a day group were cured compared to 8/10 in the twice a day group (RR 0.87, 95% CI 0.54 to 1.39).

Secondary outcomes

Relapse or recurrence

Not assessed.

Adverse effects

Only three participants in total experienced adverse effects, however, data were not reported separately for participants with tinea cruris and tinea corporis. One participant had burning and irritation and needed to stop treatment, and two participants had minor and reversible side effects.

Duration of treatment until clinical cure

Not assessed.

Participant-judged cure

Not assessed.

2 Allylamines

2.1 Allylamines versus placebo

Data from all of the studies comparing allylamine with placebo could not be pooled due to substantial heterogeneity between the studies. Individual comparisons are detailed below.

(17) Terbinafine (1%) cream/gel versus placebo cream each applied once a day

Eight studies compared and provided data for these interventions (Budimulja 2001; Cordero 1992; Evans 1992; Greer 1990; Lebwohl 2001; Millikan 1990; van Heerden 1997; Zaias 1993). Data for participants with tinea cruris and tinea corporis were combined and reported together in all of the studies, with the exception of Greer 1990 and Millikan 1990, which only included participants with tinea cruris. Terbinafine was applied once daily in all studies with the exception of a twice-daily application in Greer 1990 and Millikan 1990. In all studies this was applied as a cream except in Lebwohl 2001 as a lotion, and as a gel in van Heerden 1997.

Primary outcomes

Rate of mycological cure

All of the studies except Zaias 1993 provided usable data for this outcome. The studies were not pooled as heterogeneity remained substantial (I^2 = 76%), despite fully exploring for possible causes of clinical and methodological differences between studies. Budimulja 2001; Cordero 1992; Greer 1990; Millikan 1990 and van Heerden 1997 all significantly favoured terbinafine over placebo. Evans 1992 and Lebwohl 2001 favoured terbinafine but there was no significant difference. See Analysis 2.1 for individual studies with their respective risk ratios.

Clinical cure

Clinical cure was determined by either investigator- or participant-judged scoring systems consisting of items based on clinical signs and symptoms.

Five studies (Greer 1990; Lebwohl 2001; Millikan 1990; van Heerden 1997 and Zaias 1993) provided usable outcome data. Overall, 104/134 participants in the terbinafine group were cured compared to 23/139 in the placebo group, a result significantly favouring terbinafine (RR 4.51, 95% CI 3.10 to 6.56; P < 0.00001; NNT 3, 95% CI 2 to 4). See Analysis 2.2.

A sensitivity analysis omitting studies at high risk of attrition bias (Lebwohl 2001; Millikan 1990 and Zaias 1993) had minimal impact on the effect estimate (RR 4.38, 95% CI 2.02 to 9.52; P = 0.00002; NNT 2, 95% CI 1 to 7). See Analysis 2.3.

The three other studies did not provide clinical cure rates, but only reported the mean change in signs and symptoms scores.

- In Budimulja 2001, at day 14, the mean clinical signs and symptoms score in the terbinafine group was 1 compared to a score of 6 in the placebo group. For each symptom (e.g. itch, pustules) a 4-point scale was used, 0 being non-existent, up to 3 for severe. Each symptom score was added up for each participant and the mean score used. Therefore a score of 0-1 would have to represent very mild disease although it is impossible to quantify exactly how many people would be cured, and there may well be participants with more severe disease. A score of 6 in the placebo group would therefore indicate that the average participant in that group would have some symptoms of disease, although it is not possible to clarify how severe these are, nor if there were any cured cases.
- In Cordero 1992, at three weeks, the total signs and symptoms score reduced from 7.8 to 1.0 in the terbinafine group compared to 7.6 to 4.1 in the placebo group, suggesting better clinical improvement in the terbinafine group.
- In Evans 1992, at day 14, the mean signs and symptoms score was just under 2 in the terbinafine group, suggesting minimal evidence of disease, compared with a score of greater than 4 in the placebo group.

Overall, terbinafine appeared to be more effective than placebo in achieving clinical cure.

Secondary outcomes

Relapse or recurrence

This outcome was not assessed in Cordero 1992; Evans 1992; Greer 1990 or Lebwohl 2001. Although not a prespecified outcome in Budimulja 2001, data reported at day 56 suggest there was no relapse in either group. In van Heerden 1997, data were reported for follow-up visits but due to the large number of drop-outs, it was not possible to confirm if any relapse occurred. In Millikan 1990, 2/9 participants in the terbinafine group appeared to have a relapse, with insufficient data reported to confirm if any relapse occurred in the placebo group.

Adverse effects

These were assessed and reported in all of the studies with the exception of Zaias 1993. Pooled data from seven trials indicated that, 8/232 participants who received terbinafine reported an adverse effect compared to 23/237 with placebo, a result favouring terbinafine (RR 0.43, 95% CI 0.20 to 0.92; P = 0.03; NNT 22, 95% CI 15 to 150). See Analysis 2.4. Adverse effects were generally mild, consisting of pruritus and dermatitis.

Overall, terbinafine was better tolerated than placebo.

Duration of treatment until clinical cure

This was not assessed in any of the studies.

Participant-judged cure

- Not assessed in Cordero 1992; Evans 1992; Greer 1990; Lebwohl 2001; Millikan 1990 or van Heerden 1997.
- In Budimulja 2001, 48/56 of participants in the terbinafine group described the treatment as 'good' or 'very good' compared to 9/58 in placebo group (RR 5.52, 95% CI 3.00 to 10.17; P <0.00001; NNT 2, 95% CI 2 to 2).
- In Zaias 1993, 62/66 of participants in the terbinafine group judged the treatment as 'good' or 'very good' compared with 17/73 in the placebo group (RR 4.03, 95% CI 2.65 to 6.14; P <0.00001; NNT 2, 95% CI 2 to 2).

Participant-judged cure favoured terbinafine over placebo when pooling these data, with 110/122 in the terbinafine group describing treatment as 'good' or 'very good' compared to 26/131 in the placebo group (RR 4.46, 95% CI 3.16 to 6.31; P < 0.00001; NNT 2, 95% CI 1 to 3). See Analysis 2.5.

(18) Naftifine 1% cream once or twice daily versus placebo once or twice daily

Three studies compared and reported data for these interventions (Dobson 1991; Gip 1987; Jordon 1990).

Primary outcomes

Rate of mycological cure

Naftifine 1% cream was more effective than placebo in achieving mycological cure based on negative KOH or negative culture. In the naftifine cream group, 83/95 participants were cured after two to four weeks versus 33/92 in the placebo group (RR 2.38, 95% CI 1.80 to 3.14; P < 0.00001, NNT 3, 95% CI 2 to 4, see Analysis 3.1. This difference is statistically significant.
A sensitivity analysis omitting the one study at high risk of attrition bias (Dobson 1991) had minimal impact on the effect estimate (RR 2.32, 95% CI 1.69 to 3.20; P < 0.00001; NNT 2, 95% CI 2 to 4), see Analysis 3.2.

Clinical cure

One study (Dobson 1991), only reported data on improvement rather than clinical cure but these data were in concordance with the mycological cure rates. A further study Jordon 1990 did not report clinical cure, only the clearing of specific symptoms. In Gip 1987 25/32 participants in the naftifine group reported clinical cure compared to 10/31 in the placebo group (RR 2.42, 95% CI 1.41 to 4.16; P = 0.001; NNT 3, 95% CI 2 to 5). The results were statistically significant, favouring naftifine over placebo.

Secondary outcomes

Relapse or recurrence

Only one of the studies (Gip 1987) addressed this outcome and reported no relapse in the naftifine group (0 of 30 that had negative culture), and 3/14 in the placebo group (RR 0.07, 95% CI 0.00 to 1.25).

Adverse effects

Side effects were mild to moderate in severity and consisted mainly of erythema, pruritus and stinging in both groups. Adverse events were reported by 3/99 participants in the naftifine group compared to 7/96 in the placebo group (RR 0.44, 95% CI 0.13 to 1.57) see Analysis 3.3.

Duration of treatment until clinical cure

Not assessed.

Participant-judged cure

Not assessed.

(19) Naftifine 2% cream versus placebo cream each applied once daily

One study provided data on participants with tinea cruris (Parish 2011).

Primary outcomes

Rate of mycological cure

After two weeks, 50/75 participants in the naftifine group were cured based on negative microscopy and culture, compared to 8/71 in the placebo group (RR 5.92, 95% CI 3.02 to 11.59; P < 0.00001; NNT 2, 95% CI 2 to 3), a result significantly favouring naftifine.

Clinical cure

After two weeks, successful clinical treatment was reported in 53/75 participants in the naftifine group compared to 3/71 in the placebo group (RR 16.72, 95% CI 5.47 to 51.10; P < 0.00001; NNT 2, 95% CI 2 to 2), significantly favouring naftifine.

Secondary outcomes

Relapse or recurrence

Not assessed.

Adverse effects

One or more treatment-related adverse effects were experienced by 7/166 in the naftifine group compared to 4/168 in the placebo

group, a non-significant difference (RR 1.77, 95% CI 0.53 to 5.94; P = 0.35).

Duration of treatment until clinical cure

Not assessed.

Participant-judged cure

Not assessed.

2.2 Comparisons of same allylamines with different dosing regimens

(20) Terbinafine (1%) cream single daily application for one day versus single application daily for three, five and seven days

One study, which compared the four regimens, reported usable data (Evans 1994). Outcome data for participants with tinea cruris and tinea corporis were not reported separately.

Primary outcomes

Rate of mycological cure

Mycological cure at day 28 was assessed by negative KOH microscopy and culture. In the one-day group, 4/4 participants were cured compared to; 2/4 in the three-day group, 1/2 in the five-day group and 4/4 in the seven-day group.

Clinical cure

Participants were considered clinically cured if there were minimal or no signs or symptoms. At day 28, 4/4 in the one-day group were cured compared to 1/4 in the three-day group, 1/2 in the five-day group and 3/4 in the seven-day group.

Secondary outcomes

Relapse or recurrence

At day 84, 1/4 of the participants had evidence of mycological relapse in the one-day intervention group. There was no evidence of relapse in any of the other groups.

Adverse effects

No adverse effects were reported in any of the participants with tinea corporis or tinea cruris.

Duration of treatment until clinical cure

Not assessed.

Participant-judged cure

Not assessed.

3 Azoles versus allylamines

Data were not pooled from studies comparing azoles with allylamines for mycological cure (Budimulja 1998; Hantschke 1980; Haroon 1996; Jerajani 2013; Kagawa 1987; Wang 1995; Wang 2000) due to substantial heterogeneity (I^2 = 75%). There was no difference between groups in all studies with the exception of Kagawa 1987, which found allylamines more effective (see Analysis 4.1).

Similarly, data could not be pooled for clinical cure due to heterogeneity (I^2 = 75%) (Budimulja 1998; Hantschke 1980; Jerajani 2013; Kagawa 1987; Wang 1995; Wang 2000), see Analysis 4.2 for individual risk ratios. Omitting studies with a high risk of attrition bias in a sensitivity analysis (Haroon 1996; Jerajani 2013; Kagawa 1987), removed the previously observed heterogeneity, and these pooled data showed no difference between groups for mycological cure (RR 0.99, 95% CI 0.95 to 1.03) (I^2 = 0%), or clinical cure (RR 0.97, 95% CI 0.92 to 1.02)) (I^2 = 0%) (Analysis 4.3; Analysis 4.4).

The number of adverse effects were comparable for the different groups (RR 0.70, 95% CI 0.18 to 2.68; P = 0.60), see Analysis 4.5.

3.1 Comparisons of azoles and terbinafine

(21) Terbinafine (1%) cream/powder versus miconazole (2%) cream/powder each applied twice daily

Two studies reported usable data for these interventions (Wang 1995; Wang 2000). Outcome data for tinea cruris and tinea corporis were combined in Wang 1995 and reported separately in the other study (Wang 2000). One of the studies included three treatment arms; terbinafine for one week, for two weeks and miconazole for two weeks (Wang 1995).

Primary outcomes

Rate of mycological cure

In Wang 1995, microscopy and culture were negative in 33/35 participants in the terbinafine one-week group when assessed at week four. In the terbinafine two-week group 9/10 participants were mycologically cured at week four, and 27/30 participants in the miconazole two-week group were cured at week four.

In Wang 2000, at the end of two to three weeks, negative microscopy and culture was achieved in all (26/26) of the participants with tinea cruris in the terbinafine powder group, compared to 23/24 in the miconazole powder group (RR 1.04, 95% CI 0.93 to 1.17). All participants with tinea corporis were mycologically cured: 4/4 in the terbinafine group and 5/5 in the miconazole group.

Clinical cure

In Wang 1995, clinical cure as assessed at week four was achieved in 32/35 of the terbinafine one-week group, compared to 9/10 of participants in the terbinafine two-week group, and 27/30 in the miconazole group.

In Wang 2000, at the end of 2-3 weeks, cure was achieved in 15/26 of participants with tinea cruris in the terbinafine group compared to 13/24 in the miconazole group (RR 1.07, 95% CI 0.65 to 1.75). In participants with tinea corporis, 0/4 in the terbinafine group were cured compared to 1/5 in the miconazole group (RR 0.40, 95% CI 0.02 to 7.82).

Secondary outcomes

Relapse or recurrence

Not assessed.

Adverse effects

In Wang 1995, only one adverse effect was experienced in the terbinafine one-week group - one participant out of the 35 suffered from stinging. There were no adverse effects reported in the other groups. In Wang 2000, there were no separate adverse effects data reported for the participants with tinea cruris or tinea corporis, but the combined adverse effect rate was 4.8% in the terbinafine group compared to 4.7% in the miconazole group.

Duration of treatment until clinical cure

Not assessed.

Participant-judged cure

Not assessed.

(22) Sertaconazole (1%) cream versus terbinafine (1%) cream versus luliconazole (1%) cream applied once or twice daily

One study compared these interventions in both tinea cruris and tinea corporis (Jerajani 2013). Data were not reported separately for each condition.

Primary outcomes

Rate of mycological cure

At the end of the treatment period, all participants were reported to have negative KOH microscopy; 20/20 in sertaconazole group after four weeks, 22/22 in terbinafine group after two weeks and 20/20 in luliconazole group after two weeks.

Clinical cure

Clinical cure as judged by physician's global assessment was achieved at the end of treatment in all (20/20) of participants in the sertaconazole group, 19/22 in the terbinafine group and 19/20 in the luliconazole group.

Secondary outcomes

Relapse or recurrence

No mycological relapse was reported at the follow-up visit two weeks after the end of treatment in any of the participants. Individual symptom scores suggest that there was no clinical relapse in any of the participants.

Adverse effects

A single participant in the sertaconazole group developed an allergic contact dermatitis. There were no adverse effects reported in the other two intervention groups.

Duration of treatment until clinical cure

Not assessed.

Participant-judged cure

Not assessed.

(23) Terbinafine (1%) cream versus bifonazole (1%) cream each applied once daily

One study compared these interventions in participants with tinea cruris (Budimulja 1998).

Primary outcomes

Rate of mycological cure

After three weeks, KOH microscopy was negative in 87/89 participants in the terbinafine group compared to 83/86 in the bifonazole group (RR 1.01, 95% CI 0.96 to 1.07). Negative cultures were achieved in 87/89 of the terbinafine group compared to 84/86 of the bifonazole group (RR 1.00, 95% CI 0.96 to 1.05).

Clinical cure

After three weeks, 88/89 of the terbinafine group were clinically cured compared to 82/86 of the bifonazole group (RR 1.04, 95% CI 0.98 to 1.09).

Secondary outcomes

Relapse or recurrence

In both groups there appeared to be a number of mycological relapses at week eight, although it was not possible to confirm the precise number in view of the drop-outs occurring between week three and week eight.

Adverse effects

In the terbinafine group, 1/93 participants experienced contact dermatitis but there were no reports of adverse effects in the bifonazole group (RR 2.97, 95% CI 0.12 to 71.93).

Duration of treatment until clinical cure

Not assessed.

Participant-judged cure

Not assessed.

3.2 Comparisons of azoles and naftifine

(24) Naftifine (1%) cream versus clotrimazole (1%) cream each applied twice daily

Only one study in participants with tinea pedis, tinea corporis and tinea cruris provided usable data for these interventions (Kagawa 1987).

Primary outcomes

Rate of mycological cure

Tinea cruris: 44/51 in the naftifine cream group achieved a mycological cure based on negative KOH smear, compared to 42/55 in the clotrimazole cream group (RR 1.13, 95% CI 0.94 to 1.36).

Tinea corporis: cure rates were comparable, with 46/56 in the naftifine versus 46/62 in the clotrimazole group (RR 1.11, 95% CI 0.91 to 1.34).

Clinical cure

Clinical cure rates defined as "highly effective" on the global efficacy 5-point rating scale, were almost identical to the mycological cure rates. For tinea cruris the cure rates were 44/51 for the people treated with naftifine compared to 40/55 for the participants on clotrimazole cream (RR 1.19, 95% CI 0.98 to 1.44). In the people with tinea corporis the rates were 46/56 versus 44/62 (RR 1.16, 95% CI 0.95 to 1.41).

Secondary outcomes

Relapse or recurrence

Not assessed.

Adverse effects

Data are combined with tinea pedis and no separate data are reported for participants with tinea cruris and tinea corporis.

Duration of treatment until clinical cure

Not assessed.

Participant-judged cure

Not assessed.

(25) Naftifine (1%) cream versus tioconazole (1%) each applied twice daily

Only one study, which included participants with tinea cruris, compared and reported data for these interventions (Haroon 1996).

Primary outcomes

Rate of mycological cure

After four weeks both treatments resulted in a 100% cure rate (15/15 naftifine cream; 18/18 tioconazole cream) based on negative mycology (RR 1.00, 95% CI 0.89 to 1.12).

Clinical cure

Only the mean sum of clinical scores for each symptom were reported graphically. In the naftifine group the estimated mean score was 0.25 at four weeks, and 0.21 in the tioconazole group (0 = no symptoms, 1 = mild symptoms up to 3 = severe). After eight weeks these scores reduced to 0.12 in both groups.

Secondary outcomes

Relapse or recurrence

There were no recurrences reported in both groups.

Adverse effects

One participant out of the 15 experienced transient itching during the treatment with naftifine cream as well as 1/18 in the tioconazole cream group (RR 1.20, 95% CI 0.08 to 17.60).

Duration of treatment until clinical cure

Not assessed.

Participant-judged cure

Not assessed.

(26) Naftifine (1%) cream versus econazole (1%) each applied twice daily

One study compared and reported data for these interventions (Millikan 1988).

Primary outcomes

Rate of mycological cure

Data for mycological cure were presented together with clinical cure.

Clinical cure

Only the mean sum of clinical scores for each symptom were reported (erythema, scaling and pruritus) graphically. In the naftifine group after four weeks these scores were estimated to be 0.17, 0.08 and 0.10 respectively. In the econazole group these were 0.24, 0.26 and 0 (0 = no symptoms, 1 = mild symptoms, 2 = moderate, 3 = severe).

Secondary outcomes

Relapse or recurrence

Not assessed.

Adverse effects

In the naftifine group, 2/64 participants reported an adverse effect (one mild burning, one mild itching) compared to 8/62 in the econazole group (burning, itching, swelling, contact dermatitis) (RR 0.24, 95% CI 0.05 to 1.10; P = 0.07).

Duration of treatment until clinical cure

Not assessed.

Participant-judged cure

Not assessed.

4 Corticosteroid-combined therapies - studies combining topical antifungals with topical corticosteroids

4.1 Azoles versus corticosteroid and azole combination

Data from six studies comparing azoles with moderate to potent strength corticosteroid and azole combinations were pooled (Katz 1984; Li 2004; Pariser 1995; Shen 2002; Wang 2000a; Wortzel 1982).

There was no difference in the rate of mycological cure between the groups (RR 0.99, 95% CI 0.93 to 1.05), see Analysis 5.1. A sensitivity analysis based on excluding the one study at high risk of attrition bias (Pariser 1995) had minimal impact on the effect estimate (RR 0.99, 95% CI 0.92 to 1.07), see Analysis 5.2. I^2 = 0% in both analyses.

Clinical cure favoured corticosteroid and azole combinations in all studies except Li 2004, resulting in substantial heterogeneity and thus data were not pooled (I^2 = 63%) see Analysis 5.3. Assessments of clinical cure were made at the end of the treatment period in all of the studies with the exception of Li 2004 in which they were delayed for one week following treatment. This delay in assessment is potentially responsible for the degree of heterogeneity observed between the six studies that evaluated this comparison. Exclusion of this single study (Li 2004) as part of a sensitivity analysis reduced the level of heterogeneity across the remaining five studies (I^2 = 46%). The resulting effect estimate strongly favoured corticosteroid and azole combinations (RR 0.67, 95% CI 0.53 to 0.84; P = 0.0006, NNT 6, 95% CI 5 to 13), Analysis 5.4.

There was no difference between groups in terms of adverse effects (RR 1.36, 95% CI 0.68 to 2.69) see Analysis 5.5.

(27) Miconazole (2%) cream versus econazole nitrate (1%) with triamcinolone acetonide (0.1%) each applied twice daily

One study compared these interventions and provided usable data (Shen 2002). Outcome data for participants with tinea cruris and tinea corporis were not reported separately.

Primary outcomes

Rate of mycological cure

Out of the participants with a positive culture at baseline, 22/23 in the miconazole group had negative microscopy and culture results at week three compared to 17/19 in the econazole with triamcinolone group (RR 1.07, 95% CI 0.90 to 1.28).

Clinical cure

At week three, clinical cure based on absence of clinical signs and symptoms was reported by 22/32 participants in the miconazole group compared to 27/31 in the econazole with triamcinolone group (RR 0.79, 95% CI 0.60 to 1.03).

Secondary outcomes

Relapse or recurrence

Not assessed.

Adverse effects

Diffuse erythema and papules, which necessitated a discontinuation of treatment, were reported by 1/35 of participants in the miconazole group compared to 1/34 in the econazole with triamcinolone group (worsening rash) (RR 0.97, 95% CI 0.06 to 14.91).

Duration of treatment until clinical cure

Not assessed.

Participant-judged cure

Not assessed.

(28) Clotrimazole (1%) hydrocortisone (1%) cream versus naftifine (1%) cream each applied twice daily

Only one study compared these interventions and reported usable data (Evans 1993). Participants included those with either tinea pedis or tinea cruris or corporis and the report provided data for those with tinea cruris and tinea corporis.

Primary outcomes

Rate of mycological cure

In participants with a mycologically-confirmed infection at baseline, negative microscopy and culture results were recorded in 13/15 of the naftifine group compared to 8/10 of the clotrimazole with hydrocortisone group at the end of treatment (RR 1.08, 95% CI 0.75 to 1.57).

Clinical cure

Mean total clinical symptom scores were reported but no actual cure rates. In participants with mycologically-confirmed tinea cruris and tinea corporis, after four weeks of treatment the mean score in both intervention groups suggested participants had very mild symptoms. In participants without mycological confirmation, from four weeks onwards the mean score in both groups was similar suggesting participants continued to have mild symptoms (more symptomatic than the mycologically-confirmed group).

Secondary outcomes

Relapse or recurrence

It was not possible to determine if any relapse took place at 12 weeks as few participants attended this follow-up visit.

Adverse effects

No separate data were available on adverse effects for participants with tinea cruris and tinea corporis. Out of the total number of participants in the study, 20/137 in the clotrimazole with hydrocortisone group suffered an adverse effect compared to 18/132 in the naftifine group, with nine of these effects thought to be directly related to the study interventions.

Duration of treatment until clinical cure

In participants with mycologically-confirmed tinea cruris or tinea corporis, the mean symptom score was zero at week six (day 42) in both groups.

Participant-judged cure

Not assessed.

(29) Clotrimazole (1%) with betamethasone dipropionate (0.05%) cream versus clotrimazole (1%) cream versus betamethasone dipropionate (0.05%) cream each applied twice daily

Two studies compared these interventions (Katz 1984; Wortzel 1982). Only participants with tinea cruris were included in Wortzel 1982. Data were reported separately for tinea cruris and tinea corporis in Katz 1984.

Primary outcomes

Rate of mycological cure

Tinea cruris: after two weeks of treatment 39/60 of the participants in the clotrimazole with betamethasone group had negative KOH microscopy and culture, compared to 34/51 in the clotrimazole group and 4/48 in the betamethasone group (Katz 1984).

Tinea corporis: 32/51 of the participants in the clotrimazole with betamethasone group were mycologically cured compared to 25/49 in the clotrimazole group, and 12/38 in the betamethasone group (Katz 1984).

In Wortzel 1982, after two weeks of treatment, 13/15 of participants with tinea cruris in the clotrimazole with betamethasone group had negative KOH microscopy and culture results compared to 15/15 in the clotrimazole only, and 6/15 in the betamethasone only group.

Clinical cure

Mean clinical symptom scores were reported throughout the duration of the study period in Katz 1984. Data suggest that for both tinea cruris and tinea corporis, clotrimazole with betamethasone was more effective than clotrimazole alone, which in turn was more effective than betamethasone, but no data on actual clinical cure were provided in the report.

In Wortzel 1982, after two weeks of treatment, 12/15 of the clotrimazole with betamethasone group were considered cured or had an excellent response to treatment, compared with 3/15 in the clotrimazole group, and 2/15 in the betamethasone group.

Secondary outcomes

Relapse or recurrence

Not assessed.

Adverse effects

In Katz 1984, adverse effects were reported by 2/112 of participants in the clotrimazole with betamethasone group consisting of mild maculopapular eruption (1) and mild paraesthesia (tingling sensations) (1). Mild to moderate paraesthesia was reported by 3/113 of participants in the clotrimazole group with one participant

discontinuing treatment. In the betamethasone group adverse effects were reported in 9/106 of the participants consisting of paraesthesia (7), and painful follicular eruption (2).

In Wortzel 1982, no adverse effects were noted in the clotrimazole with betamethasone and clotrimazole groups. In the betamethasone group, one participant reported burning and tingling for a couple of hours during the second week of treatment.

Duration of treatment until clinical cure

Not assessed.

Participant-judged cure

Not assessed.

(30) Clotrimazole (1%) with betamethasone dipropionate (0.05%) cream versus ketoconazole (2%) cream each applied twice daily

One study involving participants with tinea cruris reported data for these interventions (Pariser 1995), however, in view of the significant losses to follow-up, the study results should be interpreted with caution.

Primary outcomes

Rate of mycological cure

After two weeks of treatment, 78/93 of the clotrimazole with betamethasone group had negative KOH microscopy and culture compared to 81/99 in the ketoconazole group (RR 1.03, 95% CI 0.90 to 1.17).

Clinical cure

After two weeks, 65/93 of the clotrimazole with betamethasone group were completely clear of signs and symptoms compared to 44/99 in the ketoconazole group, which was statistically significant and favoured clotrimazole with betamethasone (RR 1.57, 95% CI 1.22 to 2.03; P = 0.0006; NNT 4, 95% CI 3 to 9).

Secondary outcomes

Relapse or recurrence

Not assessed.

Adverse effects

Adverse effects were considered to have possibly or probably been related to treatment in 10/128 in the clotrimazole with betamethasone group: application site reactions (3), paraesthesia (3), pruritus (3), unreported (1). In the ketoconazole group 14/131 reported: application site reactions (4), paraesthesia (6) and pruritus (4). There was no significant difference between groups (RR 0.73, 95% CI 0.34 to 1.59; P = 0.43).

Duration of treatment until clinical cure

Not assessed.

Participant-judged cure

Assessment was based on a 4-point symptom scale, however nothing was reported other than: 'Patient-rated symptom severity scores were not statistically significant, but they favoured the clotrimazole/betamethasone dipropionate group over the ketoconazole group.'

(31) Econazole nitrate (1%) with triamcinolone acetonide (0.1%) cream versus econazole (1%) ointment each applied twice daily

Two studies included participants with both tinea cruris and tinea corporis and reported usable data (Li 2004; Wang 2000a). Outcome data for participants with tinea cruris and tinea corporis were not reported separately.

Primary outcomes

Rate of mycological cure

Microscopy was negative at weeks three to four in 39/41 participants in the econazole with triamcinolone group compared to 37/41 in the econazole group (RR 1.05, 95% CI 0.93 to 1.19)(Li 2004). Microscopy and fungal culture were negative at the end of week two in 30/33 of econazole with triamcinolone, compared with 31/35 of the econazole group (RR 1.03, 95% CI 0.87 to 1.21)(Wang 2000a).

Clinical cure

In Li 2004, 23/43 participants in the econazole with triamcinolone group were cured at weeks three to four compared to 25/42 in the econazole group (RR 0.90, 95% CI 0.62 to 1.31). In Wang 2000a, 29/33 were cured or had an excellent response at week two in the econazole with triamcinolone group compared with 21/35 in the econazole group, which was statistically significant and favoured econazole with triamcinolone (RR 1.46, 95% CI 1.09 to 1.97; P = 0.01; NNT 4, 95% CI 2 to 13).

Secondary outcomes

Relapse or recurrence

Not assessed.

Adverse effects

No serious adverse effects were reported in either intervention group in (Li 2004). No separate adverse events data were reported for participants with tinea cruris, tinea corporis or tinea pedis in (Wang 2000a).

Duration of treatment until clinical cure

Not assessed.

Participant-judged cure

Not assessed.

(32) Econazole nitrate (1%) with triamcinolone acetonide (0.1%) versus miconazole (2%) with clobetasol (0.5%) each applied twice daily

One study, which only included participants with tinea cruris, compared these interventions and reported usable data (Su 2001).

Primary outcomes

Rate of mycological cure

At week three, 74/75 of participants in the econazole with triamcinolone group had negative KOH microscopy compared with 63/75 of the miconazole with clobetasol group. This was statistically significant in favour of the econazole with triamcinolone group (RR 1.17, 95% CI 1.06 to 1.30; P = 0.002; NNT 7, 95% CI 5 to 16).

Clinical cure

Clinical cure was significantly higher in the econazole with triamcinolone group, at week three, 66/75 were cured in this group compared with 47/75 in the miconazole with clobetasol group (RR 1.40, 95% CI 1.16 to 1.70; P = 0.0006; NNT 4, 95% CI 3 to 9).

Secondary outcomes

Relapse or recurrence

Not assessed.

Adverse effects

No data reported for this outcome.

Duration of treatment until clinical cure

Not assessed.

Participant-judged cure

Not assessed.

5 Other topical antifungals

5.1 Comparisons of azoles and other topical antifungals

(33) Ciclopirox olamine (1%) cream versus clotrimazole (1%) each applied twice daily

A single study, which included participants with tinea cruris and tinea corporis, compared the effectiveness and safety of these interventions (Bogaert 1986; study 2). Outcome data for participants with tinea cruris and tinea corporis were not reported separately.

Primary outcomes

Rate of mycological cure

Cure was based on negative KOH smear and negative culture. At four weeks 33/40 participants in the ciclopirox olamine cream group had a negative KOH smear compared to 43/50 in the clotrimazole cream group (RR 0.96, 95% CI 0.80 to 1.15). Rates for negative cultures were 34/39 participants in the ciclopirox olamine cream group versus 39/45 in the clotrimazole cream group (RR 1.01, 95% CI 0.85 to 1.19).

Clinical cure

Clinical cure rates were in concordance with the mycological cure rates. At four weeks, 28/40 participants in the ciclopirox olamine cream group had no evidence of disease compared to 34/50 in the clotrimazole cream group (RR 1.03, 95% CI 0.78 to 1.36).

Secondary outcomes

Relapse or recurrence

Not assessed.

Adverse effects

One participant in each group experienced an adverse event (burning/stinging); 1/40 in the ciclopirox olamine cream group and 1/50 in the clotrimazole group (RR 1.25, 95% CI 0.08 to 19.37).

Duration of treatment until clinical cure

Not assessed.

Participant-judged cure

Not assessed.

(34) Amorolfine (0.25%) cream versus clotrimazole (1%) cream each applied twice daily

One study compared and reported data for these interventions (Banerjee 2011).

Primary outcomes

Rate of mycological cure

Both treatments showed similar results for mycological cure with 30/38 participants with tinea corporis in the amorolfine group and 34/42 in the clotrimazole cream group (RR 1.04, 95% CI 0.82 to 1.31).

Clinical cure

The clinical cure rates based on physician's assessment of "effectivity" (good/excellent) were somewhat better than the mycological cure rates 35/38 versus 40/42 respectively (RR 0.97, 95% CI 0.86 to 1.09).

Secondary outcomes

Relapse or recurrence

Although only three participants in the clotrimazole group and six in the amorolfine group attended for follow-up on day 56, none experienced a relapse.

Adverse effects

None of the 48 participants randomised to amorolfine treatment reported an adverse event, and just 1/51 in the clotrimazole group reported increased erythema (RR 0.35, 95% CI 0.01 to 8.48).

Duration of treatment until clinical cure

Not assessed.

Participant-judged cure

In the amorolfine group 34/38 considered themselves cured compared to 38/42 in the clotrimazole cream group (RR 0.99, 95% CI 0.85 to 1.15).

(35) Whitfield's ointment versus clotrimazole (1%) cream each applied three times a day

A single four-armed study compared these interventions and reported usable data (Sivayathorn 1979) (see also comparison 7, 37, 38, 45 and 55).

Primary outcomes

Rate of mycological cure

Based on a negative culture after two weeks, Whitfield's ointment was less effective than clotrimazole (6/28 compared to 16/27 with a RR of 0.36, 95% CI 0.17 to 0.79; P = 0.01; NNT 3, 95% CI 2 to 9)

Clinical cure

Whitfield's ointment was less effective than clotrimazole after two weeks, with 14/28 of participants judged as 'marked improvement' to 'healed' compared with 21/27 participants (RR 0.64, 95% CI 0.42 to 0.98; P = 0.04; NNT 4; 95% CI 2 to 47).

Secondary outcomes

Relapse or recurrence

Not assessed.

Adverse effects

No adverse event was reported in either of these groups.

Duration of treatment until clinical cure

Not assessed.

Participant-judged cure

Not assessed.

(36) Clotrimazole (1%) cream versus tolnaftate (1%) cream versus naftifine (1%) cream each applied twice daily

Only one study provided very limited outcome data for this comparison (Hantschke 1980). Seven participants with tinea corporis were included, six with tinea cruris, and other dermatomycoses were also included. Treatment was continued until clinical cure was achieved.

Primary outcomes

Rate of mycological cure

Mycological cure based on a negative culture was achieved after six weeks for the single participant with tinea corporis in the clotrimazole cream arm, while of the two participants with tinea cruris, one was cured after two weeks and the other one after four weeks. In the tolnaftate cream group the single participant with tinea corporis was cured at week six, and the two participants with tinea cruris after two weeks. Cure was attained in the naftifine cream group in four to seven weeks for the five people with tinea corporis. The two participants with tinea cruris required two and three weeks to be cured mycologically.

Clinical cure

The data for clinical cure were comparable to the data for mycological cure except that clinical healing was delayed for one to two weeks in several participants.

Secondary outcomes

Relapse or recurrence

The single participant with tinea corporis in the clotrimazole group and 1/5 with tinea corporis in the naftifine groups relapsed within two weeks. There were no recurrences in any of the participants with tinea cruris in any group.

Adverse effects

No side effects were reported with clotrimazole cream but a burning sensation was reported by 1/3 participants assigned to tolnaftate cream and 1/7 with naftifine cream

Duration of treatment until clinical cure

Clinical cure was achieved at three weeks for the two participants with tinea cruris in the clotrimazole group (the one participant with tinea corporis did not reach clinical cure, only mycological cure). In the tolnaftate cream group it took eight weeks for the participant with tinea corporis to attain clinical cure and for the participants with tinea cruris four weeks. For the naftifine groups it took seven to eight weeks for tinea corporis and five weeks for tinea cruris.

Participant-judged cure

Not assessed.

(37) Clotrimazole (1%) cream versus tolnaftate (1%) cream each applied twice daily to three times daily

Two studies providing limited usable data compared these interventions (Thomas 1976 and Sivayathorn 1979). Participants with tinea cruris, tinea pedis or both were included in Thomas 1976. Sivayathorn 1979 was a four-armed study (see also comparison 7, 35, 38, 45 and 55).

Primary outcomes

Rate of mycological cure

No separate data available for tinea cruris in Thomas 1976.

In Sivayathorn 1979, negative microscopy was seen in 16/27 of the clotrimazole group compared to 12/19 of the tolnaftate group after two weeks (RR 0.94, 95% CI 0.59 to 1.49).

Clinical cure

In Thomas 1976, two weeks after the completion of treatment, all participants (6/6) in the clotrimazole cream group and (10/10) of the participants in the tolnaftate cream group were cured, defined as clearance of the signs (RR 1.00, 95% CI 0.78 to 1.27).

In Sivayathorn 1979, clotrimazole and tolnaftate showed comparable results for clinical ratings ranging from 'marked improvement' to 'healed' (21/27 compared to 14/19 (RR 1.06, 95% CI 0.75 to 1.48).

Secondary outcomes

Relapse or recurrence

In Thomas 1976, six weeks after completion of treatment there were no relapses in the clotrimazole cream group compared to 1/10 in the tolnaftate cream group (RR 0.07, 95% CI 0.01 to 1.08). This outcome was not assessed in Sivayathorn 1979.

Adverse effects

No separate data were available for tinea cruris in Thomas 1976. There were no adverse effects reported in Sivayathorn 1979.

Duration of treatment until clinical cure

Not assessed.

Participant-judged cure

Not assessed.

(38) Miconazole (2%) cream versus tolnaftate (2%) lotion each applied twice daily to three times daily

Two studies reported usable data for these comparisons (Thulin 1975 and Sivayathorn 1979), but participants with other dermatophytoses and pityriasis versicolor were also included. In Thulin 1975, the interventions were applied twice daily and in Sivayathorn 1979, three times daily. Data were not pooled due to marked differences in treatment regimens. Sivayathorn 1979 was a four-armed study (see also comparison 7, 35, 37, 45 and 55).

Primary outcomes

Rate of mycological cure

Data were reported separately for tinea cruris and tinea corporis in Thulin 1975:

Tinea cruris: 7/8 participants in the miconazole cream group had a negative KOH smear and culture versus 6/7 in the tolnaftate lotion group (RR 1.02, 95% CI 0.68 to 1.52).

Tinea corporis: 3/3 participants in the miconazole cream group had a negative KOH smear and culture versus 3/4 in the tolnaftate lotion group (RR 1.25, 95% CI 0.63 to 2.47).

In Sivayathorn 1979, 21/27 participants in the miconazole cream group had negative microscopy compared to 12/19 in the tolnaftate ointment group (RR 1.23, 95% CI 0.83 to 1.83).

Clinical cure

Clinical cure rates were similar to the mycological cure rates in both studies. In Thulin 1975:

Tinea cruris: 6/8 in the miconazole cream group had complete disappearance of the lesions compared to 5/7 in the tolnaftate lotion group (RR 1.05, 95% CI 0.57 to 1.94).

Tinea corporis: 2/3 miconazole cream group versus 2/4 tolnaftate lotion group (RR 1.33, 95% CI 0.38 to 4.72).

In Sivayathorn 1979, 22/27 of the miconazole group were cured at two weeks compared to 14/19 in the tolnaftate group (RR 1.11, 95% CI 0.80 to 1.53).

Secondary outcomes

Relapse or recurrence

Not assessed.

Adverse effects

No adverse reactions to miconazole cream were reported but of the three adverse events in the tolnaftate group in Thulin 1975, it was unclear if these occurred in participants with tinea cruris and tinea corporis or in participants with other dermatophytoses. No adverse effects were reported in Sivayathorn 1979.

Duration of treatment until clinical cure

No separate data reported for the participants that matched our inclusion criteria.

Participant-judged cure

Not assessed.

(39) Oxiconazole (1%) cream versus tolnaftate (1%) cream each applied twice daily

One study compared and reported data for these interventions (Machado-Pinto 1987). This study did not only include participants with tinea cruris and corporis, but also included participants with tinea pedis and tinea manuum.

Primary outcomes

Rate of mycological cure

Tinea cruris: 4/4 in the oxiconazole cream group had negative microscopy after 40 days compared to 4/5 in the tolnaftate cream group (RR 1.20, 95% CI 0.72 to 1.39).

Tinea corporis: 6/6 oxiconazole cream compared to 4/4 tolnaftate cream (RR 1.00, 95% CI 0.70 to 1.43).

Clinical cure

The rates for clinical cure were identical to those for mycological cure in both tinea groups and both treatment groups.

Secondary outcomes

Relapse or recurrence

Not assessed.

Adverse effects

No separate data were reported for participants with tinea corporis and tinea cruris.

Duration of treatment until clinical cure

Not assessed.

Participant-judged cure

Not assessed.

(40) Haloprogin (1%) ointment versus miconazole (2%) cream each applied twice daily

A single study, which included participants with tinea cruris in addition to other types of infections, provided very limited outcome data for this comparison (Clayton 1979).

Primary outcomes

Rate of mycological cure

Cure based on microscopy and culture was achieved after four weeks of treatment in 8/9 participants in both treatment groups (RR 1.00, 95% CI 0.72 to 1.39).

Clinical cure

No separate data were reported for tinea cruris.

Secondary outcomes

Relapse or recurrence

Recurrences occurred in 1/8 participants in the haloprogin ointment group compared to 0/8 in the miconazole group (RR 3.00, 95% CI 0.14 to 64.26).

Adverse effects

No separate data were reported for tinea cruris.

Duration of treatment until clinical cure

Not assessed.

Participant-judged cure

Not assessed.

(41) Haloprogin (1%) lotion versus clotrimazole (1%) lotion each applied twice daily

Two studies provided data for this comparison (VanDersarl 1977 and Weitgasser 1977). Participants with tinea cruris were included in VanDersarl 1977, whilst the other (Weitgasser 1977), described two studies in participants with tinea cruris and corporis, but also other types of tinea infections.

Primary outcomes

Rate of mycological cure

The VanDersarl 1977 study reported relevant outcome data, whereas Weitgasser 1977 did not report separate data for participants with tinea corporis and tinea cruris, only cure rates according to causative organism. In the VanDersarl 1977 study, 29/34 participants with tinea cruris in the clotrimazole lotion group had a negative KOH and culture after two weeks of treatment compared to 20/32 in the haloprogin lotion group. This difference was statistically significant in favour of clotrimazole lotion (RR 1.36, 95% CI 1.01 to 1.85; P = 0.04; NNT 5, 95% CI 3 to 50).

Clinical cure

The clinical cure rates VanDersarl 1977 were slightly lower than the mycological cure rates; 22/34 for the clotrimazole lotion group and 18/32 for the haloprogin lotion group (RR 1.15, 95% CI 0.78 to 1.71). The data for clinical cure rate were combined for tinea cruris and corporis in both studies in Weitgasser 1977. In these two studies a total of 18/22 participants in the haloprogin lotion group were considered clinically cured compared to 16/20 in the clotrimazole lotion group (RR 1.02, 95% CI 0.76 to 1.37).

Secondary outcomes

Relapse or recurrence

Not assessed.

Adverse effects

In the VanDersarl 1977 study, more adverse events (mainly stinging) were reported with haloprogin than clotrimazole. None (0/40) of the participants in the clotrimazole group reported any adverse event compared to 15/40 in the haloprogin lotion group (RR 0.03, 95% CI 0.00 to 0.52; P = 0.02; NNT 3, 95% CI 2 to 5). In (Weitgasser 1977), the adverse events in both studies were combined for all tinea infections, therefore not presented here.

Duration of treatment until clinical cure

Not assessed.

Participant-judged cure

Participant-judged cure was included in the clinical evaluation in VanDersarl 1977 and not reported separately, while it was not assessed in Weitgasser 1977.

(42) Kakawate/madre de cacao (50%) ointment Gliricidia sepium versus miconazole (2%) cream each applied twice daily

Only one study compared and reported data for these interventions (Guillano 2005).

Primary outcomes

Rate of mycological cure

After three weeks 5/12 participants in the kakawate/madre de cacao ointment group were cured based on a negative KOH versus 11/18 in the miconazole group (RR 0.68, 95% CI 0.32 to 1.46).

Clinical cure

No exact data were provided but the investigators reported that their global response assessment improved in both treatment groups (reported P < 0.001) and between the groups miconazole had significantly higher scores than the kakawate/madre de cacao ointment group (P = 0.001).

Secondary outcomes

Relapse or recurrence

Not assessed.

Adverse effects

More participants experienced adverse events in the kakawate/madre de cacao ointment group than in the miconazole group. Five adverse events (erythema, stinging, oedema, itchiness and burning were reported in 15 participants, but it was unclear how many participants had more than one adverse event, while only one participant reported an adverse event (transient erythema) in the miconazole group.

Duration of treatment until clinical cure

Not assessed.

Participant-judged cure

Although no exact data were reported, the investigators indicated that there was improvement in both groups, but the participants considered miconazole more effective than kakawate/madre de cacao ointment (P = 0.012).

5.2 Comparisons of azoles and benzylamines

Data pooled from studies comparing azoles and benzylamines (Li 2006; Ramam 2003; Singal 2005) showed no difference in the rate of mycological cure (RR 1.01, 95% CI 0.94 to 1.07), see Analysis 6.1.

Two of the studies (Li 2006; Singal 2005), reported data on clinical cure illustrating no difference in the rate between the two interventions compared in each study. In Li 2006, 23/59 participants were cured in the azole group compared to 19/58 in the benzylamine group (RR 1.19, 95% CI 0.73 to 1.94). In Singal 2005, 24/25 of the azole group were cured compared to 26/27 in the benzylamine group (RR 1.00, 95% CI 0.89 to 1.11). The studies were not pooled due to substantial heterogeneity.

There was no significant difference in adverse effects between the two groups (RR 0.85, 95% CI 0.41 to 1.76), see Analysis 6.2.

(43) Butenafine (1%) cream once daily versus clotrimazole (1%) cream twice daily

These interventions were compared in two studies (Ramam 2003; Singal 2005).

Primary outcomes

Rate of mycological cure

Across both studies, mycological cure based on a negative KOH smear was reported in 46/49 participants in the butenafine cream group and in 50/53 in the clotrimazole cream group (RR is 1.00, 95% CI 0.90 to 1.10).

Based on a negative culture in Singal 2005, there was a 100% cure rate in the butenafine cream group (27/27) and 96% cure rate in the clotrimazole cream group (24/25), which showed that both preparations are highly effective (RR 1.04, 95% CI 0.94 to 1.16).

Clinical cure

There were no assessments of clinical cure in Ramam 2003 only a reduction in symptom score was reported, therefore only data from Singal 2005 could be used for this outcome. After four weeks, 26/27 participants in the butenafine cream group were cured and 24/25 in the clotrimazole group (RR 1.00, 95% CI 0.90 to 1.12), which is in agreement with the mycological cure rates.

Secondary outcomes

Relapse or recurrence

Relapse rates were low for both treatment groups in both studies. In the butenafine group, 2/47 participants experienced a relapse compared to 4/51 in the clotrimazole group (RR 0.54, 95% CI 0.10 to 2.83).

Adverse effects

Adverse events were mild and consisted of transient pruritus and burning, and did not lead to withdrawal of the participants. In the butenafine cream group, 8/77 had an adverse event, and in the clotrimazole group 7/78 (RR 1.16, 95% CI 0.44 to 3.04).

Duration of treatment until clinical cure

Not assessed.

Participant-judged cure

Not assessed.

(44) Butenafine (1%) cream versus bifonazole (1%) cream each applied once daily

One study compared the effects of these interventions (Li 2006).

Primary outcomes

Rate of mycological cure

Both interventions yielded high rates of negative KOH and cultures with 54/58 participants in the butenafine cream group and 56/59 in the bifonazole cream group (RR 0.98, 95% CI 0.90 to 1.08).

Clinical cure

The clinical cure rates, based on resolution of signs and symptoms on a 4-point Likert scale, were much lower than the mycological cure rates; 19/58 were clinically cured in the butenafine group compared to 23/59 in the bifonazole group (RR 0.84, 95% CI 0.52 to 1.37).

Secondary outcomes

Relapse or recurrence

No recurrences were seen in any of the two groups.

Adverse effects

In the butenafine group, 6/58 participants reported adverse effects (erythema, burning, stinging, pruritus and oedema) compared to 5/59 in the bifonazole group (RR 1.22, 95% CI 0.39 to 3.78).

Duration of treatment until clinical cure

Not assessed.

Participant-judged cure

Not assessed.

(45) Whitfield's ointment versus miconazole (2%) cream each applied three to four times a day

These interventions were compared in two studies (Voravutinon 1993 and Sivayathorn 1979. In Voravutinon 1993, treatment was applied four times daily and in Sivayathorn 1979 three times daily. Sivayathorn 1979 was a four-armed study (see also comparison 7, 35, 37, 38 and 55).

Primary outcomes

Rate of mycological cure

Voravutinon 1993: In the Whitfield's ointment group, 41/44 participants were cured based on a negative KOH compared to 40/42 in the miconazole group (RR 0.98, 95% CI 0.88 to 1.09). These data were confirmed with a negative culture; 39/44 versus 39/42 respectively (RR 0.95, 95% CI 0.83 to 1.09).

In Sivayathorn 1979, miconazole was more effective in achieving mycological cure compared to Whitfield's ointment, with 21/27 cured compared with 6/28 (RR 3.63, 95% CI 1.74 to 7.59; P = 0.0006; NNT 2, 95% CI 2 to 4).

Data were not pooled due to substantial statistical heterogeneity (I^2 = 96%).

Clinical cure

In Voravutinon 1993, although the investigators used a 4-point Likert scale to compare four different symptoms and their improvement during the treatment period, no actual cure rates were reported. In Sivayathorn 1979, miconazole was more effective in achieving clinical cure, with 22/27 cured compared with 14/28 in the Whitfield's ointment group (RR 1.63, 95% CI 1.08 to 2.46; P = 0.02; NNT 4, 95% CI 2 to 16).

Secondary outcomes

Relapse or recurrence

In Voravutinon 1993, four weeks after the end of treatment 2/39 of the Whitfield's ointment group relapsed versus 1/39 in the miconazole group (RR 2.00, 95% CI 0.19 to 21.16). This outcome was not assessed in Sivayathorn 1979.

Adverse effects

Three out of the 48 participants in the Whitfield's ointment group experienced mild adverse events such as erythema and mild burning versus none of the 48 in the miconazole group (RR 7.00,

95% CI 0.37 to 131.96). In Sivayathorn 1979 no adverse effects were reported.

Duration of treatment until clinical cure

Not assessed.

Participant-judged cure

Not assessed.

5.3 Comparisons of other antifungals and placebo

(46) Ciclopirox olamine (1%) cream versus vehicle each applied twice daily

A single study, which included participants with tinea cruris and tinea corporis, provided usable data for this comparison (Bogaert 1986; study 1). Outcome data for participants with tinea cruris and tinea corporis were not reported separately.

Primary outcomes

Rate of mycological cure

The effect of the vehicle on mycological cure rates was greater than would normally be expected. While 57/70 (81%) participants In the ciclopirox olamine cream group had a negative KOH smear at week four, in the vehicle group 31/69 (45%) had a negative KOH smear although the difference was statistically significant in favour of the active treatment (RR 1.81, 95% CI 1.36 to 2.41; P < 0.0001; NNT 3, 95% CI 2 to 5). Rates for negative culture were 61/70 versus 39/69 (RR 1.81, 95% CI 1.36 to 2.41; P = 0.0002; NNT 4, 95% CI 3 to 7).

Clinical cure

Absence of signs and symptoms of disease was noted by 50/70 participants in the ciclopirox olamine cream group compared to 12/69 in the vehicle group (RR 4.11, 95% CI 2.41 to 7.01; NNT 2, 95% CI 2 to 3). This difference was statistically significant.

Secondary outcomes

Relapse or recurrence

Not assessed.

Adverse effects

A single participant (1/69) in the vehicle group complained of transient burning versus none (0/70) in the active treatment group (RR 3.04, 95% CI 0.13 to 73.43).

Duration of treatment until clinical cure

Not assessed.

Participant-judged cure

Not assessed.

(47) Butenafine (1%) cream versus vehicle each applied once daily

Two studies compared butenafine (1%) cream versus vehicle (Greer 1997; Lesher 1997). One study (Greer 1997), only included participants with tinea corporis and the other (Lesher 1997) only tinea cruris. The studies were not pooled due to statistical heterogeneity.

Primary outcomes

Rate of mycological cure

In the study on participants with tinea corporis (Greer 1997), there was a statistically significant difference in mycological cure rate between the group that had received butenafine cream (37/42) and the group that received vehicle cream (10/36) (RR 3.17, 95% CI 1.85 to 5.43; P < 0.0001; NNT 2, 95% CI 2 to 3). In the Lesher 1997 study, butenafine also appeared to be more effective; 29/37 participants had negative KOH smears and cultures compared to 4/38 in the vehicle group (RR 7.45, 95% CI 2.20 to 19.11; P < 0.0001; NNT 2, 95% CI 2 to 3).

Clinical cure

The results of the clinical cure rates were in agreement with the mycological cure rates. Of the 42 participants treated with butenafine cream in (Greer 1997), 24 were considered cured compared to 9/36 in the vehicle group (RR 2.29, 95% CI 1.23 to 4.26; P = 0.009; NNT 4, 95% CI 2 to 10). Similar results were noted in (Lesher 1997) where 23/37 of the participants were cured compared to 6/38 respectively (RR 3.94, 95% CI 1.81 to 8.55; P = 0.0005; NNT 3, 95% CI 2 to 4).

Secondary outcomes

Relapse or recurrence

Relapse or recurrence was not a prespecified outcome in one study Greer 1997, however in Lesher 1997, there were no relapses reported in either group.

Adverse effects

No side effects occurred in both groups in Greer 1997 and in Lesher 1997 just one participant out of the 46 treated with butenafine reported a burning sensation after application while no adverse events were reported in the vehicle group (0/45) (RR 2.94, 95% CI 0.12 to 70.23).

Duration of treatment until clinical cure

Not assessed.

Participant-judged cure

According to the participants in Greer 1997, 39/42 in the butenafine cream group considered their infection greatly improved versus 10/36 in the vehicle group (RR 3.34, 95% CI 1.96 to 5.70; P < 0.00001; NNT 2, 95% CI 2 to 3). In the study of Lesher 1997, the numbers were 25/37 versus 9/39 after two weeks (RR 2.93, 95% CI 1.58 to 5.42; P = 0.0006; NNT 3, 95% CI 2 to 5), but after six weeks these had increased to 29/37 versus 8/39 (RR 3.82, 95% CI 2.01 to 7.25; P < 0.0001; NNT 2, 95% CI 2 to 3).

(48) Griseofulvin (1%) solution versus vehicle lotion each applied once daily

One study examined this comparison (Macasaet 1991).

Primary outcomes

Rate of mycological cure

At two weeks a larger number of negative cultures was achieved in the topical griseofulvin group (21/26) than in the vehicle group (3/27) and this difference was statistically significant (RR 7.27, 95% CI 2.46 to 21.47; P = 0.0003; NNT 2, 95% CI 2 to 3).

Clinical cure

In the topical griseofulvin group, 19/26 participants were considered clinically cured (no residual signs or symptoms) compared to 2/27 in the vehicle group (RR 9.87, 95% CI 2.55 to 38.20; P = 0.0009; NNT 2, 95% CI 2 to 3), representing cure rates similar to mycological cure.

Secondary outcomes

Relapse or recurrence

Not assessed.

Adverse effects

One participant out of the 26 in the topical griseofulvin group reported erythema and irritation and 3/27 in the vehicle group reported adverse effects: two had erythema and irritation and one reported dry skin. The difference in the total number of adverse events was not statistically significant (RR 0.35, 95% CI 0.04 to 3.12).

Duration of treatment until clinical cure

Not assessed.

Participant-judged cure

Not assessed.

(49) Senna alata soap versus placebo soap each used twice daily

One study reported limited data for this comparison (Oladele 2010). Only six participants had tinea corporis and matched our inclusion criteria; five were in the Senna alata soap group and one in the placebo soap group.

Primary outcomes

Rate of mycological cure

Not assessed.

Clinical cure

All five participants with tinea corporis in the Senna alata group were cured at week four, while the one participant with tinea corporis in the placebo group was not cured.

Secondary outcomes

Relapse or recurrence

Not assessed.

Adverse effects

Not assessed.

Duration of treatment until clinical cure

It took four weeks for the five participants with tinea corporis to be cured in the Senna alata group, and the single patient in the placebo group was not cured.

Participant-judged cure

Not assessed.

5.4 Comparisons of all other antifungals

(50) Tetrandrine (2%) cream with ketoconazole (2%) cream versus tetrandrine (2%) cream versus ketoconazole (2%) cream each applied twice daily

A single study provided outcome data for this comparison (Shi 2011).

Primary outcomes

Rate of mycological cure

After two weeks of treatment the combined therapy of ketoconazole with tetrandrine appeared most effective with 14/16 participants attaining negative KOH and culture compared to 7/15 in the ketoconazole alone group and 0/12 in the tetrandrine alone group.

When making a direct comparison between ketoconazole with tetrandrine and ketoconazole, the former was slightly more effective at achieving mycological cure (14/16 versus 7/15 (RR 1.88, 95% CI 1.06 to 3.32; P = 0.03; NNT 3, 95% CI 2 to 13)

Ketoconazole with tetrandrine was more effective than placebo (14/16 versus 0/12 with a RR of 22.18, 95% CI 1.45 to 338.38; P = 0.03; NNT 2, 95%CI 2 to 2).

Clinical cure

Rates of clinical cure were in agreement with mycological cure rates; 12/16 were cured in the combined therapy group, 5/15 in the ketoconazole group and 0/12 in the tetrandrine group.

Directly comparing ketoconazole with tetrandrine and ketoconazole alone, ketoconazole with tetrandrine was slightly more effective at achieving clinical cure, with 12/16 participants cured compared to 5/15 in the ketoconazole alone group (RR 2.25, 95% CI 1.04 to 4.86; P = 0.04; NNT 3, 95% CI 2 to 17).

Ketoconazole with tetrandrine was more effective than placebo in achieving clinical cure (12/16 versus 0/12 with a RR of 19.12, 95% CI 1.24 to 293.98; P = 0.03; NNT 2, 95% CI 2 to 3).

Secondary outcomes

Relapse or recurrence

None of the participants in the combined therapy relapsed, while two relapsed in the ketoconazole group, and as none were cured in the tetrandrine group, relapse does not apply here.

Adverse effects

No adverse events were reported in any of the groups.

Duration of treatment until clinical cure

Not assessed.

Participant-judged cure

Not assessed.

(51) Xianglian lotion (5.58% to 10%) wash once a day, and Xianglian cream (22.32% to 30%), twice daily versus potassium

permanganate 0.02%, wash once a day, and clotrimazole cream (3%), twice daily

Two studies compared these interventions and provided limited usable data (Fan 1991; Fan 1994).

Primary outcomes

Rate of mycological cure

Across both studies, at the end of treatment, 68/87 participants with tinea cruris in the Xianglian lotion/Xianglian cream group had negative cultures versus 33/57 in the potassium permanganate/clotrimazole group, which was a statistically significant difference (RR 1.35, 95% CI 1.05 to 1.73; P = 0.02; NNT 5, 95% CI 3 to 21). In the participants with tinea corporis (only data from Fan 1994), these rates were 14/15 versus 2/4 respectively (RR 1.87, 95% CI 0.69 to 5.02).

Clinical cure

In one study (Fan 1991), the data for clinical cure were combined with mycological cure. However, the other study (Fan 1994) reported a complete disappearance of signs and symptoms after four weeks in 10/35 of the participants with tinea cruris treated with Xianglian lotion/Xianglian cream compared to 4/12 of the participants treated with potassium permanganate/clotrimazole (RR 0.86, 95% CI 0.33 to 2.23) and for the participants with tinea corporis these rates were 11/15 compared to 2/4 respectively (RR 1.47, 95% CI 0.53 to 4.09).

Secondary outcomes

Relapse or recurrence

This outcome was not assessed in one of the studies Fan 1991, whereas in Fan 1994 it was reported that in the Xianglian lotion/Xianglian cream group 3/8 with tinea cruris relapsed and 0/7 with tinea corporis but no data were available for the comparison group.

Adverse effects

Not assessed.

Duration of treatment until clinical cure

Not assessed.

Participant-judged cure

Not assessed.

(52) Ajoene (0.6%) gel versus terbinafine (1%) cream each applied twice daily

Only one study compared and reported data for these interventions (Ledezma 1999).

Primary outcomes

Rate of mycological cure

Based on negative KOH and culture 19/25 participants were cured 30 days after treatment in the ajoene gel group compared to 13/17 in the terbinafine group (RR 0.99, 95% CI 0.70 to 1.40).

Clinical cure

Based on a clinical score totalling individual items (itching, burning, redness, weeping, scaling, pustulation), scored on a 4-point Likert scale, all participants in both groups were cured 30 and 60 days after end of treatment.

Secondary outcomes

Relapse or recurrence

Out of the total number of participants that were effectively treated, 1/19 relapsed in the ajoene group compared to 1/13 in the terbinafine group (RR 0.68, 95% CI 0.05 to 9.48).

Adverse effects

Although not prespecified as an outcome, it is reported that both treatments were well-tolerated and that with the ajoene gel slight transient burning was experienced (unclear how many participants experienced this) and two participants in the terbinafine group suffered from erythema and intense itching.

Duration of treatment until clinical cure

Not assessed.

Participant-judged cure

Not assessed.

(53) Triclosan soap versus plain soap each applied once a day

A single study compared and provided data for these interventions (Dinkela 2007). One primary outcome was reported and none of the secondary outcomes were assessed. Only 15 of the participants had tinea corporis and thus matched our inclusion criteria.

Primary outcomes

Rate of mycological cure

After two months, 6/7 participants who had washed with Triclosan were cured based on a negative KOH compared to 3/7 participants who washed with plain soap (RR 2.00, 95% CI 0.81 to 4.96).

Clinical cure

No precise data could be extracted from the report for participants with only tinea corporis.

Secondary outcomes

Nothing reported.

(54) Whitfield's ointment versus pecilocin each applied once a day

Two participants with tinea corporis were included in this trial (the remainder were diagnosed with tinea pedis) (Holti 1970). Both of the participants were assigned to pecilocin.

Primary outcomes

Rate of mycological cure

Scrapings of the two participants with tinea corporis showed a negative culture after 12 weeks of treatment with pecilocin, there were no participants with tinea corporis in the Whitfield's ointment treatment arm.

Clinical cure

Both participants showed a clinical cure after 12 weeks.

Secondary outcomes

Relapse or recurrence

The two participants in the pecilocin group did not relapse within six months after the end of treatment.

Adverse effects

Not assessed.

Duration of treatment until clinical cure

Not assessed.

Participant-judged cure

Not assessed.

(55) Whitfield's ointment versus tolnaftate (2%) ointment each applied three times a day

A single four-armed study compared these interventions and reported usable data (Sivayathorn 1979) (see also comparison 7, 35, 37, 38, and 45).

Primary outcomes

Rate of mycological cure

Based on a negative culture after two weeks, Whitfield's ointment was less effective than tolnaftate in achieving mycological cure, with 6/28 cured compared to 12/19 (RR 0.34, 95% CI 0.15 to 0.75; P = 0.007; NNT 3, 95% CI 2 to 8).

Clinical cure

Whitfield's ointment was also less effective at achieving clinical cure than tolnaftate, with 14/28 in the Whitfield's group considered 'marked improvement' to 'healed' compared to 14/19 in the tolnaftate group (RR 0.68, 95% CI 0.43 to 1.07).

Secondary outcomes

Relapse or recurrence

Not assessed.

Adverse effects

No adverse event was reported in either of these groups.

Duration of treatment until clinical cure

Not assessed.

Participant-judged cure

Not assessed.

DISCUSSION

Although optimal cure rates would appear to be achievable with some of these interventions, multiple applications and the length of treatment required might lead to poor compliance and, consequently, a less than successful outcome. Topical agents administered once daily over a shorter period may well provide more readily attainable and sustained results.

Summary of main results

This review included 129 trials, many of which were more than 20 years old and a substantial number (around 25%) were at least partially industry funded. These trials provided some evidence to support the clinical effectiveness and safety of several commonly used topical antifungal treatments for tinea cruris and corporis. Due to the large number of different interventions, it was only possible to pool data for several outcomes for terbinafine against placebo and naftifine 1% against placebo. The quality of the evidence was considered to be low for these comparisons. Naftifine 2% also appeared to be an effective treatment, requiring a lesser number of applications compared to the 1% formulation, however, the 2% formulation is only registered for use in the USA.

Almost all other active interventions were effective at achieving mycological cure after two to four weeks compared with placebo. There appeared to be little difference between active interventions in achieving this outcome, although duration of treatment varied. Clinical cure was also assessed in most studies, and similarly, most active interventions were superior when compared with placebo. Where data were available, no substantial differences were seen in the treatment effects between tinea cruris and tinea corporis.

Once-daily versus twice-daily applications were evaluated in two studies (del Palacio 1995 - eberconazole), (Ramelet 1987 - oxiconazole) and there were no differences between dosing regimens for any of the outcomes assessed in these studies. Similarly, comparative results were seen in studies assessing twice-daily applications of terbinafine versus placebo (Greer 1990; Millikan 1990) and once-daily terbinafine versus placebo. Results were also similar in the study of Jordon 1990 assessing naftifine 1% versus placebo when compared to the studies assessing a twice-daily application (Dobson 1991; Gip 1987). Once-daily applications may increase patient compliance and satisfaction with treatment and therefore the assessment of efficacy of such dosing regimens is important.

Meta-analyses comparing active interventions were only possible for three treatment classes of antifungals. These results suggested that topical azoles, allylamines, benzylamines and also azoles combined with corticosteroids all achieved high mycological cure rates. There was limited difference between groups in the comparisons of azoles with allylamines, azoles with benzylamines, and azoles with corticosteroid and azole combinations. It was only possible to pool data from a small number of trials investigating these comparisons and the majority of these trials were also judged as at an 'unclear risk' of bias and thus the quality of the evidence was rated as low to very low for these comparisons.There was evidence, albeit rated as very low quality, that moderate to potent strength corticosteroids combined with azoles achieved a higher rate of clinical cure compared to azoles alone at the end of treatment, but this was not reflected in the mycological cure rate. Eradication of the organism does not always confer immediate clinical cure, possibly due to delay in skin regeneration following infection, or the time for skin-mediated inflammatory responses to settle, or both. It is conceivable therefore that the comparable mycological cure rates between azoles and corticosteroid with azole combinations represent similar effects of the azole component of the treatment in eradicating the organism, and that the corticosteroid component may be more effective than azole alone in the treatment of associated skin inflammation.

This review provided a very limited insight into the comparative effectiveness of Whitfield's ointment and azole creams, with only two studies evaluating these comparisons. These studies reported mixed results, with one (Sivayathorn 1979) suggesting that azoles

were more effective, and Voravutinon 1993 indicating no difference between miconazole and Whitfield's ointment. It was somewhat disappointing to see so few trials evaluating what is still a widely used treatment in many parts of the world.

All interventions appeared to be well-tolerated with a low rate of mild, local adverse effects, and no reports of systemic side effects. In particular, there was no increase in side effects seen with the corticosteroid and azole combination creams. In some instances, participants discontinued treatment due to adverse effects, but this number was minimal.

For further details see the 'Summary of findings for the main comparison; Summary of findings 2; Summary of findings 4; Summary of findings 3; Summary of findings 5; Summary of findings 6'

Overall completeness and applicability of evidence

A range of interventions were covered, the majority of which were evaluated in single studies, a few of which addressed just a limited number of our outcomes and illustrated the existing gaps in the overall completeness of the evidence. The quality of data reporting was very variable across the studies, and in several, it was unclear to what extent the impact of industry sponsorship may have had on the direction and completeness of the results. The limited data reported in many of the studies did not enable fair and reliable comparisons to be made for any one single intervention against another for a specific outcome, with the exception of terbinafine and naftifine. Based on the evidence available, these two interventions would appear to be safe and effective in the treatment of tinea corporis and tinea cruris (Summary of findings for the main comparison; Summary of findings 2).

Quality of the evidence

The quality of the evidence as summarised in the 'Summary of findings for the main comparison; Summary of findings 2; Summary of findings 4; Summary of findings 3; Summary of findings 5; Summary of findings 6' was rated as low to very low. The important reasons for downgrading for each outcome were; limitations in study design or execution (risk of bias), and imprecision mainly due to low sample sizes. Due to indirectness, we downgraded the quality of evidence for clinical and mycological cure in the comparisons of azoles with allylamines, azoles with benzylamines, azoles with corticosteroid and azole combinations and azoles with placebo comparisons because they covered several different treatments within each of the groups. The reasons for downgrading the quality of evidence are discussed in the following sections.

Limitations in study design and implementation

Although study design in the included studies appeared to have been at best adequate, our study-level assessments of the risk of bias for a number of the domains in several of these studies revealed some of the limitations in their implementation, which have been reported in the 'Risk of bias in included studies' section of this review.

There was considerable variation in how well the studies were reported, and in particular the methods used to generate the sequence, to conceal the allocation, and the measures taken to blind investigators and participants. These factors, compounded with unsuccessful attempts to contact many of the investigators for additional information, created difficulties in making accurate assessments of the risk of bias in almost half of the included studies. Additionally, in many instances the key outcomes that were assessed in the included studies only provided limited data, much of which could not be pooled, and, consequently, did not allow any wider assessment or comparison of the effects of the interventions across the studies.

A number of the included studies (18) excluded participants after randomisation due to negative mycological culture i.e. because those participants no longer met the inclusion criteria. If the losses between the groups were balanced and moderate we considered this represented a relatively low risk of bias and was unlikely to have a significant impact on the intervention effect estimate (ICH Expert Working Group 1998). However, it should be taken into account that in routine clinical practice cultures are generally not taken from a participant with a clinical diagnosis of a tinea infection and antifungal treatment is prescribed immediately. An analysis including the participants in the context of the real life clinical situation i.e. on the basis of a solely clinical diagnosis might taper the effect of the antifungal treatment as opposed to an analysis based on participants with both a clinically- and mycologically-confirmed diagnosis (Fergusson 2002). Ideally, the primary analysis in these studies should have been according to the intention-to-treat (ITT) principle, taking into account all participants randomised in the study, and which would most likely contribute additional data on safety and any potential harms associated with the interventions. A subsequent secondary analysis of only those randomised participants with confirmed eligibility, would be more likely to provide increased precision in any estimates of treatment effect.

Indirectness of the evidence

Although there was a degree of variability in the inclusion criteria selected by the trialists in the included studies, in general these matched the eligibility criteria for this review.

The participants were a fairly representative sample, as prespecified in 'Types of participants' (although most participants would have been recruited in a secondary care setting) and therefore we did not have any significant concerns about the directness of the evidence relating to the participants identified in the review. In view of the more extensive and varied differences in clinical presentation, the evidence for the effects of these interventions cannot and should not be extrapolated directly to immunocompromised participants or those using immunosuppressing drugs, who may require additional systemic antifungal therapy. This would also be applicable to participants with clinical conditions where there has been minimal response to topical treatment or if extensive surfaces are affected, and switching to a systemic antifungal treatment might be a more appropriate option (Gupta 2004; Weinstein 2002).

Head-to-head comparisons of interventions predominated, and were evaluated in over 100 studies, but the level of clinical heterogeneity between the studies did not permit pooling of data for almost all of these comparisons. Consequently, the review does not provide sufficient evidence to enable reliable and confident decision-making in the selection of one intervention over another. Comparisons of azoles with allylamines, azoles with benzylamines, azoles with placebo and azoles with corticosteroid and azole combinations were pooled in the review. As these included

different treatments within the same groups, we downgraded the quality of the evidence for indirectness related to the outcomes in these comparisons.

Hardly any of the included studies assessed duration of treatment until clinical cure, however in several studies it was possible to utilise data that reported assessments at different time points to provide reasonable estimates of time until clinical cure. One of the key patient reported outcomes (PRO); participant judged cure that would have provided important direct evidence of the impact of these interventions on people with tinea corporis or tinea cruris, was largely unreported or ignored. The importance of these PROs appears to have been largely underestimated by most of the trial investigators.

Inconsistency of the results

Most of the comparisons were evaluated in single studies, which precluded any assessment of consistency of results across studies assessing similar interventions, with the exception of terbinafine versus placebo and naftifine versus placebo, and for mycological cure, clotrimazole versus placebo. Inconsistency in treatment effect for mycological cure between the studies comparing terbinafine versus placebo was attributed to unexplained heterogeneity and therefore these data were not pooled. However, for the other outcomes in the comparison of terbinafine versus placebo, the results appeared fairly consistent. Downgrading of the quality of evidence for the interventions comparing azoles versus allylamines and azoles versus placebo was as a result of the substantial heterogeneity between the studies for both mycological cure and clinical cure for these comparisons. This applied equally to clinical cure in the comparison of azoles versus allylamines.

Imprecision of the results

The paucity of studies included in this review that compared similar interventions, provided limited opportunities for data synthesis and therefore any substantive assessment of the degree of precision of effect was not feasible. We have exercised caution when extracting data from the primary research studies and have provided confidence intervals to indicate the strength of the data on which conclusions might be drawn. In Summary of findings for the main comparison; Summary of findings 2; Summary of findings 4; Summary of findings 3; Summary of findings 5; Summary of findings 6, we downgraded the quality of evidence due to imprecision in each comparison for one or more outcomes. Mostly this was associated with too small, or very small sample sizes, or that the confidence intervals included no effect and appreciable harm or appreciable benefit.

Publication bias

Although it would be reasonable to assume that the comprehensive searches will have identified all existing randomised controlled trials, and thereby helped to limit bias in the conduct of this review, the comparative absence of published trials over the last 10 to 15 years may be a cause for some concern. A further indication was that the majority, 118 out of 129, of the studies included in this review were in fact conducted before the year 2000. Although formal assessment of publication bias was not feasible largely due to the low number (< 10) of included studies that compared similar interventions, we did identify a very small number of duplicate reports in our searches. See 'Results of the search'.

Potential biases in the review process

We made every attempt to limit bias in the review process by ensuring a comprehensive search for potentially eligible studies. The review authors' independent assessments of eligibility of studies for inclusion in this review and the extraction of data minimised the potential for additional bias beyond that detailed in the 'Risk of bias in included studies' tables. The incompleteness of some of the reports and our inability to obtain clarification of certain trial details or to resolve ambiguities in the reports may have contributed to some bias in their assessment, but, where these conditions applied, this was explicitly stated in the text of our review. The effects of language bias on the identification and selection of studies for inclusion in a systematic review is widely recognised; therefore, we ensured that any studies that were not in the English language were translated so that they could be adequately assessed for eligibility.

Agreements and disagreements with other studies or reviews

We identified five literature reviews (Gupta 2004; Havlickova 2008a; Moriarty 2012; Nadalo 2006; Weinstein 2002) and three systematic reviews (Rotta 2012; Rotta 2012B; Rotta 2013), of the effectiveness of treatments for tinea infections.

The literature reviews provided a wealth of background information covering the different types of tinea infections, to include epidemiological data and specific sites of predilection as well as the associated risk factors. However, none of these reviews undertook a comprehensive and systematic search of the literature, nor gave any indication of how studies were selected and evaluated. Therefore they cannot be considered reliable sources of evidence and the basis for recommendations and guidance. There was broad agreement between the reviews that most topical antifungals are effective but that there was also insufficient clear evidence to support the outright superiority of any specific antifungal over another. However, the recommendations from two of the reviews (Moriarty 2012; Nadalo 2006) were that allylamines should be the first line of treatment, based on their rapid mode of action and shorter treatment period, but with the disadvantage of increased cost (Nadalo 2006). Two of the reviews (Havlickova 2008a; Weinstein 2002) recommended a combined therapy of a topical antifungal with a topical corticosteroid for infections associated with severe inflammation. Conversely the authors in (Gupta 2004) stated that the addition of a corticosteroid to an antifungal; should be considered "mistreatment", as it might mask the signs of tinea infection and lead to tinea incognito. Several recent reports were supportive of this statement (Fox 2008; Goldstein 2013; Greenberg 2002; Moriarty 2012) and even suggested that the use of these combinations may be associated with persistent or recurrent infection (Alston 2003). The prescribing behaviour of dermatologists and non-dermatologists of these combined agents has been evaluated (Smith 1998) and it was reported that non-dermatologists were more likely to prescribe combination agents (34.1%) than dermatologists (4.8%, P = 0.001). Possible reasons suggested were that non-dermatologists were less accurate in diagnosing a fungal infection and also less aware of potential side effects. The adverse events associated with topical steroids are fairly well-recognised and include skin atrophy, secondary skin infection and telangiectasia. Systemic side effects are more likely to occur when large areas of skin are treated, or if treatment is prolonged. As the majority of studies investigating these combined

therapies did not exceed three weeks it was not possible to confirm or refute the reports and comments on the extent and impact of these potential adverse effects. In clinical practice, duration of treatment might be prolonged when large areas are affected or when the diagnosis is incorrect. Accordingly, the effectiveness and safety of combination treatments of a topical antifungal with a topical corticosteroid remain a continuing debate.

While we are in broad agreement with the conclusions reported in the three systematic reviews (Rotta 2012; Rotta 2012B; Rotta 2013), we express concern with the methods used to reach these conclusions, which are not reflective of a robust and comprehensive process used to synthesise the totality of the available evidence for this clinical topic. Our major areas of concern are with the exclusion of studies based on language of publication, and the assessment and reporting of the methodological quality in terms of risk of bias of the included studies. Although the search appeared to be comprehensive in these reviews, the language of publication was a restriction i.e. only English, Spanish, or Portuguese studies were included. Similar language restrictions in our review would have reduced the number of included studies by a not insignificant 20%. The authors in these three reviews assessed and reported methodological quality using the Jadad Scale which has well-documented and widely acknowledged limitations (Herbison 2006; Olivo 2008), but they also indicated they had used the Cochrane 'Risk of bias' tool although they failed to report any of these assessments. The authors in (Rotta 2013) stated that 'absence of information about the allocation should not have affected the confidence of the results', which added further to our concerns with the methodological rigour of their review (Fedorowicz 2013). Inadequate reporting of key quality items such as sequence generation and allocation concealment should necessitate assessments of 'unclear risk of bias' in contrast to 'low risk of bias' for these domains. A further area of discordance with our review was the lack of detail reported by the review authors confirming how blinding was achieved and deemed to be effective in the trials included in their review. They only reported that 'half of the included studies, were satisfactorily blinded', without providing any indication how blinding was implemented or ensured, which contrasted somewhat with our more detailed exploration of this important source of bias.

In our search for additional studies and reviews, we also examined six clinical references and sources for guidelines and systematic reviews; Agency for Healthcare Research and Quality (http://www.ahrq.gov/, DynaMed (https://dynamed.ebscohost.com/), National Guidelines Clearinghouse (http://www.guideline.gov/), National Institute for Health and Clinical Excellence (http://www.nice.org.uk/), Scottish Intercollegiate Guidelines Network (http://www.sign.ac.uk/index.html), UK Database of Uncertainties about the Effects of Treatments (http://www.library.nhs.uk/duets/), and UpToDate (http://www.uptodate.com/home). The relevant NICE CKS (Clinical Knowledge Summaries) (http://cks.nice.org.uk/) which "provide primary care practitioners with a readily accessible summary of the current evidence base and practical guidance on best practice", was last updated in 2009. However, study design appeared to be the sole criterion used to determine the level of evidence to support any of the clinical recommendations in the summary. It was surprising to find that, with the exception of DynaMed, the majority of these clinical references did not address this clinical topic or provided very limited current information that could aid clinical decision-making. DynaMed, a clinical reference derived from systematic literature surveillance with explicit critical appraisal criteria, provided summaries of two large systematic reviews covering multiple tinea infection sites (Rotta 2012; Rotta 2013) and two randomised trials specific to tinea cruris (Lebwohl 2001; Parish 2011). The results were in agreement with our review but the distinction between empiric treatment and treatment of microbiologically confirmed cases was further highlighted.

AUTHORS' CONCLUSIONS

Implications for practice

In selecting a topical treatment for tinea corporis or tinea cruris, clinicians need to consider a number of factors which include effectiveness, availability, cost, tolerability and patient compliance, although the order of importance of these factors may vary depending on clinical setting.

Our results suggest that all classes of commonly used topical antifungals achieve substantial mycological and clinical cure rates. However, there is currently insufficient evidence available to determine if one particular class or individual topical antifungal is superior in terms of mycological cure and clinical cure to another. Although there is widespread, global availability of many of the interventions evaluated in this review (or at least some of the individual treatments within each class), in reality many people, particularly in resource-poor countries, may only have access to older treatments such as Whitfield's ointment or even Castellani's paint. If available, an azole cream would be preferable as it is likely to be more effective, and more acceptable in view of the reduced number of applications that are required. However, even older azole creams such as clotrimazole may be significantly more expensive in some settings and thus may present an obstacle to the provision of optimal treatment. Access to different treatments by patients may vary widely both at national and regional level, such that a treatment available for purchase over the counter in one country may be available only on prescription elsewhere.

Our findings provide evidence, rated as very low quality, that azoles when combined with corticosteroids achieve slightly better rates of clinical cure (with equivalent mycological cure) compared to azoles at the end of treatment and as suggested may be due to the effect on the associated inflammation of the skin. Easing of erythema and itch by corticosteroids might be interpreted as a ‘cure’ by patients, therefore if these are the predominant symptoms this may in turn encourage satisfaction and compliance with treatment. Combination treatments may be considered appropriate in such cases, although only for short periods of time to avoid the potential of adverse effects from corticosteroid overuse.

Tolerability does not appear to be a problem with topical antifungal treatments, however, compliance with topical treatments for dermatological conditions, including tinea infections, can be poor and is often a barrier to successful treatment. Decreased frequency of application and shorter durations of treatment could reduce these compliance issues (Weinberg 2009). Our review did not find enough evidence to determine optimal dosing regimens or duration of treatment and the effect of these factors on relapse rates also remains unclear.

In clinical practice (particularly within a primary care setting), it may not be routine to confirm the diagnosis by microscopy or

culture, so there is a potential for misdiagnosis. The estimates of benefit described in this review, which included only studies where the diagnosis was confirmed, may therefore overestimate the benefit seen in such clinical settings.

Naftifine 1% and terbinafine 1% have both been shown to be effective treatments, however, the quality of evidence for these comparisons versus placebo was rated as low. Clotrimazole 1% was shown to be effective in achieving mycological cure compared with placebo. Naftifine 2% and terbinafine 1% appear to be effective in a once-daily application and with a shorter duration of treatment compared with azoles. Mild adverse effects were reported infrequently. These two treatments are more expensive.

Implications for research

A review of topical antifungal treatments for tinea cruris and corporis provides an example of the implications for research when a limited number of high-quality eligible studies had been found. This review highlights the need for randomised controlled trials to evaluate the effects of these interventions, which can ultimately provide reliable evidence to help inform clinical decision-making.

Any future randomised controlled trials must be well-designed, well-conducted, and adequately delivered with subsequent reporting, including high-quality descriptions of all aspects of methodology. Reporting should conform to the Consolidated Standards of Reporting Trials (CONSORT) statement (http://www.consort-statement.org/), which will enable appraisal and interpretation of results, and accurate judgements to be made about the risk of bias, and the overall quality of the evidence. Although it is uncertain whether reported quality mirrors actual study conduct, it is noteworthy that studies with unclear methodology have been shown to produce biased estimates of treatment effects (Schulz 1995).

Despite the limitations in the main findings of this review, it would appear that most active interventions exert a sufficient therapeutic effect, and can be considered safe to use, which would therefore negate the need for a placebo comparison in future randomised controlled trials.

For further research recommendations based on the EPICOT (evidence, population, intervention, comparison, outcomes, and time) format (Brown 2006), see Table 4.

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* Indicates the major publication for the study

CHARACTERISTICS OF STUDIES

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

Abdul Bari 2012

Methods	Randomised, double-blind, active-controlled trial Setting Baghdad College of Pharmacy, Baghdad, Iraq Date of study Not reported. Duration of intervention 2 weeks with follow-up at 2 weeks
Participants	N = 96 (42 male/54 female) Age range 14-72 years **Inclusion criteria of the trial** • superficial mycosis disease (confirmed by KOH and culture) **Exclusion criteria of the trial** • antibiotic or antifungal treatment < 90 days prior to study entry Randomised N = 96 Withdrawals/losses to follow-up No losses to follow-up reported Baseline data Nothing reported

Abdul Bari 2012 *(Continued)*

Interventions	**Intervention** • butenafine (1%) cream b.i.d. for 2 weeks (48) **Comparator** • bifonazole (1%) cream b.i.d. for 2 weeks (48)
Outcomes	Assessments (3): baseline, at 2 weeks and at 2 weeks follow-up **Outcomes of the trial** (as reported) 1. Mycological evaluation (KOH and culture) 2. Clinical evaluation (itching, redness, papules & pustules): 4-point Likert scale# 3. Adverse events# Denotes outcomes prespecified for this review
Notes	Study included participants with tinea versicolor, tinea corporis, tinea cruris, tinea manuum, and tinea pedis. No separate data provided for different tinea infections, see Table 3

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote (page 151): "..randomized.." Comment: Insufficient detail was reported about the method used to generate the allocation sequence to allow a clear assessment of whether it would produce comparable groups.
Allocation concealment (selection bias)	Unclear risk	The method used to conceal the allocation sequence, that is to determine whether intervention allocations could have been foreseen in advance of, or during, enrolment, was not reported. Comment: There was insufficient information to permit a clear judgement.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote (page 151): "..double-blind.." Comment: The report did not provide sufficient detail about the specific measures used to blind study participants and personnel from knowledge of which intervention a participant received, to permit a clear judgement.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote (page 151): "..double-blind.." Comment: The report did not provide sufficient detail about the specific measures used to blind study participants and personnel. It was unclear therefore, whether the outcome measurement was likely to be influenced by the lack of blinding.
Incomplete outcome data (attrition bias) All outcomes	Low risk	No losses to follow-up reported. Comment: We judged this as a low risk of bias.
Selective reporting (reporting bias)	Low risk	The protocol for the study was not available, but the prespecified outcomes and those mentioned in the methods section appeared to have been reported. Comment: We judged this as at a low risk of bias.
Other bias	Low risk	The study appeared to be free of other forms of bias.

Alomar 1992

Methods	Randomised, double-blind, active-controlled trial Setting Multi-centre (13), Spain Date of study June 1988 - June 1989. Duration of the intervention 4 weeks with follow-up at 5 weeks
Participants	N = 631 (gender and age unreported) **Inclusion criteria of the trial** • 18-70 years • superficial mycotic skin infection confirmed by KOH and culture **Exclusion criteria of the trial** • pregnant or lactating women • hypersensitivity to topical azolic products • use of topical treatments, especially antifungals < 1 week prior to study entry • systemic antimicrobial or antifungal treatment < 4 weeks prior to study entry • onychomycosis, tinea capitis, pityriasis versicolor with a severity not treatable solely with topical treatment • severe organic or psychiatric disease that could interfere with progress of the trial • participants incapable of understanding the nature of the trial Randomised N = 631 Withdrawals/losses to follow-up 62/631 (10%); sertaconazole (22), miconazole (40) • treatment failure; sertaconazole (2), miconazole (17) • loss to follow-up; sertaconazole (9), miconazole (16) • adverse drug reaction; sertaconazole (2), miconazole (4) • concomitant disease; sertaconazole (3), miconazole (0) • others; sertaconazole (6), miconazole (3) Baseline data Tinea pedis: sertaconazole (91), miconazole (75) Tinea corporis: sertaconazole (103), miconazole (102) Tinea barbae: sertaconazole (9), miconazole (9) Tinea manuum: sertaconazole (28), miconazole (20) Tinea cruris: sertaconazole (102), miconazole (106)
Interventions	**Intervention** • sertaconazole (2%) cream b.i.d. for 28 days (358) **Comparator**

Alomar 1992 *(Continued)*

- miconazole (2%) cream b.i.d. for 28 days (334)

Outcomes	Assessments (6): baseline, weeks 1, 2, 3, 4 and 5 **Outcomes of the trial** (as reported) 1. Mycological evaluation (KOH and culture) 2. Clinical evaluation: 6-point Likert scale# 3. Adverse events# 4. Tolerance Denotes outcomes prespecified for this review
Notes	We only included data on participants with tinea corporis and cruris. See Table 3

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote (page 769): "The medication was allocated by randomization tables according to centres and in blocks." Comment: Probably done.
Allocation concealment (selection bias)	Unclear risk	The method used to conceal the allocation sequence, that is to determine whether intervention allocations could have been foreseen in advance of, or during, enrolment, was not reported. Comment: There was insufficient information to permit a clear judgement.
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote (page 769): ".. double-blind.." and ".. same colour, smell, and consistency and in identical packaging..". Comment: The report provided sufficient detail about the measures used to blind study participants and personnel from knowledge of which intervention a participant received, to permit a clear judgement.
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Outcomes were investigator-assessed as well as participant-assessed. Blinding of participants and key study personnel was ensured, and it is unlikely that the blinding could have been broken. Comment: We judged this as at a low risk of bias.
Incomplete outcome data (attrition bias) All outcomes	Low risk	62/631 (10%); sertaconazole (22), miconazole (40). Per-protocol analysis. Comment: Low and reasonably balanced number of drop-outs at follow-up, and although per-protocol analysis considered to be at low risk of bias.
Selective reporting (reporting bias)	Low risk	The protocol for the study was not available, but the prespecified outcomes and those mentioned in the methods section appeared to have been reported. Comment: We judged this as at a low risk of bias.
Other bias	High risk	One of the authors was employed by Research Centre Ferrer Group, the manufacturer of sertaconazole. Comment: A potential risk of bias cannot be excluded.

Altmeyer 1990

Methods	Randomised, double-blind, active-controlled trial Setting Unclear but appears to be multi-centre in Germany Date of study Not reported. Duration of intervention 2-4 weeks with follow-up at 2-3 weeks after end of treatment
Participants	N = 100 (76 male/24 female) Mean age = 38, range 16-65 years **Inclusion criteria of the trial** • cutaneous mycotic infections confirmed by KOH 'and' or 'or' culture **Exclusion criteria of the trial** • antimycotic treatment < 2 weeks prior to study entry • pregnant and breast feeding women • serious systemic or metabolic diseases • hypersensitivity to imidazole derivatives or topical agents in general • non-compliant participants Randomised N = 100 Withdrawals/losses to follow-up • fenticonazole (1/50) interrupted treatment, cyclopyroxolamine (0/50) Baseline data Localisation: Hands: fenticonazole (3), cyclopyroxolamine (2) Feet: fenticonazole (37), cyclopyroxolamine (39) Hands and feet: fenticonazole (1), cyclopyroxolamine (0) Face: fenticonazole (0), cyclopyroxolamine (1) Groin: fenticonazole (3), cyclopyroxolamine (8) Trunk: fenticonazole (6), cyclopyroxolamine (0)
Interventions	**Intervention** • fenticonazole (2%) solution in a spray once daily during 2-4 weeks (50) **Comparator** • cyclopyroxolamine (1%) solution in a spray once daily during 2-4 weeks (50)
Outcomes	Assessments (6): baseline, weeks 1, 2, 3, 4 and 2-3 weeks after end of treatment **Outcomes of the trial** (as reported) 1. Mycological evaluation (KOH and culture)

Altmeyer 1990 *(Continued)*

2. Clinical evaluation of sign and symptoms (itching, burning, pain, erythema, exudation, weeping, pustules, scaling, rhagades and keratosis): 5-point Likert scale#
3. Global therapeutic efficacy: 5-point Likert scale#
4. Relapse
5. Adverse events#

Denotes outcomes prespecified for this review

Notes	We only included participants with tinea cruris and corporis. See Table 3

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote (page 62): ".. were randomized.." Comment: Insufficient detail was reported about the method used to generate the allocation sequence to allow a clear assessment of whether it would produce comparable groups.
Allocation concealment (selection bias)	Unclear risk	The method used to conceal the allocation sequence, that is to determine whether intervention allocations could have been foreseen in advance of, or during, enrolment, was not reported. Comment: There was insufficient information to permit a clear judgement.
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote (page 61-62): ".. double-blind.." and ".. supplied in identical containers..". Comment: The report provided sufficient detail about the measures used to blind study participants and personnel from knowledge of which intervention a participant received, to permit a clear judgement.
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Outcomes were investigator-assessed as well as participant-assessed. Blinding of participants and key study personnel was ensured, and it is unlikely that the blinding could have been broken. Comment: We judged this as at a low risk of bias.
Incomplete outcome data (attrition bias) All outcomes	Low risk	1/100 (fenticonazole group) interrupted treatment "due to slight itching". Per-protocol analysis. Comment: We judged this as at low risk of bias.
Selective reporting (reporting bias)	Low risk	The protocol for the study was not available, but the prespecified outcomes and those mentioned in the methods section appeared to have been reported. Comment: We judged this as at a low risk of bias.
Other bias	High risk	One of the authors was employed by Recordati Industria Chimica e Farmaceutica SpA, the manufacturer of fenticonazole. Comment: A potential risk of bias cannot be excluded.

Athow-Frost 1986

Methods	Randomised, double-blind, active-controlled trial Setting

Athow-Frost 1986 *(Continued)*

	Multi-centre (4), Germany and UK Date of study Unreported. Duration of intervention up to for weeks with follow-up at 6 and 10 weeks
Participants	N = 60 (35 male/18 female; 7 gender unreported) Mean age = 30 years **Inclusion criteria of the trial** • dermatophytosis (ringworm) of hands, feet or other parts of the body, or from pityriasis versicolor confirmed by KOH and culture • > 14 years **Exclusion criteria of the trial** • tinea unguium alone • (possibly) pregnant or lactating women • antifungal therapy < 2 weeks prior to study entry • history of hypersensitivity to miconazole or related preparations • history of multiple hypersensitivity reactions to locally applied medications Randomised N = 60 Delayed exclusions: • 5/60, unclear from which groups: negative culture for dermatophytes Withdrawals/losses to follow-up • miconazole (2): defaulted from follow-up at early stages in the trial Baseline data Diagnosis: Tinea pedis: fenticonazole (15), miconazole (17) Tinea cruris: fenticonazole (3), miconazole (2) Tinea manuum: fenticonazole (3), miconazole (2) Tinea corporis: fenticonazole (0), miconazole (2) Pityriasis versicolor: fenticonazole (7), miconazole (2)
Interventions	**Intervention** • fenticonazole (2%) cream b.i.d. for up to 4 weeks (28) **Comparator** • miconazole (2%) cream b.i.d. for up to 4 weeks (25) No antifungal or other topical skin therapy apart from trial medication permitted
Outcomes	Assessments (7): baseline, weekly 1-4, and 2, 6 weeks after discontinuation of treatment **Outcomes of the trial** (as reported) 1. Mycological evaluation (KOH and culture) 2. Clinical evaluation of signs and symptoms (erythema, itching, desquamation, vesicular eruption and oedema): 4-point Likert scale# 3. Overall clinical assessment: 3-point Likert scale#

Athow-Frost 1986 *(Continued)*

4. Routine laboratory haematological and biochemical screening
5. Adverse effects

Denotes outcomes prespecified for this review

Notes	We only considered data from participants with tinea corporis or cruris. See Table 3

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote (page 109): "On entry, patients were allocated the next available treatment number which determined, according to a randomization code...". Comment: Insufficient detail was reported about the method used to generate the allocation sequence to allow a clear assessment of whether it would produce comparable groups.
Allocation concealment (selection bias)	Unclear risk	The method used to conceal the allocation sequence, that is to determine whether intervention allocations could have been foreseen in advance of, or during, enrolment, was not reported. Comment: There was insufficient information to permit a clear judgement.
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote (page 109): "The appearance and packaging of both drugs were identical, so that neither patients nor investigators were aware of which treatment was being received". Comment: The report provided sufficient detail about the measures used to blind study participants and personnel from knowledge of which intervention a participant received, to permit a clear judgement.
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Outcomes were investigator-assessed as well as participant-assessed. Blinding of participants and key study personnel was ensured, and it is unlikely that the blinding could have been broken. Comment: We judged this as at a low risk of bias.
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Losses after randomisation due to negative baseline culture: 5/60 (8%) unclear from which group. Failed to attend for follow-up : (2) miconazole group. Per-protocol analysis Comment: Total of 7/60 (12%) combined with the per-protocol analysis poses an unclear risk of bias for this domain.
Selective reporting (reporting bias)	Low risk	The protocol for the study was not available, but the prespecified outcomes and those mentioned in the methods section appeared to have been reported. Comment: We judged this as at a low risk of bias.
Other bias	Unclear risk	Quote (page 116): "We are indebted toRecordati SPA, Milan, for advice, support and supplies of fenticonazole". Comment: Insufficient information to assess whether important risk of bias exists.

Avila 1985

Methods	Randomised, double-blind, active-controlled trial Setting Dermatology Department of Hospital, Lima, Peru Date of study Not reported. Duration of the intervention 3 weeks with follow-up at 5 weeks
Participants	N = 40 (34 male/6 female) Mean age = 39, range 21-67 years **Inclusion criteria of the trial** • clinical fungal disease confirmed by KOH **Exclusion criteria of the trial** • tinea capitis, pityriasis versicolor, onychomycosis • unstable diabetes, impaired immune function, chronic moccasin type tinea pedis > 6 months • use of griseofulvin or other antifungal treatment < 1 week prior to study entry Randomised N = 40 Withdrawals/losses to follow-up • no drop-outs Baseline data Diagnosis: Tinea pedis: sulconazole (15), miconazole (18) Tinea cruris: sulconazole (3), miconazole (2) Tinea corporis: sulconazole (1), miconazole (0) Tinea manuum: sulconazole (1), miconazole (0)
Interventions	**Intervention** • sulconazole nitrate (1%) cream b.i.d. for 3 weeks (20) **Comparator** • miconazole nitrate (2%) cream b.i.d. for 3 weeks (20)
Outcomes	Assessments (5): baseline, weeks 1, 2, 3, and 5 **Outcomes of the trial** (as reported) 1. Mycological evaluation (KOH and culture) 2. Clinical evaluation of signs and symptoms (erythema, scales, itchiness, macerations, vesicles, fissures and pustules: 4-point Likert scale# 3. Overall clinical improvement: 5-point Likert scale# 4. Relapse 5. Adverse events#

Avila 1985 *(Continued)*

Denotes outcomes prespecified for this review

Notes	We only included participants with tinea cruris and corporis. See Table 3

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote (page 330): "..two randomly allocated treatments..". Comment: Insufficient detail was reported about the method used to generate the allocation sequence to allow a clear assessment of whether it would produce comparable groups.
Allocation concealment (selection bias)	Unclear risk	The method used to conceal the allocation sequence, that is to determine whether intervention allocations could have been foreseen in advance of, or during, enrolment, was not reported. Comment: There was insufficient information to permit a clear judgement.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote (page 329): "..double-blind.." Comment: The report did not provide sufficient detail about the specific measures used to blind study participants and personnel from knowledge of which intervention a participant received, to permit a clear judgement.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote (page 329): "..double-blind.." Comment: The report did not provide sufficient detail about the specific measures used to blind study participants and personnel. It was unclear therefore, whether the outcome measurement was likely to be influenced by the lack of blinding.
Incomplete outcome data (attrition bias) All outcomes	Low risk	No losses to follow-up. Comment: We judged this as at low risk of bias.
Selective reporting (reporting bias)	Low risk	The protocol for the study was not available, but the prespecified outcomes and those mentioned in the methods section appeared to have been reported. Comment: We judged this as at a low risk of bias.
Other bias	Low risk	The study appeared to be free of other forms of bias.

Bagatell 1986

Methods	Randomised, placebo (vehicle)-controlled trial Setting Not reported, USA Date of study Not reported. Duration of intervention daily for 3 weeks to follow-up at 5 weeks
Participants	N = 37 (33 male/4 female) Age range 12–65, median 42 years

Bagatell 1986 *(Continued)*

Inclusion criteria of the trial

- >12 years
- clinically diagnosed and mycologically confirmed (KOH and scrapings for cultures) tinea corporis/cruris of trunk, groin or perianal region

Exclusion criteria of the trial

- haematological, hepatic, renal or cardiac disease
- pregnant or nursing females
- hypersensitivity to imidazoles
- concomitant topical/systemic antifungal therapy
- chemotherapeutic medications
- no topical medications previous 7 days or systemic antimycotics previous 30 days

Randomised

N = 37

Withdrawals/losses to follow-up

- vehicle (3), lost to follow-up at week 3
- bifonazole (1), not evaluated at week 3

Baseline data

Disease duration in months:

- < 1; bifonazole (5), vehicle (2)
- > 1-6; bifonazole (4), vehicle (5)
- > 6-12; bifonazole (1), vehicle (1)
- > 12; bifonazole (10), vehicle (9)
- unknown; bifonazole (0), vehicle (3)

Use of previous medication for tinea corporis/cruris (type, timing and duration unreported)

- bifonazole (13/20), vehicle (9/17)

Interventions	**Intervention** • bifonazole (1%) cream once a day for 3 weeks (20) **Comparator** • vehicle once a day for 3 weeks (17)
Outcomes	Assessments (5): baseline, weeks 1, 2, 3, and 5 **Outcomes of the trial** (as reported) 1. Clinical sign and symptoms: 3-point Likert scale# 2. Mycological evaluation (KOH and culture) 3. Overall rate of response Denotes outcomes prespecified for this review
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement

Bagatell 1986 *(Continued)*

Random sequence generation (selection bias)	Unclear risk	Quote (page 295): "..were randomly assigned to treatment..". Comment: Insufficient detail was reported about the method used to generate the allocation sequence to allow a clear assessment of whether it would produce comparable groups.
Allocation concealment (selection bias)	Unclear risk	The method used to conceal the allocation sequence, that is to determine whether intervention allocations could have been foreseen in advance of, or during, enrolment, was not reported. Comment: There was insufficient information to permit a clear judgement.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote (page 295): "..double-blind.." Comment: The report did not provide sufficient detail about the specific measures used to blind study participants and personnel from knowledge of which intervention a participant received, to permit a clear judgement.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote (page 295): "..double-blind.." Comment: The report did not provide sufficient detail about the specific measures used to blind study participants and personnel. It was unclear therefore, whether the outcome measurement was likely to be influenced by the lack of blinding.
Incomplete outcome data (attrition bias) All outcomes	High risk	3/17 lost to follow-up in the vehicle group. Per-protocol analysis. Comment: Losses in vehicle group are likely to be due to lack of effect which combined with the per-protocol analysis, represents a potential high risk of bias.
Selective reporting (reporting bias)	Low risk	The protocol for the study was not available, but the prespecified outcomes and those mentioned in the methods section appeared to have been reported. Comment: We judged this as at a low risk of bias.
Other bias	Low risk	The study appeared to be free of other forms of bias.

Banerjee 2011

Methods	Randomised, controlled trial with 3 parallel treatment arms Setting Dermatology outdoor clinic of School of Tropical Medicine, Kolkata, India Date of study Not reported. Duration of intervention 4 weeks to follow-up 8 weeks
Participants	N = 150 (85 male/65 female) Age range 18–65, mean 31 years **Inclusion criteria of the trial** • clinical diagnosis of mild to moderate grades of tinea corporis • mycologically confirmed presence of fungal hyphae **Exclusion criteria of the trial**

Banerjee 2011 *(Continued)*

- uncontrolled diabetes
- HIV infection
- suffering from concomitant bacterial infection
- pregnant or lactating mothers; females reproductive age practicing unreliable methods of contraception
- systemic 'and' or 'or' topical antifungal agents use during previous month
- negative skin scraping for fungus from a clinically suspected lesion at baseline visit

Randomised

N = 150

Withdrawals/losses to follow-up

- amorolfine group 10/48 (21%) reasons unreported
- clotrimazole group 9/51 (17.6%) for non compliance or lost to follow-up
- fluconazole group 10/51 (19.6%) for non compliance or lost to follow-up

Baseline data

Not reported

Interventions	**Intervention** • amorolfine (0.25%) cream b.i.d. for 4 weeks (48) **Comparator 1** • clotrimazole (1%) cream b.i.d. for 4 weeks (51) **Comparator 2** • fluconazole (0.5%) gel b.i.d. for 4 weeks (51) No concomitant other antifungal; any other topical medication or systemic antifungals, antihistamines and corticosteroids were permitted.
Outcomes	Assessments (4): baseline, days 14, 28, 56 **Outcomes of the trial** (as reported) 1. Mycological cure rate# 2. Clinical improvement of itching, erythema and scaling: 4-point Likert scale# 3. Physician's global clinical assessment of "effectivity and tolerability": 4-point Likert scale# 4. Participant's assessment of "effectivity and acceptability" of treatment: 4-point Likert scale# 5. Adverse events# Denotes outcomes prespecified for this review
Notes	Data for fluconazole (0.5%) gel treatment arm reported separately in Banerjee 2012 (See primary reference Banerjee 2011)

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote (page 658): "..randomized, controlled trial...." and "divided into three groups randomly...."

Banerjee 2011 *(Continued)*

		Comment: Insufficient detail was reported about the method used to generate the allocation sequence to allow a clear assessment of whether it would produce comparable groups. After e-mail contact: "Randomization was achieved through Random Number Table and patients were accordingly allocated to the respective groups." Comment: Probably done.
Allocation concealment (selection bias)	Unclear risk	The method used to conceal the allocation sequence, that is to determine whether intervention allocations could have been foreseen in advance of, or during, enrolment, was not reported. Comment: There was insufficient information to permit a clear judgement. After e-mail contact: "However, drug allotment and clinical assessment of patients were done by different set of researchers and the data were kept separately till the end of the studies." Comment: It remains unclear if the allocation concealment was adequate.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote (page 658): "amorolfine has been recommended by the manufacturer for once daily use, we have recommended its use in the study patients twice daily for the purpose of blinding the evaluation of its effectivity and adverse effects". Comment: The impact of incomplete or possibly inadequate blinding of participants and trialists was unclear. After e-mail contact: "we could not procure the medicines in identical containers" Comment: The impact of incomplete or possibly inadequate blinding of participants and trialists remains unclear.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote (page 658): "We tried to single blind the study by engaging an investigator for evaluating the patients during selection and follow-up, but was kept blinded regarding the molecule used by the patient". Comment: Reasonable attempts appear to have been made to blind the personnel (outcomes assessors) at follow-up, but participants who were also outcomes assessors may not have been adequately blinded. Unclear to what extent this had an impact on participant-assessed outcomes.
Incomplete outcome data (attrition bias) All outcomes	High risk	Missing outcome data: clotrimazole group 9/51 (17.6%) for non compliance or lost to follow-up, amorolfine group 10/48 (21%) and fluconazole group 10/51 (19.6%) for non compliance or lost to follow-up. Comment: Although balanced across groups, the high drop-out rate with per-protocol analysis represents a potential high risk of bias.
Selective reporting (reporting bias)	Low risk	The protocol for the study was not available, but the prespecified outcomes and those mentioned in the methods section appeared to have been reported. Comment: We judged this as at a low risk of bias.
Other bias	Low risk	The study appeared to be free of other forms of bias.

Björnberg 1986

Methods	Randomised, double-blind, active-controlled, within-patient comparison trial

Björnberg 1986 *(Continued)*

	Setting Department of Dermatology, University of Lund, Sweden Date of study Not reported. Duration of intervention up to 4 weeks
Participants	N = 26 (25 male/1 female) Age range = 16-65 years **Inclusion criteria of the trial** • bilateral symmetric lesions tinea pedis and cruris confirmed by KOH **Exclusion criteria of the trial** • not reported Randomised N = 26 Withdrawals/losses to follow-up • 2/26 reasons not known Baseline data Tinea pedis: 6 Tinea cruris: 20
Interventions	**Intervention** • miconazole (2%) cream b.i.d. for up to 4 weeks (26) **Comparator** • miconazole (2%)-hydrocortisone (1%) cream b.i.d. for up to 4 weeks (26)
Outcomes	Assessments (3): baseline, weeks 2 and 4 **Outcomes of the trial** (as reported) 1. Clinical evaluation: 5-point Likert scale# 2. Adverse events# Denotes outcomes prespecified for this review
Notes	We only included data on participants with tinea cruris. See Table 3

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote (page 471): "..randomized.." Comment: Insufficient detail was reported about the method used to generate the allocation sequence to allow a clear assessment of whether it would produce comparable groups.

Björnberg 1986 *(Continued)*

Allocation concealment (selection bias)	Unclear risk	The method used to conceal the allocation sequence, that is to determine whether intervention allocations could have been foreseen in advance of, or during, enrolment, was not reported. Comment: There was insufficient information to permit a clear judgement.
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote (page 471): ".. received two tubes of cream with identical appearance.." Comment: The report provided sufficient detail about the measures used to blind study participants and personnel from knowledge of which intervention a participant received, to permit a clear judgement.
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Outcomes were investigator-assessed as well as participant-assessed. Blinding of participants and key study personnel was ensured, and it is unlikely that the blinding could have been broken. Comment: We judged this as at a low risk of bias.
Incomplete outcome data (attrition bias) All outcomes	Low risk	2/26 were lost to follow-up for unknown reasons. Within-patient comparison. Comment: We judged this as at low risk of bias.
Selective reporting (reporting bias)	Low risk	The protocol for the study was not available, but the prespecified outcomes and those mentioned in the methods section appeared to have been reported. Comment: We judged this as at a low risk of bias.
Other bias	Low risk	The study appeared to be free of other forms of bias.

Bogaert 1986

Methods	Randomised, double-blind, controlled (vehicle and active intervention) trials (2 studies) Setting Multi-centre, Dominican Republic, Guatemala, USA Date of study Not reported. Duration of intervention 4 weeks to follow-up 2 weeks post treatment
Participants	Study 1: ciclopirox olamine cream versus vehicle (N = 139). Study 2: ciclopirox olamine cream versus clotrimazole (N = 90) Age and gender unreported **Inclusion criteria of the trial** • >10 yrs old (vehicle controlled); >3 years old (clotrimazole controlled) • clinical and mycological diagnosis (KOH and culture) of tinea cruris or corporis **Exclusion criteria of the trial** • pregnancy • antifungal therapy prior 7 days Randomised Study 1; N = 139; Study 2; N = 90

Bogaert 1986 *(Continued)*

	Withdrawals/losses to follow-up • Study 1: at end of study all patients evaluated, at 5/6 weeks (4/70) ciclopirox olamine group and (3/69) vehicle group lost to follow-up. Reasons not reported • Study 2: at end of study all patients evaluated, at 5/6 weeks (7/40) ciclopirox olamine group and (14/50) clotrimazole group lost to follow-up. Reasons not reported Baseline data Nothing reported
Interventions	**Study 1** **Intervention** • ciclopirox olamine (1%) cream b.i.d. over 4 weeks (70) **Comparator** • vehicle over 4 weeks b.i.d. (69) **Study 2** **Intervention** • ciclopirox olamine (1%) cream over 4 weeks (40) **Comparator** • clotrimazole (1%) cream over 4 weeks (50) No concomitant topical or systemic antifungal or corticosteroid permitted.
Outcomes	Assessments (6): baseline, weeks 1, 2, 3, 4, 5 or 6 **Outcomes of the trial** (as reported) 1. Clinical evaluation (overall severity, as well as severity of scaling, pruritus, vesiculation, inflammation, erythema, oedema, fissures, exudation and maceration): 4-point Likert scale# 2. Assessment of treatment response: 3 point Likert scale# 3. Mycological evaluation (KOH and culture) 4. Adverse events ("safety" and "tolerance") Denotes outcomes prespecified for this review
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote (page 211): "..randomly allocated to treatment groups..". Comment: Insufficient detail was reported (both studies) about the method used to generate the allocation sequence to allow a clear assessment of whether it would produce comparable groups.
Allocation concealment (selection bias)	Unclear risk	The method used to conceal the allocation sequence, that is to determine whether intervention allocations could have been foreseen in advance of, or during, enrolment, was not reported (both studies). Comment: There was insufficient information to permit a clear judgement.

Bogaert 1986 *(Continued)*

Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote (page 210): "..double-blind..". Comment: The report (both studies) did not provide sufficient detail about the specific measures used to blind study participants and personnel from knowledge of which intervention a participant received, to permit a clear judgement.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote (page 211): "..clinical and mycological assessment..". Comment: Uncertainty with the effectiveness of blinding of outcomes assessors (participants/healthcare providers) during the study. Insufficient information to permit a clear judgement.
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Both studies no drop-outs at the end of treatment evaluations week 4. Losses to follow-up in treatment-free period at 5/6 weeks: Study 1: ciclopirox olamine group (4/70) and vehicle group (3/69). Reasons not reported. Study 2: ciclopirox olamine group(7/40) and clotrimazole group (14/50). Reasons not reported. Comment: Study 1 (5%) low numbers balanced across the groups. Study 2 (23%) higher numbers and unbalanced. Unclear if losses to follow-up due to discontinuation of treatment or lack of treatment effect. We judged this at unclear risk of bias.
Selective reporting (reporting bias)	Low risk	The protocol for the study was not available, but the prespecified outcomes and those mentioned in the methods section appeared to have been reported. Comment: We judged this as at a low risk of bias.
Other bias	Low risk	The study appeared to be free of other forms of bias.

Borelli 2007

Methods	Randomised, open-label, active-controlled, non-inferiority study Setting Multi-centre, dermatology practices (24) in Germany Date of study Not reported. Duration of intervention 1-2 weeks to follow-up at 4 weeks
Participants	N = 535 (male/female numbers unreported) Age range 18–70 years **Inclusion criteria of the trial** • positive culture test at the pretreatment visit for tinea corporis or tinea pedis as a result of dermatophytes, or a candidosis • clinical signs and symptoms indicative of the various target diseases • investigator assessed: Total Clinical Score (TCS) ≥6; erythema, desquamation, vesicles, pustules, and itch (0 = absent, 1 = mild, 2 = moderate, and 3 = severe) • positive finding on direct microscopic examination **Exclusion criteria of the trial**

Borelli 2007 *(Continued)*

- systemic mycosis or mycosis of the hands, face, or scalp, oropharyngeal mycosis 'and' or 'or' vaginal mycosis
- fungal skin infection located on an adjacent skin area
- pretreatment with antifungal drugs (previous 14 days) and immunosuppressive agents (30 days)
- pregnancy, lactation, or inadequate contraception in women of child-bearing potential
- severe psychiatric illnesses
- allergy to sertaconazole or vehicle ingredients
- participation in another study 30 days prior to study commencement

Randomised

N = 535

Delayed exclusions:

222/535 (41%): negative culture for dermatophytes. Excluded from ITT analysis. Full analysis set (FAS) = 313 participants, sertaconazole solution (160) group; sertaconazole cream (153) group

Withdrawals/losses to follow-up:

- sertaconazole solution (36/160); sertaconazole cream (43/153). Total:79/313, protocol violations (68), premature termination (11)

Baseline data

- dermatophytes in culture: solution (147/185); cream (138/185) groups
- Candida spp in culture: solution (8/12); cream (12/20) groups
- dermatophytes and Candida spp in culture: solution (5/8); cream (3/8) groups
- 80/313 trunk or groin (35 solution, 45 cream group), 233 tinea pedis

Interventions	**Intervention** • sertaconazole (2%) solution b.i.d. for 28 days (160) **Comparator** • sertaconazole (2%) cream b.i.d. for 28 days (153)
Outcomes	Assessments (3): pretreatment, weeks 2 and 4 **Outcomes of the trial** (as reported) 1. Culture 2. Total clinical score (erythema, desquamation, vesicles, pustules, and itch): 4-point Likert scale# 3. Adverse events# Denotes outcomes prespecified for this review
Notes	We only considered data from participants with tinea corporis or cruris, however the report unclear how many infections of the trunk and groin were caused by dermatophytes. See 'Contact with Investigators' Table 1 and Table 3

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote (page 372): "..randomly assigned to one of the two therapy groups..".

Borelli 2007 *(Continued)*

		Comment: Insufficient detail was reported about the method used to generate the allocation sequence to allow a clear assessment of whether it would produce comparable groups.
Allocation concealment (selection bias)	Unclear risk	The method used to conceal the allocation sequence, that is to determine whether intervention allocations could have been foreseen in advance of, or during, enrolment, was not reported. Comment: There was insufficient information to permit a clear judgement.
Blinding of participants and personnel (performance bias) All outcomes	High risk	Quote (page 371): "..open-label..". Comment: The outcome was likely to be influenced by the lack of blinding.
Blinding of outcome assessment (detection bias) All outcomes	High risk	Quote (page 371): "..open-label..". Comment: The outcome measurement was likely to be influenced by the lack of blinding.
Incomplete outcome data (attrition bias) All outcomes	High risk	Losses after randomisation due to negative baseline culture: 41% participants failed criterion of 'positive culture test at pretreatment visit' and were not included in the full analysis set (FAS). FAS = 313 participants, 160 in sertaconazole solution group and 153 in sertaconazole cream group. Withdrawals/losses to follow-up: sertaconazole solution (36/160); sertaconazole cream (43/153). Total:79/313 (25%), protocol violations (68), premature termination (11). Comment: Entry criterion (culture specimen) measured prior to randomisation. The delayed exclusions are well-balanced between groups, no attrition bias between the groups. See ICH Expert Working Group 1998. Large and although well balanced number of drop-outs at follow-up, combined with per-protocol analysis considered to be at high risk of bias.
Selective reporting (reporting bias)	Low risk	The protocol for the study was not available, but the prespecified outcomes and those mentioned in the methods section appeared to have been reported. Comment: We judged this as at a low risk of bias.
Other bias	High risk	Quote (page 377): "trial funded by Dr R Pfleger GmbH, Bamberg, Germany and Ferrer International, Barcelona, Spain". One of the investigators was an employee and "some of the authors and study group members received compensation for their contribution to the trial". Comment: A potential risk of bias cannot be excluded.

Budimulja 1998

Methods	Randomised, double-blind, active-controlled trial Setting Multi-centre (unspecified) in Indonesia Date of study Not reported. Duration of intervention 1 week and placebo 2 weeks and 3 weeks for comparator to follow-up at 8 weeks

Budimulja 1998 *(Continued)*

Participants	N = 185 (100 male/85 female) Age range 18–64, 50% in the 25-44 age group **Inclusion criteria of the trial** • clinical diagnosis of tinea cruris and a positive mycologic examination **Exclusion criteria of the trial** • nothing reported Randomised N = 185 Withdrawals/losses to follow-up • week 3: (10/185); bifonazole (6); terbinafine (4). Reasons: loss to follow-up (9) and developed contact dermatitis terbinafine group (1) • week 8: (16/185) bifonazole (8); terbinafine (8) nothing further reported Baseline data Duration of disease: • <1 month terbinafine 29/93 (31.2%); bifonazole 30/92 (32.6%) groups • 1–6 months terbinafine 33/93 (35.5%); bifonazole 37/92 (40.2%) groups • >6 months terbinafine 31/93 (33.3%); bifonazole 25/92 (27.2%) groups
Interventions	**Intervention** • terbinafine cream (1%) once daily for 1 week and 2 weeks placebo (93) **Comparator** • bifonazole cream (1%) applied once daily for 3 weeks (92)
Outcomes	Assessments (4): baseline, weeks 1, 2, 3 and 8 **Outcomes of the trial** (as reported) 1. Assessments of clinical signs and symptoms (pruritus, erythema, papules): 3-point Likert scale# 2. Global assessment of effectiveness: 3-point Likert scale# 3. Mycologic cure rate# 4. Tolerability of the study medication 5. Adverse events (at each follow-up visit) 6. Relapse rate at week 8# Denotes outcomes prespecified for this review
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote (page 871): "..double-blind randomized..".

Budimulja 1998 *(Continued)*

		Comment: Insufficient detail was reported about the method used to generate the allocation sequence to allow a clear assessment of whether it would produce comparable groups.
Allocation concealment (selection bias)	Unclear risk	The method used to conceal the allocation sequence, that is to determine whether intervention allocations could have been foreseen in advance of, or during, enrolment, was not reported. Comment: There was insufficient information to permit a clear judgement.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote (page 871): "..double-blind..". Comment: The report did not provide sufficient detail about the specific measures used to blind study participants and personnel from knowledge of which intervention a participant received, to permit a clear judgement.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote (page 871): "..double-blind..". Comment: There was insufficient information to permit clear judgement of risk of bias.
Incomplete outcome data (attrition bias) All outcomes	Low risk	Drop-outs at week 3: bifonazole group (6); terbinafine group (4). Reasons: loss to follow-up (9); contact dermatitis (1). Data analysis per-protocol Comment: Low and well balanced number of drop-outs, and although per-protocol analysis considered to be at low risk of bias.
Selective reporting (reporting bias)	High risk	Tolerability unreported and adverse events minimally and incompletely reported. Comment: We judged this as at a high risk of bias.
Other bias	Unclear risk	Quote: "Sandoz Biochemie Farma Indonesia provided support". Comment: The investigators did not confirm what support was provided, but one of the interventions under investigation was terbinafine (Sandoz), thus a potential risk of bias cannot be excluded.

Budimulja 2001

Methods	Randomised, double-blind, active-controlled study Setting Two centres in Indonesia Date of study Not reported. Duration of intervention 7 days to follow-up 7 weeks
Participants	N = 120, gender reported for only 117 (53 male/ 64 female) Age range 15–70, mean 35.5 years **Inclusion criteria of the trial** • clinical diagnosis of tinea corporis/cruris confirmed by microscopy detection of fungal hyphae on a KOH wet mount **Exclusion criteria of the trial** • topical antifungal agent use within 28 days, or oral antifungal treatment prior 6 weeks • history of radiation therapy

Budimulja 2001 *(Continued)*

- systemic therapy with cytostatic or immunosuppressive drugs prior 2 weeks
- use of antibacterial, antiviral, or antihelminthic drugs prior 2 weeks
- pregnancy and lactation
- history of drug or alcohol abuse
- hypersensitivity to terbinafine
- immunodeficiency

Randomised

N = 120

Delayed exclusions:

Terbinafine (3): negative culture for dermatophytes (1); no day 1 assessment of efficacy following commencement of treatment (2). Excluded from ITT analysis

Withdrawals/losses to follow-up

16/117 (13%), terbinafine group (4) placebo group (12)

- protocol violation (1 in each group)
- lost to follow-up terbinafine group (3), placebo group (1)
- adverse events placebo group (2)
- unsatisfactory therapeutic effect placebo group (8)

Baseline data

Trichophyton rubrum infection (109)
Epidermophyton Floccosum infection (8)

Trichophyton mentagrophytes infection (2)

Interventions	**Intervention** • terbinafine (1%) cream once daily for 7 days (60) **Comparator** • placebo once daily for 7 days (60)
Outcomes	Assessments (5): baseline, days 8, 14, 42, and 56 **Outcomes of the trial** (as reported) 1. Mycological cure (KOH and culture) 2. Total clinical signs and symptoms score (erythema, scaling, pruritus, vesiculation, pustules, exudation, crusting, and papules: 4-point Likert scale# 3. Clinical response 4. Overall assessment of efficacy and tolerability: 5-point Likert scale# 5. Adverse events# Denotes outcomes prespecified for this review
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote (page 44): "..randomized to treatment..".

Budimulja 2001 *(Continued)*

		Comment: Insufficient detail was reported about the method used to generate the allocation sequence to allow a clear assessment of whether it would produce comparable groups.
Allocation concealment (selection bias)	Unclear risk	The method used to conceal the allocation sequence, that is to determine whether intervention allocations could have been foreseen in advance of, or during, enrolment, was not reported. Comment: There was insufficient information to permit a clear judgement.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote (page 301): "..double-blind..". Comment: The report did not provide sufficient detail about the specific measures used to blind study participants and personnel from knowledge of which intervention a participant received, to permit a clear judgement.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote page (301): "..double-blind..". Comment: The report did not provide sufficient detail about the measures used to blind study participants and personnel. It was unclear therefore, whether the outcome measurement was likely to be influenced by the lack of blinding.
Incomplete outcome data (attrition bias) All outcomes	Low risk	3 terbinafine group were excluded after randomisation and not included in intention-to-treat analysis. Further 16 lost to follow-up: placebo 12 (20%). All included in intention-to-treat analysis. Comment: We judged this as at a low risk of bias.
Selective reporting (reporting bias)	Low risk	The protocol for the study was not available, but the prespecified outcomes and those mentioned in the methods section appeared to have been reported. Comment: We judged this as at a low risk of bias.
Other bias	Low risk	The study appeared to be free of other forms of bias.

Califano 1999

Methods	Randomised, open, active-controlled study Setting Dermatology departments of 2 hospitals in Messina and Lucca, Italy Date of study Not reported. Duration of intervention 1-3 weeks with 4 weeks follow-up
Participants	N = 61 (28 male/33 female) Median age = 39.5 years **Inclusion criteria of the trial** • localised dermatomycosis (tinea cruris, tinea corporis and tinea pedis) • confirmation by KOH and culture **Exclusion criteria of the trial** • participants with pityriasis versicolor

Califano 1999 *(Continued)*

- other skin infection
- other antimycotic treatment prior to study
- allergy to antimycotics
- concomitant treatment with barbiturates, coumarin anticoagulants, antidiabetic medication
- concomitant use of antibiotics for bacterial infection

Randomised

N = 61

Withdrawals/losses to follow-up

- fluconazole (1/32) due to protocol violation, econazole (0/29)

Baseline data

Tinea pedis: fluconazole (3), econazole (4)

Tinea corporis: fluconazole (20), econazole (19)

Tinea cruris: fluconazole (0), econazole (3)

Other: fluconazole (9), econazole (3)

Interventions	**Intervention** • topical fluconazole (0.5%) once a day for 1 up to 3 weeks (32) **Comparator** • topical econazole lipo gel (1%) once a day for 1 up to 3 weeks (29)
Outcomes	Assessments (4-6): baseline, weeks 1-3 and 2 and 4 weeks after end of treatment **Outcomes of the trial** (as reported) 1. Clinical evaluation (burning, erythema, pruritus, exudation, desquamation): 4-point Likert scale# 2. Mycological evaluation (KOH and culture) 3. Adverse events (tolerance) Denotes outcomes prespecified for this review
Notes	Only considered data from participants with tinea corporis or cruris. See Table 3

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote (page 264): "Ogni centro di sperimentazione ha arruolato i pazienti seguendo la lista di randomizzazione fornita dalla Roerig farmaceutici." Comment: Probably done.
Allocation concealment (selection bias)	Low risk	Comment: Sequence was generated by the sponsor, a form of central randomisation. Probably done; judged at a low risk of bias.
Blinding of participants and personnel (performance bias) All outcomes	High risk	Quote (page 263): "..open, comparative..". Comment: The outcome was likely to be influenced by the lack of blinding.

Califano 1999 *(Continued)*

Blinding of outcome assessment (detection bias) All outcomes	High risk	Quote (page 263): "..open, comparative..". Comment: The outcome measurement was likely to be influenced by the lack of blinding.
Incomplete outcome data (attrition bias) All outcomes	Low risk	Drop-out: fluconazole group (1/32) protocol violation. Per-protocol analysis. Comment: We judged this at a low risk of bias.
Selective reporting (reporting bias)	Low risk	The protocol for the study was not available, but the prespecified outcomes and those mentioned in the methods section appeared to have been reported. Comment: We judged this as at a low risk of bias.
Other bias	Unclear risk	Involvement of Roerig farmaceutici (manufacturer of both interventions) unreported, other than in sequence generation. Comment: Insufficient information to assess whether important risk of bias exists.

Clayton 1973

Methods	Randomised, double-blind, active-controlled trial Setting Mycology Department, St Thomas' Hospital UK Date of study Over a 4-month period, date unreported. Duration of intervention 4 weeks to follow-up 8 weeks
Participants	N = 43 (29 male/3 female;11 gender unreported) Age range 13–63 years **Inclusion criteria of the trial** • positive microscopy of skin scrapings for ringworm fungi **Exclusion criteria of the trial** • if first skin scrapings were negative on culture Randomised N = 43 Withdrawals/losses to follow-up • 11/43 (25.6%), reasons and group not reported Baseline data For the 32 who completed the study (16 in each group): • Feet infected: clotrimazole group (4), Whitfield's cream group (6) • Feet and body: clotrimazole group (0), Whitfield's cream group (3) • Feet and groins: clotrimazole group (7), Whitfield's cream group (5) • Groin: clotrimazole group (4), Whitfield's cream group (2) • Groin and body: clotrimazole group (1), Whitfield's cream group (0)

Clayton 1973 *(Continued)*

Interventions	**Intervention** • clotrimazole (1%) b.i.d. for 4 weeks (16) **Comparator** • Whitfield's cream b.i.d. for 4 weeks (16)
Outcomes	Assessments (4): baseline, weeks 2, 4, 8 **Outcomes of the trial** (as reported) 1. Microscopy and culture (1 organism present; ½ organism scanty; 0 organism absent) 2. Clinician's opinion as to effectiveness (1 good; ½ partial; 0 none)# 3. Patient's opinion on acceptability (1 good; ½ moderate; 0 poor) Denotes outcomes prespecified for this review
Notes	Ringworm group included participants with tinea pedis. We only included participants with (additional) tinea corporis or cruris. See Table 3. Study included 3 additional groups of participants (pityriasis versicolor, erythrasma and Candida infections).

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote (page 298): "..were randomized to treatments..". Comment: Insufficient detail was reported about the method used to generate the allocation sequence to allow a clear assessment of whether it would produce comparable groups.
Allocation concealment (selection bias)	Unclear risk	The method used to conceal the allocation sequence, that is to determine whether intervention allocations could have been foreseen in advance of, or during, enrolment, was not reported. Comment: There was insufficient information to permit a clear judgement.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote (page 298): "Neither the clinician, the mycologist, the pharmacist, nor the patient, knew which preparation was being used". Comment: The report did not provide sufficient detail about the specific measures used to blind study participants and personnel from knowledge of which intervention a participant received, to permit a clear judgement.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote (page 298): "Neither the clinician, the mycologist, the pharmacist, nor the patient, knew which preparation was being used". Both investigator and participants were the outcomes assessors. Comment: Uncertainty with the effectiveness of blinding of outcomes assessors (participants/healthcare providers) during the study. Insufficient information to permit a clear judgement.
Incomplete outcome data (attrition bias) All outcomes	High risk	Lost to follow-up: 11/43 (25.6%) reasons not reported, unclear from which groups. Per-protocol analysis. Comment: Judged as at a high risk of bias.
Selective reporting (reporting bias)	Low risk	The protocol for the study was not available, but the prespecified outcomes and those mentioned in the methods section appeared to have been reported. Comment: We judged this as at a low risk of bias.

Clayton 1973 *(Continued)*

Other bias	Unclear risk	Quote (page 302): "We are grateful to Bayer Pharmaceuticals Ltd, for the supply of drugs and for help in organizing the trial". Comment: Insufficient information to assess whether important risk of bias exists.

Clayton 1976

Methods	Randomised, double-blind, active-controlled trial Setting St John's Hospital for Diseases of the Skin, London, UK Date of study Not reported. Duration of the intervention 4 weeks with follow-up at 8 weeks
Participants	N = 136 (74 male/44 female; 18 gender unreported) Age range = 5-62 years **Inclusion criteria of the trial** • participants with dermatophytes (ringworm fungi), Malassezia furfur, Candida yeasts or corynebacteria confirmed by KOH **Exclusion criteria of the trial** • participants with scalp or nail infections Randomised N = 136 Withdrawals/losses to follow-up At week 8: 56/136 (41%) lost to follow-up • dermatophytes infection:12/57 (21%); miconazole (4), clotrimazole (3) needed griseofulvin after 4 weeks: 6 were lost to follow-up (inconsistently reported) • pityriasis versicolor: unclear how many enrolled; 37 completed 4 weeks of treatment, 7 did not return at 8 weeks; 2 were given alternative therapy, 5 were lost to follow-up • candida infection: unclear how many were enrolled; 13 completed 4 weeks of treatment, 4 did not return at 8 weeks; lost to follow-up • erythrasma infection 2/11 did not return at follow-up at week 8 Baseline data Localisation of dermatophytes infection: Feet: miconazole (9), clotrimazole (5) Feet and groins: miconazole (9), clotrimazole (6) Groins: miconazole (6), clotrimazole (5) Hands: miconazole (2), clotrimazole (1) Some participants had multiple infection sites
Interventions	**Intervention**

Clayton 1976 *(Continued)*

- miconazole (2%) cream b.i.d. for 4 weeks (total number unclear)

Comparator

- clotrimazole (1%) cream b.i.d. for 4 weeks (total number unclear)

Outcomes	Assessments (4): baseline, weeks 2, 4 and 8 **Outcomes of the trial** (as reported) 1. Clinical evaluation: 3-point Likert scale# 2. Mycological evaluation (KOH and culture) 3. Relapse 4. Acceptability 5. Adverse events# Denotes outcomes prespecified for this review
Notes	Study included participants with malassezia furfur, erythrasma and candida infections. We only considered tinea corporis and cruris.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote (page 226): "..were randomized into one of the two treatment groups..". Comment: Insufficient detail was reported about the method used to generate the allocation sequence to allow a clear assessment of whether it would produce comparable groups.
Allocation concealment (selection bias)	Unclear risk	The method used to conceal the allocation sequence, that is to determine whether intervention allocations could have been foreseen in advance of, or during, enrolment, was not reported. Comment: There was insufficient information to permit a clear judgement.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote (page 225-6): "..double-blind study.." and "Neither the clinician, the mycologist, the pharmacist nor the patient knew which preparation was being used". Comment: The report did not provide sufficient detail about the measures used to blind study participants and personnel from knowledge of which intervention a participant received, to permit a clear judgement.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote (page 225-6): "..double-blind..." and "Neither the clinician, the mycologist, the pharmacist nor the patient knew which preparation was being used". Comment: Uncertainty with the effectiveness of blinding of outcomes assessors (participants/healthcare providers) during the study. Insufficient information to permit a clear judgement.
Incomplete outcome data (attrition bias) All outcomes	High risk	Unclear how many enrolled for each type of infection. At week 8 56/136 (41%) lost to follow-up. Per-protocol analysis. Comment: We judged this as at a high risk of bias.
Selective reporting (reporting bias)	Low risk	The protocol for the study was not available, but the prespecified outcomes and those mentioned in the methods section appeared to have been reported. Comment: We judged this as at a low risk of bias.

Clayton 1976 *(Continued)*

Other bias	Unclear risk	Quote (page 231): "We are grateful to Janssen Pharmaceutical Ltd. and to Bayer UK Pharmaceutical Division for the supply of drugs and for help in organizing the trial." Comment: Insufficient information to assess whether important risk of bias exists.

Clayton 1979

Methods	Randomised, double-blind, active-controlled trial Setting Department of Mycology, St John's Hospital for Diseases of the Skin, London, UK Date of study Not reported. Duration of intervention 4 weeks with follow-up at 8 weeks
Participants	N = 112 (64 male/27 female; 21 gender unreported) Age range 18-70 years **Inclusion criteria of the trial** • dermatophytes (ringworm fungi), Malassezia furfur, Candida yeasts or corynebacteria confirmed by KOH **Exclusion criteria of the trial** • scalp or nail infections Randomised N = 112 Withdrawals/losses to follow-up • haloprogin14/50 (28%): due to non-attendance at the appropriate time (11), failure to apply the ointment as directed (1); side effects necessitating withdrawal (2) • miconazole 15/62 (24%): due to nonattendance (13), failure to comply with instructions (1); side effects (1) Baseline data Candida infections: haloprogin (6), miconazole (7) Erythrasma: haloprogin (unclear), miconazole (unclear) Pityriasis versicolor: haloprogin (11), miconazole (17) Site of the dermatophytes infections: Feet: haloprogin (9), miconazole (9) Feet and hands: haloprogin (2), miconazole (2) Feet and groins: haloprogin (4), miconazole (2) Groins: haloprogin (5), miconazole (7) Hands: haloprogin (0), miconazole (3) Face: haloprogin (1), miconazole (0)

Clayton 1979 *(Continued)*

	Submammary: haloprogin (0), miconazole (1)
Interventions	**Intervention** • haloprogin (1%) ointment b.i.d. for 4 weeks (50) **Comparator** • miconazole (2%) cream b.i.d. for 4 weeks (62)
Outcomes	Assessments (4): baseline, weeks 2, 4 and 8 **Outcomes of the trial** (as reported) 1. Mycological and bacteriological evaluation (KOH and culture) 2. Clinical evaluation 3. Relapse 4. Adverse effects Denotes outcomes prespecified for this review
Notes	Study included participants with malassezia furfur, and candida infections as well. We only considered tinea corporis and cruris.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote (page 66): "Patients were randomized into one of the two treatment groups.." Comment: Insufficient detail was reported about the method used to generate the allocation sequence to allow a clear assessment of whether it would produce comparable groups.
Allocation concealment (selection bias)	Unclear risk	The method used to conceal the allocation sequence, that is to determine whether intervention allocations could have been foreseen in advance of, or during, enrolment, was not reported. Comment: There was insufficient information to permit a clear judgement.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote (page 65-6): "..double-blind study.." and "The clinician, the mycologist, the pharmacist or the patient did not know which preparation was being used". Comment: The report did not provide sufficient detail about the measures used to blind study participants and personnel from knowledge of which intervention a participant received, to permit a clear judgement.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote (page 65-6): "..double-blind study.." and "The clinician, the mycologist, the pharmacist or the patient did not know which preparation was being used". Comment: Uncertainty with the effectiveness of blinding of outcomes assessors (participants/healthcare providers) during the study. Insufficient information to permit a clear judgement.
Incomplete outcome data (attrition bias) All outcomes	High risk	Lost to follow-up: Haloprogin 14/50 (28%), miconazole 15/62 (24%). Per-protocol analysis. Comment: We judged this as at a high risk of bias.

Clayton 1979 *(Continued)*

Selective reporting (reporting bias)	Low risk	The protocol for the study was not available, but the prespecified outcomes and those mentioned in the methods section appeared to have been reported. Comment: We judged this as at a low risk of bias.
Other bias	Unclear risk	Quote (page 72): "We are very grateful to Dr C. Edwards of Schering Chemicals Limited for his valuable help throughout the trial and for arranging the supply of drugs. Comment: Insufficient information to assess whether important risk of bias exists.

Clayton 1982

Methods	Randomised, double-blind, active-controlled trial Setting St John's Hospital for Diseases of the Skin, London, UK Date of study Not reported. Duration of intervention 4 weeks with follow-up at 8 weeks
Participants	N = 99 (88 male/11 female) Mean age = 34 years males, 39 years females **Inclusion criteria of the trial** • fungal infections or erythrasma **Exclusion criteria of the trial** • not reported Randomised N = 99 Withdrawals/losses to follow-up • tioconazole 13/50 (26%), miconazole 8/49 (16%) lost to follow-up Baseline data Localisation of the dermatophytes infections: Feet: tioconazole (10), miconazole (9) Groins: tioconazole (11), miconazole (13) Hands: tioconazole (1), miconazole (8) Body: tioconazole (7), miconazole (3)
Interventions	**Intervention** • tioconazole (2%) b.i.d. for 4 weeks (50) **Comparator** • miconazole (2%) b.i.d. for 4 weeks (49)
Outcomes	Assessments (4): baseline, weeks 2, 4 and 8

Clayton 1982 *(Continued)*

Outcomes of the trial (as reported)

1. Mycological and bacteriological evaluation (KOH and culture)
2. Clinical evaluation
3. Relapse
4. Acceptability of the cream
5. Adverse effects

Denotes outcomes prespecified for this review

Notes	Study included participants with malassezia furfur, and candida infections . We only considered tinea corporis and cruris. See Table 3

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote (page 544): "..were allocated randomly to.." Comment: Insufficient detail was reported about the method used to generate the allocation sequence to allow a clear assessment of whether it would produce comparable groups.
Allocation concealment (selection bias)	Unclear risk	The method used to conceal the allocation sequence, that is to determine whether intervention allocations could have been foreseen in advance of, or during, enrolment, was not reported. Comment: There was insufficient information to permit a clear judgement.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote (page 544): "..double-blind study.." Comment: The report did not provide sufficient detail about the measures used to blind study participants and personnel from knowledge of which intervention a participant received, to permit a clear judgement.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote (page 544): "..double-blind..." Comment: Uncertainty with the effectiveness of blinding of outcomes assessors (participants/healthcare providers) during the study. Insufficient information to permit a clear judgement.
Incomplete outcome data (attrition bias) All outcomes	High risk	Lost to follow-up 21/99 (21%): tioconazole 13/50 (26%), miconazole 8/49 (16%). Per-protocol analysis. Comment: We judged this as at a high risk of bias.
Selective reporting (reporting bias)	Low risk	The protocol for the study was not available, but the prespecified outcomes and those mentioned in the methods section appeared to have been reported. Comment: We judged this as at a low risk of bias.
Other bias	Unclear risk	Quote (page 549): "We are very grateful to Dr J. Henderson of Pfizer Ltd for help throughout the trial and for the supply of drugs." Comment: Insufficient information to assess whether important risk of bias exists.

Clerico 1987

Methods	Randomised, open, active-controlled, within-patient comparison trial Setting Institute of Clinical Dermatology, University of Rome, Rome, Italy Date of study Not reported. Duration of intervention 30 days
Participants	N = 40 (3 male/37 female) Age range = 7-74 years **Inclusion criteria of the trial** • clinical diagnosis of superficial dermatomycosis **Exclusion criteria of the trial** • not reported Randomised N = 40 Withdrawals/losses to follow-up • 1/40 discontinued treatment Baseline data Diagnosis: Tinea cruris: 1 Tinea corporis: 3 Candidiasis or pityriasis versicolor, or other tinea infections: 37
Interventions	**Intervention** • fenticonazole (2%) cream b.i.d. for 30 days (20) **Comparator** • miconazole (2%) cream b.i.d. for 30 days (20)
Outcomes	Assessments (2): baseline and day 30 **Outcomes of the trial** (as reported) 1. Clinical evaluation 2. Mycological evaluation 3. Adverse events# Denotes outcomes prespecified for this review
Notes	Only 4 participants with tinea cruris/corporis. In 6 participants a within-patient comparison was carried out.
Risk of bias	

Clerico 1987 *(Continued)*

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote (page 79): "..according to a randomized scheme..". Comment: Insufficient detail was reported about the method used to generate the allocation sequence to allow a clear assessment of whether it would produce comparable groups.
Allocation concealment (selection bias)	Unclear risk	The method used to conceal the allocation sequence, that is to determine whether intervention allocations could have been foreseen in advance of, or during, enrolment, was not reported. Comment: There was insufficient information to permit a clear judgement.
Blinding of participants and personnel (performance bias) All outcomes	High risk	Open trial. Comment: The outcome was likely to be influenced by the lack of blinding.
Blinding of outcome assessment (detection bias) All outcomes	High risk	Open trial. Comment: The outcome measurement was likely to be influenced by the lack of blinding.
Incomplete outcome data (attrition bias) All outcomes	Low risk	1 lost to follow-up. Comment: We judged this as at a low risk of bias.
Selective reporting (reporting bias)	Low risk	Very limited data are provided. The protocol for the study was not available, but the prespecified outcomes and those mentioned in the methods section appeared to have been reported. Comment: We judged this as at a low risk of bias
Other bias	Low risk	The study appears to be free from other forms of bias.

Cordero 1992

Methods	Randomised, double-blind, placebo-controlled trial Setting Multi-centre, Dominican Republic, Guatemala, Panama, USA Date of study Not reported. Duration of intervention 1 week to follow-up at 4 weeks
Participants	N = 74 (36 male/29 female; 9 gender unreported) Age range 5–76, median 31 years (terbinafine); 40 years (placebo) **Inclusion criteria of the trial** • tinea cruris/ corporis confirmed by culture **Exclusion criteria of the trial** • nothing reported

Cordero 1992 *(Continued)*

	Randomised N = 74 Withdrawals/losses to follow-up • report unclear but missing data at 2 weeks follow-up: terbinafine group 7/36 (19%); 22/38 (58%) in placebo group Baseline data Not reported
Interventions	**Intervention** • topical terbinafine (1%) once daily for 1 week (36) **Comparator** • placebo once daily for 1 week (38)
Outcomes	Assessments (4): baseline, week 1 (end of treatment), weeks 3 and 5 **Outcomes of the trial** (as reported) 1. Mycologic evaluation (KOH and culture) 2. Clinical assessment (sum of the sign-and-symptom scores)# Denotes outcomes prespecified for this review
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote (page 23): "..were randomized to receive.." Comment: Insufficient detail was reported about the method used to generate the allocation sequence to allow a clear assessment of whether it would produce comparable groups.
Allocation concealment (selection bias)	Unclear risk	The method used to conceal the allocation sequence, that is to determine whether intervention allocations could have been foreseen in advance of, or during, enrolment, was not reported. Comment: There was insufficient information to permit a clear judgement.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote (page 23): "..double-blind study.." Comment: The report did not provide sufficient detail about the measures used to blind study participants and personnel from knowledge of which intervention a participant received, to permit a clear judgement.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote (page 24): "..clinical and mycological assessment..." Comment: Uncertainty with the effectiveness of blinding of outcomes assessors (participants/healthcare providers) during the study. Insufficient information to permit a clear judgement.
Incomplete outcome data (attrition bias) All outcomes	High risk	Missing data at 2-week follow-up: terbinafine group 7/36 (19%); 22/34 (58%) in placebo group. Per-protocol analysis.

Cordero 1992 *(Continued)*

		Comment: We judged this as at a high risk of bias.
Selective reporting (reporting bias)	Low risk	Although only minimal data were reported, the outcomes listed in the 'Methods' section appeared comparable to the reported results. Comment: We judged this as at a low risk of bias.
Other bias	Unclear risk	The study appeared to be free of other forms of bias.

Cucè 1980

Methods	Randomised, double-blind, active-controlled, within-patient comparison trial Setting Dermatology Department Sâo Paulo University Medical School, Brazil Date of study Not reported. Duration of intervention until negative parasitology, mean duration 3 weeks to follow-up at 4 weeks
Participants	N= 81 (36 male/45 female) Mean age = 35 years **Inclusion criteria of the trial** • microscopy (KOH) and culture **Exclusion criteria of the trial** • systemic or topical use of antimycotic agents, without adequate wash out period • bacterial superinfection • uncooperative subjects Randomised N= 81 Withdrawals/losses to follow-up • nothing reported Baseline data Tinea corporis (20) Tinea cruris (20) Tinea pedis (20) Pityriasis versicolor (21)
Interventions	Half in each group were treated with one or other intervention **Intervention** • tolciclate (1%) cream b.i.d. or three times daily until negative mycology (42) **Comparator**

Cucè 1980 *(Continued)*

	• miconazole (2%) cream b.i.d. or three times daily until negative mycology (39)
Outcomes	Assessments (5): baseline and thereafter roughly once a week up to 4 weeks **Outcomes of the trial** (as reported) 1. Mycological cure (KOH and culture) 2. Clinical assessment (erythema, scaling, blistering and itching): 4-point Likert scale# 3. Subjective symptoms (burning, itching) 4. Disappearance time# 5. Combined evaluation of investigator and participants of the treatment Denotes outcomes prespecified for this review
Notes	We only included data from participants with tinea corporis or cruris. See Table 3. Study included 2 additional groups of participants (pityriasis versicolor and tinea pedis).

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote (page 145): "..the allocation of the two treatments was randomized". Comment: Insufficient detail was reported about the method used to generate the allocation sequence to allow a clear assessment of whether it would produce comparable groups.
Allocation concealment (selection bias)	Unclear risk	The method used to conceal the allocation sequence, that is to determine whether intervention allocations could have been foreseen in advance of, or during, enrolment, was not reported. Comment: There was insufficient information to permit a clear judgement.
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote (page 145): "..double-blind basis.....supplied in identical preparations.." Comment: Probably done.
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Blinding of outcomes assessors, key personnel and participants was ensured, and it was unlikely that the blinding could have been broken. Comment: We judged this as at a low risk of bias.
Incomplete outcome data (attrition bias) All outcomes	Low risk	No attrition or exclusions from data analysis. Comment: We judged this as at a low risk of bias.
Selective reporting (reporting bias)	Low risk	Although only minimal outcomes data were reported, the outcomes listed in the 'Methods' section appeared comparable to the reported results. Comment: We judged this as at a low risk of bias.
Other bias	Low risk	The study appeared to be free of other forms of bias.

del Palacio 1989

Methods	Randomised, double-blind, active-controlled trial Setting

del Palacio 1989 *(Continued)*

	Department of Dermatology, Hospital 12 de Octubre, Madrid, Spain Date of study Not reported. Duration of intervention up to 6 weeks with follow-up 3 weeks after end of treatment
Participants	N = 40 (18 male/22 female) Mean age = 21-24, range 2-58 years **Inclusion criteria of the trial** • cutaneous candidosis and dermatophytosis confirmed by KOH and culture **Exclusion criteria of the trial** • pregnant women, women in whom pregnancy could not be excluded with certainty • secondary bacterial infection • antimycotics < 2 weeks prior to study entry Randomised N = 40 Withdrawals/losses to follow-up • amorolfine (2), bifonazole (1) due to adverse events Baseline data Location of infection: Body : amorolfine (13), bifonazole (10) Feet (interdigital spaces): amorolfine (3), bifonazole (6) Groin: amorolfine (3), bifonazole (2) Hand: amorolfine (0), bifonazole (1) Face: amorolfine (0), bifonazole (1)
Interventions	**Intervention** • amorolfine (0.5%) cream once daily up to 6 weeks (20) **Comparator** • bifonazole (1%) cream once daily up to 6 weeks (20)
Outcomes	Assessments (8): baseline, weekly up to 6 weeks and 3 weeks after end of treatment **Outcomes of the trial** (as reported) 1. Clinical evaluation of signs and symptoms (itching, burning, redness, weeping, scaling, pustulation, incrustation): 4-point Likert scale# 2. Mycological evaluation (KOH and culture) 3. Adverse events: 3-point Likert scale# 4. Clinical efficacy: 4-point Likert scale# Denotes outcomes prespecified for this review
Notes	We only considered participants with tinea corporis and tinea cruris. See Table 3

Risk of bias

Bias	Authors' judgement	Support for judgement

del Palacio 1989 *(Continued)*

Random sequence generation (selection bias)	Unclear risk	Quote (page 141): "..patients were randomized into one of the two treatment group" Comment: Insufficient detail was reported about the method used to generate the allocation sequence to allow a clear assessment of whether it would produce comparable groups.
Allocation concealment (selection bias)	Unclear risk	The method used to conceal the allocation sequence, that is to determine whether intervention allocations could have been foreseen in advance of, or during, enrolment, was not reported. Comment: There was insufficient information to permit a clear judgement.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote (page 141): "..double-blind.." Comment: The report did not provide sufficient detail about the measures used to blind study participants and personnel from knowledge of which intervention a participant received, to permit a clear judgement.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote (page 141): "..double-blind.." Comment: Uncertainty with the effectiveness of blinding of outcomes assessors (participants/healthcare providers) during the study. Insufficient information to permit a clear judgement.
Incomplete outcome data (attrition bias) All outcomes	Low risk	3/40 (8%) were lost to follow-up; amorolfine (2), bifonazole (1) due to adverse events. per-protocol analysis. Comment: Low and well balanced number of drop-outs and although per-protocol analysis considered to be at a low risk of bias.
Selective reporting (reporting bias)	Low risk	The protocol for the study was not available, but the prespecified outcomes and those mentioned in the methods section appeared to have been reported. Comment: We judged this as at a low risk of bias.
Other bias	Unclear risk	Quote (page 144): "The medication for this trial was kindly supplied by F. Hoffmann La Roche & Co., Basel, Switzerland". Comment: Hoffman La Roche & Co are the manufacturers of amorolfine. A potential risk of bias cannot be excluded.

del Palacio 1991

Methods	Randomised, double-blind, phase II dose-finding study Setting Department of Dermatology, General hospital Madrid, Spain Date of study Not reported. Duration of intervention up to maximum 6 weeks with follow-up 2 months
Participants	N = 75 (male 40, female 35) Age range 18–71, mean 37 years **Inclusion criteria of the trial** • candidosis and dermatophytosis KOH microscopy and culture

del Palacio 1991 *(Continued)*

Exclusion criteria of the trial

- pregnancy
- participants with secondary bacterial infection or onychomycosis
- use of antimycotic in prior two weeks

Randomised

N = 75

Withdrawals/losses to follow-up

Total 8/75 (11%):

Withdrawals due to adverse events/side effects: 0.125% (3); 0.25% (3); 0.5% (2)

Baseline data

1 cutaneous candidosis and 74 dermatophyte infections

Sites and concentrations:

- Face (13): 0.125% (5); 0.25% (3); 0.5% (5)
- Body (16): 0.125% (5); 0.25% (6); 0.5% (5)
- Groin (22): 0.125% (5); 0.25% (9); 0.5% (8)
- Arm/leg (16/13): 0.125% (6/5); 0.25% (5/4); 0.5% (5/4)
- Foot (5): 0.125% (1); 0.25% (1); 0.5% (3)
- Hand: 0.25% (1)

Interventions	**Intervention and Comparator** 25/group: 3 concentrations • amorolfine in 3 concentrations (0.125%, 0.25%, 0.5%) once daily up to 6 weeks
Outcomes	Assessments: baseline, once a week during treatment, end of treatment, 2 weeks, 2 months at follow-up **Outcomes of the trial** (as reported) 1. Clinical disease activity (itching, burning, redness, weeping, scaling, pustulation, crust formation and others): 4-point Likert scale# 2. Adverse effects: 3-point Likert scale# 3. Clinical efficacy: 4-point Likert scale# 4. Mycologic evaluation (KOH and culture) 5. Relapse Denotes outcomes prespecified for this review
Notes	We only included data from participants with tinea corporis or cruris. See Table 3

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote (page 299): "..double-blind randomized... patients were allocated to three parallel groups" Comment: Insufficient detail was reported about the method used to generate the allocation sequence to allow a clear assessment of whether it would produce comparable groups.

del Palacio 1991 *(Continued)*

Allocation concealment (selection bias)	Unclear risk	Quote (page 299): "..patients were allocated to three parallel groups.." The method used to conceal the allocation sequence, that is to determine whether intervention allocations could have been foreseen in advance of, or during, enrolment, was not reported. Comment: There was insufficient information to permit a clear judgement.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote (page 299): "..double-blind....neither the clinician nor the patient knew which concentration was being used....." Comment: The report did not provide sufficient detail about the measures used to blind study participants and personnel from knowledge of which intervention a participant received, to permit a clear judgement.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote (page 299): "..neither the clinician nor the patient knew which concentration was being used....." Comment: Uncertainty with the effectiveness of blinding of outcomes assessors (participants/healthcare providers) during the study. Insufficient information to permit a clear judgement.
Incomplete outcome data (attrition bias) All outcomes	Low risk	Drop-outs (8/75) due to adverse events/side effects: 0.125% (3); 0.25%(3); 0.5% (2). Per-protocol analysis. Comment: Low and well balanced number of drop-outs and although per protocol analysis considered to be at a low risk of bias.
Selective reporting (reporting bias)	High risk	Clinical disease activity one of the principal outcomes of the study was not reported at all. Comment: We judged this at a high risk of bias.
Other bias	Low risk	The study appeared to be free of other forms of bias.

del Palacio 1992

Methods	Randomised, double-blind, active-controlled dose-finding study Setting 20 centres in Europe and Latin America Date of study May 1985-November 1988. Duration of the intervention 2-6 weeks with follow-up 1 weeks after end of treatment
Participants	N = 725 (392 male/322 female; 11 gender unreported) Mean age = 39 years **Inclusion criteria of the trial** • > 16 years • diagnosis of dermatomycosis confirmed by KOH and culture **Exclusion criteria of the trial** • pregnant women and participants with a bacterial infection, onychomycosis or trichomycosis

del Palacio 1992 *(Continued)*

	• other antifungals < 2 weeks prior to study entry or requirement for other antimycotic agents during the trial Randomised N = 725 Withdrawals/losses to follow-up • 11/725 (2%) were lost to follow-up; 0.125% amorolfine (2), 0.25% amorolfine (5), 0.5% amorolfine (4) Baseline data Location of the dermatomycosis: Foot: 0.125% amorolfine (114), 0.25% amorolfine (103), 0.5% amorolfine (106) Large body area: 0.125% amorolfine (64), 0.25% amorolfine (66), 0.5% amorolfine (74) Skin fold: 0.125% amorolfine (63), 0.25% amorolfine (62), 0.5% amorolfine (58) Other: 0.125% amorolfine (0), 0.25% amorolfine (3), 0.5% amorolfine (1)
Interventions	**Intervention** • amorolfine (0.125%) cream once a day for 2-6 weeks (243) **Comparator 1** • amorolfine (0.25%) cream once a day for 2-6 weeks (239) **Comparator 2** • amorolfine (0.5%) cream once a day for 2-6 weeks (243)
Outcomes	Assessments: baseline, weekly up to 6 weeks and 1 week after end of treatment **Outcomes of the trial** (as reported) 1. Mycological evaluations (KOH and culture) 2. Clinical evaluation of signs and symptoms: 4-point Likert scale# 3. Size of target lesion: 4-point Likert scale 4. Overall assessment: 3-point Likert scale# 5. Adverse events# 6. Relapse Denotes outcomes prespecified for this review
Notes	We only included data for participants with tinea corporis and cruris. See Table 3

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote (page 50): "..was randomly allocated..". Comment: Insufficient detail was reported about the method used to generate the allocation sequence to allow a clear assessment of whether it would produce comparable groups.
Allocation concealment (selection bias)	Unclear risk	The method used to conceal the allocation sequence, that is to determine whether intervention allocations could have been foreseen in advance of, or during, enrolment, was not reported.

del Palacio 1992 *(Continued)*

		Comment: There was insufficient information to permit a clear judgement.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote (page 50): "..double-blind..". Comment: The report did not provide sufficient detail about the measures used to blind study participants and personnel from knowledge of which intervention a participant received, to permit a clear judgement.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote (page 50): "..double-blind..". Comment: Uncertainty with the effectiveness of blinding of outcomes assessors (healthcare providers and participants) during the study. Insufficient information to permit a clear judgement.
Incomplete outcome data (attrition bias) All outcomes	Low risk	11/725 (2%) were lost to follow-up; 0.125% amorolfine (2), 0.25% amorolfine (5), 0.5% amorolfine (4). Per-protocol analysis. Comment: Low and balanced number of drop-outs at follow-up, and although per-protocol analysis considered to be at a low risk of bias.
Selective reporting (reporting bias)	Low risk	The protocol for the study was not available, but the prespecified outcomes and those mentioned in the methods section appeared to have been reported. Comment: We judged this as at a low risk of bias.
Other bias	High risk	Two of the authors are employed by the Clinical Research Department, F.Hoffmann-La Roche Ltd, Basel, Switzerland, the manufacturer of amorolfine. Comment: A potential risk of bias cannot be excluded.

del Palacio 1995

Methods	Randomised, double-blind, comparative dose finding study Setting University Hospital, Madrid, Spain Date of study Not reported. Duration of intervention up to 6 weeks with follow-up 2 weeks after 'cure'
Participants	N = 60 (male 38, female 22) Mean age = 45 years across all groups except for cream (2%) b.i.d. group 27.5 years (P < 0.05) **Inclusion criteria of the trial** • dermatophytosis (tinea corporis/ tinea cruris) confirmed by KOH microscopy • age 18-65 years **Exclusion criteria of the trial** • pregnancy • onychomycosis or dermatophytosis of palms and soles • scalp ringworm • superficial widespread tinea corporis or cruris • use of antimycotic agents in prior 4 weeks Randomised

del Palacio 1995 *(Continued)*

N = 60

Withdrawals/losses to follow-up

- Total 3: cream (2%) once daily (2) due to adverse events; cream (2%) b.i.d. (1) due to appearance of multiple skin ringworm lesions
- 2 did not attend planned visit at 4 weeks in cream (1%) b.i.d. group

Baseline data

Duration of infection weeks:

- 1-28 in the 1% once daily group
- 2-53 in the 1% twice daily group
- 1-48 in the 2% once daily group
- 1-48 in the 2% twice daily group

Site
1% once daily group: groin (5), body (10)

1% twice daily group: groin (6), body (9)

2% once daily group: groin (6), body (9)

2% twice daily group: groin (10), body (5)

Interventions	**Interventions** 15/group into 4 groups • eberconazole cream (1%) once daily for up to 6 weeks • eberconazole cream (1%) twice daily for up to 6 weeks • eberconazole cream (2%) once daily for up to 6 weeks • eberconazole cream (2%) twice daily for up to 6 weeks
Outcomes	Assessments: baseline**,** once a week during treatment, end of treatment and 6 weeks at follow-up **Outcomes of the trial** (as reported) 1. Clinical disease activity (itching, burning, redness, weeping, scaling, pustulation, crust formation and others): 4-point Likert scale# 2. Adverse effects: 3-point Likert scale# 3. Mycologic evaluation (KOH and culture) Denotes outcomes prespecified for this review
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote (page 318): "..double- blind randomized.." Comment: Insufficient detail was reported about the method used to generate the allocation sequence to allow a clear assessment of whether it would produce comparable groups.
Allocation concealment (selection bias)	Unclear risk	The method used to conceal the allocation sequence, that is to determine whether intervention allocations could have been foreseen in advance of, or during, enrolment, was not reported.

del Palacio 1995 *(Continued)*

		Comment: There was insufficient information to permit a clear judgement.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote (page 318): "..neither the clinician nor the patient knew which concentration was being used..". Comment: The report did not provide sufficient detail about the measures used to blind study participants and personnel from knowledge of which intervention a participant received, to permit a clear judgement.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Comment: Uncertainty with the effectiveness of blinding of outcomes assessors (investigators and participants). Insufficient information to permit a clear judgement.
Incomplete outcome data (attrition bias) All outcomes	Low risk	Lost to follow-up (3): 2% cream once daily (2) due to adverse events, 2% cream b.i.d. (1) due to appearance of multiple skin ringworm lesions. Per-protocol analysis. Comment: Low and well balanced number of drop-outs, and although per-protocol analysis considered to be at a low risk of bias.
Selective reporting (reporting bias)	Low risk	The protocol for the study was not available, but the prespecified outcomes and those mentioned in the methods section appeared to have been reported. Comment: We judged this as at a low risk of bias.
Other bias	Low risk	The study appeared to be free of other forms of bias.

del Palacio 1999

Methods	Randomised, double-blind, active-controlled trial Setting Department of Clinical Microbiology, Hospital Universitario '12 de Octubre', Madrid, Spain Date of study Not reported. Duration of intervention 4 weeks with follow-up at 10 weeks
Participants	N = 59 (33 male/26 female) (1 participant with multiple (2) sites i.e. within-patient comparison) Mean age = 35 years ketoconazole group, 44 years flutrimazole group **Inclusion criteria of the trial** • 18-70 years • dermatophyte or Candida cutaneous infections confirmed by KOH and culture **Exclusion criteria of the trial** • pregnant women, child bearing age not using a safe contraceptive method, breast feeding women • hypersensitivity to imidazole derivatives • topical antifungals < 2 week prior to study entry • systemic drugs e.g. corticosteroids, antibiotics, immunosuppressive, antifungal, antiviral, antihelmintic or cytotoxic agents < 4 weeks prior to study entry • secondary bacterial infections, with chronic or severe liver 'and' or 'or' renal disease, with severe systemic diseases and patients on radiation therapy • participants with moccasin type of tinea pedis and those with extensive lesions not suitable for topical treatment

del Palacio 1999 *(Continued)*

	Randomised N = 59 Withdrawals/losses to follow-up • 1/30 ketoconazole due to adverse events Baseline data Infected sites (dermatophytes): Body: ketoconazole (11), flutrimazole (9) Groin: ketoconazole (7), flutrimazole (6) Toe webs: ketoconazole (7), flutrimazole (7) Infected sites (candidiasis): ketoconazole (5), flutrimazole (8)
Interventions	**Intervention** • ketoconazole (2%) cream once daily for 4 weeks (30) **Comparator** • flutrimazole (1%) cream once daily for 4 weeks (29)
Outcomes	Assessments (3): baseline, weeks 4 and 10 **Outcomes of the trial** (as reported) 1. Clinical evaluation of sign and symptoms (erythema, scaling, vesicles, pustulation, crusts, fissures, weeping, itching, burning, pain and others: 4-point Likert scale# 2. Mycological evaluation (KOH and culture) 3. Adverse events# Denotes outcomes prespecified for this review
Notes	We only considered data from participants with tinea cruris and tinea corporis. See Table 3

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote (page 650): "patients were allocated to one of two treatment groups". Comment: Insufficient detail was reported about the method used to generate the allocation sequence to allow a clear assessment of whether it would produce comparable groups.
Allocation concealment (selection bias)	Unclear risk	The method used to conceal the allocation sequence, that is to determine whether intervention allocations could have been foreseen in advance of, or during, enrolment, was not reported. Comment: There was insufficient information to permit a clear judgement.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote (page 650): "..double-blind..". Comment: The report did not provide sufficient detail about the measures used to blind study participants and personnel from knowledge of which intervention a participant received, to permit a clear judgement.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Comment: Uncertainty with the effectiveness of blinding of outcomes assessors (investigators and participants). Insufficient information to permit a clear judgement.

del Palacio 1999 *(Continued)*

Incomplete outcome data (attrition bias) All outcomes	Low risk	1/30 in ketoconazole group due to adverse events. Per-protocol analysis. Comment: Low and balanced number of drop-outs at follow-up, and although per-protocol analysis considered to be at a low risk of bias.
Selective reporting (reporting bias)	Low risk	The protocol for the study was not available, but the prespecified outcomes and those mentioned in the methods section appeared to have been reported. Comment: We judged this as at a low risk of bias.
Other bias	Unclear risk	Quote (page 655): "This study was supported by a grant from Menarini Lab. (Barcelona, Spain)." Comment: Menari Lab is manufacturer of ketoconazole, thus a potential risk of bias cannot be excluded.

del Palacio 2001

Methods	Randomised, double-blind, active-controlled trial Setting Department of Clinical Microbiology and Department of Dermatology, Hospital Universitario 12 de Octubre, Madrid, Spain Date of study Not reported. Duration of intervention 4 weeks with follow-up at 10 weeks
Participants	N = 157 (83 male/74 female) Mean age = 46, range 19-69 years **Inclusion criteria of the trial** • > 10 years and < 70 years • dermatomycoses confirmed by KOH and culture **Exclusion criteria of the trial** • pregnant or breastfeeding women • secondary bacterial infection, moccasin involvement of feet, onychomycoses • topical antifungals < 2 weeks the trial or an oral antifungal < 4 weeks prior to study entry • hepatic or renal deficiency or immunosuppressive treatment or concomitant therapy with any other antifungal agent or corticosteroid Randomised N = 157 Withdrawals/losses to follow-up • clotrimazole (4), eberconazole (4), due to adverse events Baseline data Infection sites: Body: clotrimazole (33), eberconazole (34) Groin: clotrimazole (18), eberconazole (17)

del Palacio 2001 *(Continued)*

	Face: clotrimazole (1), eberconazole (4) Feet: clotrimazole (17), eberconazole (17)
Interventions	**Intervention** • clotrimazole (1%) cream b.i.d. for 4 weeks (79) **Comparator** • eberconazole (1%) cream b.i.d. for 4 weeks (78)
Outcomes	Assessments (3): baseline, weeks 4 and 10 **Outcomes of the trial** (as reported) 1. Clinical evaluation of signs and symptoms (erythema,itching, burning, weeping, scaling, pustulation, crust formation, vesicles, fissures, pain and others): 4-point Likert scale# 2. Mycological evaluation (KOH and culture) 3. Relapse Denotes outcomes prespecified for this review
Notes	We only considered data from participants with tinea cruris. See Table 3

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote (page 174): "patients were randomized to one of two treatment groups" Comment: Insufficient detail was reported about the method used to generate the allocation sequence to allow a clear assessment of whether it would produce comparable groups.
Allocation concealment (selection bias)	Unclear risk	The method used to conceal the allocation sequence, that is to determine whether intervention allocations could have been foreseen in advance of, or during, enrolment, was not reported. Comment: There was insufficient information to permit a clear judgement.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote (page 174): "..double-blind..". Comment: The report did not provide sufficient detail about the measures used to blind study participants and personnel from knowledge of which intervention a participant received, to permit a clear judgement.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Comment: Uncertainty with the effectiveness of blinding of outcomes assessors (investigators). Insufficient information to permit a clear judgement.
Incomplete outcome data (attrition bias) All outcomes	Low risk	8/157; 4 in both groups due to adverse events. Per-protocol analysis. Comment: Low and balanced number of drop-outs at follow-up, and although per-protocol analysis considered to be at a low risk of bias.
Selective reporting (reporting bias)	Low risk	The protocol for the study was not available, but the prespecified outcomes and those mentioned in the methods section appeared to have been reported. Comment: We judged this as at a low risk of bias.

del Palacio 2001 *(Continued)*

Other bias	Low risk	The study appeared to be free of other forms of bias.

Dinkela 2007

Methods	Randomised, double-blind, active-controlled trial Setting Two primary schools in Tanzania Date of study April - July 2003. Duration of intervention 2 months
Participants	N = 244 (128 male/122 female (= 250 cases due to multiple infection sites) Age range 6-19 years **Inclusion criteria of the trial** • children with clinically diagnosed tinea versicolor, capitis, corporis, or pedis confirmed by KOH 'and' or 'or' culture **Exclusion criteria of the trial** • skin disorder required immediate treatment, or treatment other than the soap had been administered Randomised N = 244 Withdrawals/losses to follow-up • 20/244 excluded during or after the trial: their skin disorder required immediate treatment, received/used intervention < 4 times, or lost to follow-up Baseline data Tinea versicolor (174) Tinea capitis (40) Tinea corporis (15) Tinea pedis (21) A number of participants had multiple infections
Interventions	**Intervention** • soap containing Triclosan once a day for 2 months **Comparator** • plain soap once a day for 2 months
Outcomes	Assessments (2): baseline, 2 months **Outcomes of the trial** (as reported) 1. Complete body examination 2. History taking and documentation of the clinical presentation of skin disorders 3. Digital photographic documentation

Dinkela 2007 *(Continued)*

4. Skin scrapings 'and' or 'or' hair clippings and mycological evaluation (KOH)#
5. Subjective improvement

Denotes outcomes prespecified for this review

Notes	We only included and reported on data from participants with tinea corporis.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote (page 24): "The study participants were randomly assigned.." Comment: Insufficient detail was reported about the method used to generate the allocation sequence to allow a clear assessment of whether it would produce comparable groups. After e-mail response: "Randomisation was computer based and carried out by a statistician at Swiss Tropical and Public Health Institute, Basel, before the onset of the clinical trial. First verum and placebo were randomly assigned to letters A to U to the serial numbers of 1 to 400 for 400 possible study units. During the screening examination all the study participants living in one household were identified and formed one unit. A unit could consist of one or more children. At both schools the serial numbers assigned to the randomised letters were distributed in the order of the names on the list of the study participants. The list had been created by the field investigators in the order in which the children had been included in the study". Comment: Probably done.
Allocation concealment (selection bias)	Low risk	The method used to conceal the allocation sequence, that is to determine whether intervention allocations could have been foreseen in advance of, or during, enrolment, was not reported. Comment: There was insufficient information to permit a clear judgement. After e-mail response: "Every one but the statistician and those involved in the production of the soap were blinded with regard to this allocation sequence". Comment: Probably done.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote (page 23): "..double-blind..". Comment: The report did not provide sufficient detail about the measures used to blind study participants and personnel from knowledge of which intervention a participant received, to permit a clear judgement.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote (page 23): "..double-blind..". Uncertainty with the effectiveness of blinding of outcomes assessors (participants/healthcare providers) during the study. Insufficient information to permit a clear judgement.
Incomplete outcome data (attrition bias) All outcomes	High risk	Inconsistent reporting of participants randomised and outcomes assessment during follow -up. Comment: We judged this at a high risk of bias. After e-mail response: "Some children had multiple infections. In Fig. 1 the number of cases are presented, not the number of patients. Thus, the total number of cases is higher (250) than the number of study participants (224). The samples of 45 children taken during the screening examination could not be evaluated. At the follow-up examination the samples of 8 children could not

Dinkela 2007 *(Continued)*

		be evaluated in this study. In these missing cases not enough material could be collected or samples were contaminated by dust and therefore did not allow microscopic assessment". Comment: Although reasons have been provided, missing outcome data 45/224 (20%) combined with per-protocol analysis judged as at a high risk of bias.
Selective reporting (reporting bias)	High risk	Minimal data reported and partly in a narrative manner with P values but incomplete instead of providing the exact numbers. Comment: We judged this at a high risk of bias.
Other bias	Low risk	Quote (page 27): "This study was supported and financed by Ciba Specialty Chemicals Inc., who also provided the study soap." Comment: Although the study was supported and financed by Ciba Specialty Chemicals Inc., none of the investigators appear to be employed or received financial support from this company. We judged this as at low risk of bias

Dobson 1991

Methods	Randomised, double-blind, placebo-controlled trial Setting Multi-centre (5) in USA Date of study Not reported. Duration of intervention 6 weeks with follow-up at 6 weeks
Participants	N = 85 (41 male/21 female; 23 gender unreported) Mean age = 39, range 18-85 years **Inclusion criteria of the trial** • clinical diagnosis of tinea cruris or corporis confirmed by KOH **Exclusion criteria of the trial** • concomitant topical or systemic therapy with antibiotics, antimycotics, corticosteroids, antifungal therapy < 7 days (topical) or < systemic) prior to study entry • any condition interfering with diagnosis or evaluation of tinea cruris/corporis Randomised N = 85 Delayed exclusions: • 23/85 due to negative culture at baseline, unclear how many from each group Withdrawals/losses to follow-up • no losses reported Baseline data Nothing reported

Dobson 1991 *(Continued)*

Interventions	**Intervention** • naftifine (1%) cream b.i.d. for 4 weeks (34) **Comparator** • vehicle cream b.i.d. for 4 weeks (28)
Outcomes	Assessments (5): baseline, weeks 1, 2, 4 and 6 **Outcomes of the trial** (as reported) 1. Mycological evaluation (KOH and culture) 2. Clinical evaluation of signs and symptoms (erythema, scaling, papules, pustules, vesicles, pruritus, burning, fissures, macerations crusts and pain): 4-point Likert scale# 3. Overall clinical improvement: 4-point Likert scale# 4. Adverse events# Denotes outcomes prespecified for this review
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote (page 57): "..were randomly assigned..". Comment: Insufficient detail was reported about the method used to generate the allocation sequence to allow a clear assessment of whether it would produce comparable groups.
Allocation concealment (selection bias)	Unclear risk	The method used to conceal the allocation sequence, that is to determine whether intervention allocations could have been foreseen in advance of, or during, enrolment, was not reported. Comment: There was insufficient information to permit a clear judgement.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote (page 57): "..double-blind..". Comment: The report did not provide sufficient detail about the specific measures used to blind study participants and personnel from knowledge of which intervention a participant received, to permit a clear judgement.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote (page 57): "..double-blind..". Comment: The report did not provide sufficient detail about the specific measures used to blind study participants and personnel. It was unclear therefore, whether the outcome measurement was likely to be influenced by the lack of blinding.
Incomplete outcome data (attrition bias) All outcomes	High risk	Delayed exclusions 23/85 (27%) due to negative baseline culture. Unclear how many participants in each group and delayed exclusions in each group. Per-protocol analysis. Comment: Entry criterion (culture specimen) measured prior to randomisation. Under powered study combined with per-protocol analysis we judged this at a high risk of bias.
Selective reporting (reporting bias)	Low risk	The protocol for the study was not available, but the prespecified outcomes and those mentioned in the methods section appeared to have been reported.

Dobson 1991 *(Continued)*

		Comment: We judged this as at a low risk of bias.
Other bias	High risk	One investigator employed by Herbert Laboratories. Comment: A potential risk of bias cannot be excluded.

Duweb 1997

Methods	Randomised, double-blind, active-controlled trial Setting Department of Dermatology, Al Tahadi University, Libya Date of study Not reported. Duration of the intervention 2 weeks
Participants	N = 25 (age and gender unreported) **Inclusion criteria of the trial** • participants with mycologically proven tinea corporis **Exclusion criteria of the trial** • not reported Randomised N = 25 Withdrawals/losses to follow-up • not reported Baseline data Not reported
Interventions	**Intervention** • terbinafine (1%) cream b.i.d. for 2 weeks **Comparator** • clotrimazole (1%) b.i.d. for 2 weeks
Outcomes	Assessments (2): treatment weeks 1, 2 **Outcomes of the trial** (as reported) 1. Clinical evaluation 2. Mycological evaluation Denotes outcomes prespecified for this review
Notes	Abstract, very limited data in the report. See Table 3
Risk of bias	

Duweb 1997 *(Continued)*

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote (page 284): "..randomly allocated.." Comment: Insufficient detail was reported about the method used to generate the allocation sequence to allow a clear assessment of whether it would produce comparable groups.
Allocation concealment (selection bias)	Unclear risk	The method used to conceal the allocation sequence, that is to determine whether intervention allocations could have been foreseen in advance of, or during, enrolment, was not reported. Comment: There was insufficient information to permit a clear judgement.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote (page 284): "..double-blind..". Comment: The report did not provide sufficient detail about the measures used to blind study participants and personnel from knowledge of which intervention a participant received, to permit a clear judgement.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote (page 284): "..double-blind..". Comment: Uncertainty with the effectiveness of blinding of outcomes assessors (participants/healthcare providers) during the study. Insufficient information to permit a clear judgement.
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	No data reported. Comment: Insufficient information to permit a clear judgement.
Selective reporting (reporting bias)	Unclear risk	Minimal data are reported. Abstract. Comment: Insufficient information to permit a clear judgement.
Other bias	Unclear risk	Insufficient information to permit a clear judgement.

Effendy 1987

Methods	Randomised, double-blind, active-controlled trial Setting Dermatology Department, University of Marburg, Germany Date of study Not reported. Duration of intervention up to 8 weeks
Participants	N = 99 (59 male/16 female; 24 unreported) Mean age = 44 years **Inclusion criteria of the trial** • clinical sign and symptoms of dermatomycosis **Exclusion criteria of the trial** • not reported Randomised

Effendy 1987 *(Continued)*

N = 99

Delayed exclusions

24/99 (24%) due to negative culture, but unclear from which group

Withdrawals/losses to follow-up

- not reported

Baseline data

Location:

Arms: clotrimazole (2), naftifine (1)
Trunk: clotrimazole (3), naftifine (2)
Legs: clotrimazole (2), naftifine (1)
Feet: clotrimazole (24), naftifine (30)
Hands: clotrimazole 1), naftifine (1)
Inguinal region: clotrimazole (7), naftifine (4)
Buttocks: clotrimazole (0), naftifine (1)
Interdigital spaces (toes and fingers): clotrimazole (23), naftifine (24)

Interventions	**Intervention** • clotrimazole (1%) solution b.i.d. for up to 8 weeks (36) **Comparator** • naftifine (1%) solution once daily for up to 8 weeks (39)
Outcomes	Assessments (5): baseline, weeks, 2, 4, 6 and 8 **Outcomes of the trial** (as reported) 1. Clinical evaluation of signs and symptoms: 7-point Likert scale# 2. Mycological evaluation (KOH and culture) Denotes outcomes prespecified for this review
Notes	Unclear how many participants matched the inclusion criteria (sites reported but unclear which pathogens at each site). See Table 3

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote (page 106): "..randomly allocated .." Comment: Insufficient detail was reported about the method used to generate the allocation sequence to allow a clear assessment of whether it would produce comparable groups.
Allocation concealment (selection bias)	Unclear risk	The method used to conceal the allocation sequence, that is to determine whether intervention allocations could have been foreseen in advance of, or during, enrolment, was not reported. Comment: There was insufficient information to permit a clear judgement.
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote (page 106): "..double-blind.." and "The two compounds were packed in identical containers.."

Effendy 1987 *(Continued)*

		Comment: The report provided sufficient detail about the measures used to blind study participants and personnel from knowledge of which intervention a participant received, to permit a clear judgement.
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Outcomes were investigator-assessed. Blinding of participants and key study personnel was ensured, and it is unlikely that the blinding could have been broken. Comment: We judged this as at a low risk of bias.
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Delayed exclusions: 24/99 (24%) due to negative culture, but unclear from which group. At follow-up no report of losses to follow-up. Comment: Insufficient information to assess whether an important risk of bias exists.
Selective reporting (reporting bias)	Low risk	The protocol for the study was not available, but the prespecified outcomes and those mentioned in the methods section appeared to have been reported. Comment: We judged this as at a low risk of bias.
Other bias	Low risk	The study appears to be free of other forms of bias.

Evans 1992

Methods	Randomised, double-blind, vehicle-controlled study Setting General practice, UK Date of study Not reported. Duration of intervention 1 week with follow-up 4 weeks
Participants	N = 76 enrolled, full data-set unreported, available-case sub set N = 31 (male 22, female 9) Age range 19–66 , mean 39 years **Inclusion criteria of the trial** • male or female >18 years • clinical diagnosis tinea corporis or tinea cruris confirmed by positive microscopy • women of child-bearing age must be using a reliable form of contraception **Exclusion criteria of the trial** • pregnant or breast-feeding • received radiation therapy, cytostatic, or immunosuppressive drugs • systemic antifungals, antiviral or anthelminthic drugs prior 2 weeks Concomitant therapy permissible i.e. hypertension, diabetes mellitus or cardiac insufficiency but no additional topical medication Randomised 76; 3/76 failed to return after baseline visit Delayed exclusions/Withdrawals/losses to follow-up

Evans 1992 *(Continued)*

45/76 (59%)

- 23 delayed exclusions i.e. negative baseline cultures subsequent to a positive microscopy (10), with yeast infections (13),
- 16 did not meet the inclusion criteria i.e. negative mycology at baseline and erroneously entered
- 6 = lost to follow-up (3), incomplete assessment (1), treated for too long (2)

Baseline data

Disease duration in weeks (mean): terbinafine (10.3), vehicle (21.5)

Interventions	**Intervention** • terbinafine (1 %) cream once daily for 1 week (38) **Comparator** • vehicle only once daily for 1 week (35)
Outcomes	Assessment (4): baseline, weeks 1, 2 and 4 **Outcomes of the trial** (as reported) 1. Clinical evaluation, signs and symptoms of infection (erythema, pustules, desquamation, encrustation, vesiculation and pruritus): 4-point Likert scale# 2. Mycological evaluation (KOH and culture) 3. Adverse events: 3-point Likert scale# Denotes outcomes prespecified for this review
Notes	Quote (page 273): "We would like to thank Sandoz Pharmaceuticals for organizing the trial and for providing the trial medication, MGB Clinical Research Ltd for their assistance in the organization of the trial".

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote (page 181): "..randomly assigned.." Comment: Insufficient detail was reported about the method used to generate the allocation sequence to allow a clear assessment of whether it would produce comparable groups.
Allocation concealment (selection bias)	Unclear risk	The method used to conceal the allocation sequence, that is to determine whether intervention allocations could have been foreseen in advance of, or during, enrolment, was not reported. Comment: There was insufficient information to permit a clear judgement.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote (page 181): "..double-blind.." Comment: The report did not provide sufficient detail about the measures used to blind study participants and personnel from knowledge of which intervention a participant received, to permit a clear judgement.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote (page 181): "..double-blind.." Comment: Uncertainty with the effectiveness of blinding of outcomes assessors (participants/healthcare providers) during the study. Insufficient information to permit a clear judgement.

Evans 1992 *(Continued)*

Incomplete outcome data (attrition bias) All outcomes	Low risk	45/76 (59%). Losses after randomisation due to negative baseline culture or culture with other species: 39/76 (51%). Unclear how many exactly from each group, 6 more losses after this (also unclear from which group). Quote (page 182): "intention-to-treat analysis.. included all randomized patients.. with at least one assessment after the baseline visit or who withdrew prematurely before the week 1 visit.... values were carried forward for those patients who dropped out patients with incomplete data were considered as treatment failures in the overall effectiveness evaluation". Comment: Substantial losses balanced across intervention groups, analysis included LOCF. Probably done.
Selective reporting (reporting bias)	Low risk	The protocol for the study was not available, but the prespecified outcomes and those mentioned in the methods section appeared to have been reported. Comment: We judged this as at a low risk of bias.
Other bias	Unclear risk	Quote (page 183): "Sandoz Pharmaceuticals for organizing the trial and for providing the trial medication, MGB Clinical Research Ltd for their assistance in the organization of the trial". Comment: Although the investigators did not clarify precisely what assistance other than trial medication was provided, a potential risk of bias cannot be excluded.

Evans 1993

Methods	Randomised, double-blind, active-controlled trial (see Notes) Setting General Practice centres (28) in UK Date of study Not reported. Duration of intervention 4 weeks with follow-up at 12 weeks
Participants	N = 269 (Group I tinea pedis 116 male/ 41 female; Group II tinea corporis/cruris 75 male/37 female) Age range 12-81 years **Inclusion criteria of the trial** • > 12 years; clinical diagnosis of tinea pedis, tinea corporis, or tinea cruris and a symptom/sign score > 3 **Exclusion criteria of the trial** • pregnant or lactating women • women of reproductive age without using a reliable form of contraception • received radiation therapy, systemic therapy with toxic or immunosuppressive drugs, or therapy with antibacterial, antifungal, antiviral or anthelminthic drugs < 7 days prior to study entry Randomised N = 269; 2 Strata: tinea corporis/cruris 112, tinea pedis 157 Withdrawals/losses to follow-up

Evans 1993 *(Continued)*

	• 4 did not attend after baseline visit, ITT analysis based on 265, unclear from which group (I or II) or treatment arm Baseline data Diagnosis: Tinea pedis: naftifine (77), clotrimazole HC (80) Tinea corporis/cruris: naftifine (55), clotrimazole HC (57) Mycological confirmation in tinea corporis/cruris: naftifine (15), clotrimazole HC (11)
Interventions	**Intervention** • naftifine (1%) cream b.i.d. for 4 weeks (77 tinea pedis; 55 tinea corporis/cruris) **Comparator** • clotrimazole (1%) plus 1% hydrocortisone (1%) b.i.d. for 4 weeks (80 tinea pedis; 57 tinea corporis/cruris) No additional topical medication was allowed
Outcomes	Assessments (6): baseline, weeks 1, 2, 3, 4, 6 and 12 **Outcomes of the trial** (as reported) 1. Clinical evaluation of signs and symptoms (erythema, scaling, vesiculation, pustules, crusting and pruritus): 4-point Likert scale# 2. Mycological evaluation (KOH and culture) 3. Adverse events# Denotes outcomes prespecified for this review
Notes	Patients were stratified into two groups: Group I comprised patients with tinea pedis, and Group II comprised patients with tinea corporis or tinea cruris. We only included participants with tinea corporis and cruris.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote (page 438): "patients were stratified into two groups: Group I comprised patients with tinea pedis, and Group II comprised patients with tinea corporis or tinea cruris. Within each group, patients were randomly allocated to receive.." Comment: Insufficient detail was reported about the method used to generate the allocation sequence to allow a clear assessment of whether it would produce comparable groups.
Allocation concealment (selection bias)	Unclear risk	The method used to conceal the allocation sequence, that is to determine whether intervention allocations could have been foreseen in advance of, or during, enrolment, was not reported. Comment: There was insufficient information to permit a clear judgement.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote (page 437): "..double-blind.." Comment: The report did not provide sufficient detail about the measures used to blind study participants and personnel from knowledge of which intervention a participant received, to permit a clear judgement.

Evans 1993 *(Continued)*

Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote (page 437): "..double-blind.." Comment: Uncertainty with the effectiveness of blinding of outcomes assessors (participants/healthcare providers) during the study. Insufficient information to permit a clear judgement.
Incomplete outcome data (attrition bias) All outcomes	Low risk	4/269 did not return after baseline. Unclear from which Group (I or II), or which treatment arm. Intention-to treat-analysis based on 265 participants. Comment: Low number of drop-outs, we judged this as at a low risk of bias.
Selective reporting (reporting bias)	Low risk	The protocol for the study was not available, but the prespecified outcomes and those mentioned in the methods section appeared to have been reported. Comment: We judged this as at a low risk of bias.
Other bias	Unclear risk	Quote (page 442): "We would like to thank Sandoz Pharmaceuticals for the management and analysis of this study". Comment: A potential risk of bias cannot be excluded.

Evans 1994

Methods	Randomised, double-blind, parallel-group study Setting Multi-centre, general practice UK Date of study Not reported. Duration of intervention single application and 1 week with follow-up 12 weeks
Participants	N = 21 (16 male, 5 female) Age range 22-72, mean 37 years **Inclusion criteria of the trial** • > 18 years • clinical diagnosis tinea corporis or tinea cruris confirmed by positive microscopy **Exclusion criteria of the trial** • subsequently negative on culture • non-dermatophyte infections • women of child-bearing age without using a reliable form of contraception • pregnant or breast-feeding women • oral terbinafine in the previous 3 months, other systemic antifungals < 6 weeks, topical antimycotic therapy < 7 days Randomised N = 21 Delayed exclusions/Withdrawals/losses to follow-up 7/21 (34%) delayed exclusions i.e. negative baseline mycology (4), candida infection (1), pityriasis versicolor (1), failed to return after the entry visit (1)

Evans 1994 *(Continued)*

	Baseline data Nothing reported
Interventions	**Intervention** • terbinafine (1%) cream once daily for one day, placebo subsequent 6 days (4) **Comparator** • terbinafine (1%) cream once daily for 3 subsequent days, placebo subsequent 4 days (4) • terbinafine (1%) cream once daily for 5 subsequent days, placebo subsequent 2 days (2) • terbinafine (1%) cream once daily for 7 subsequent days (4)
Outcomes	Assessments (5): baseline, days 8, 14, 28 and 84 **Outcomes of the trial** (as reported) 1. Mycological evaluation (KOH and culture) 2. Clinical evaluation, signs and symptoms of infection (erythema, pustules, desquamation, encrustation, vesiculation and pruritus): 4-point Likert scale# 3. Adverse events: 3-point Likert scale# Denotes outcomes prespecified for this review
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote (page 84): "..randomized using Fisher and Yates tables". Comment: Probably done.
Allocation concealment (selection bias)	Unclear risk	The method used to conceal the allocation sequence, that is to determine whether intervention allocations could have been foreseen in advance of, or during, enrolment, was not reported. Comment: There was insufficient information to permit a clear judgement.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote (page 84): "..double-blind"..and "Each patient was given a pack containing seven tubes of cream (one for each day of the week), some containing active drug, and some only vehicle cream." Comment: The report did not provide sufficient detail about if the tubes looked identical to blind study participants and personnel from knowledge of which intervention a participant received, to permit a clear judgement.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote (page 84): "..double-blind"..and "Each patient was given a pack containing seven tubes of cream (one for each day of the week), some containing active drug, and some only vehicle cream." Comment: Uncertainty with the effectiveness of blinding of outcomes assessors (participants/healthcare providers) during the study. Insufficient information to permit a clear judgement.
Incomplete outcome data (attrition bias) All outcomes	High risk	Delayed exclusions: (6/21) negative baseline mycology or other infections. Unclear which group. Withdrawals/ failed to return: (1/21) after the entry visit. Per-protocol analysis.

Evans 1994 *(Continued)*

		Comment: Unclear how many participants/group and delayed exclusions in each group. Under powered study combined with per-protocol analysis we judged this at a high risk of bias.
Selective reporting (reporting bias)	Low risk	The protocol for the study was not available, but the prespecified outcomes and those mentioned in the methods section appeared to have been reported. Comment: We judged this as at a low risk of bias.
Other bias	High risk	Quote (page 87): "We thank Sandoz Pharmaceuticals (U.K.) Ltd for supplying terbinafine and supporting the study." Comment: Although the investigators did not clarify precisely what support other than trial medication was provided, a potential risk of bias cannot be excluded.

Fan 1991

Methods	Randomised, single-blind, active-controlled trial Setting Department of Dermatology, Second Affiliated Hospital of Guangzhou University of Traditional Chinese Medicine, Guangzhou, China Date of study Not reported. Duration of intervention 3 weeks with one week follow-up
Participants	N = 183 (77 male/93 female; 13 gender unreported) Age range 15-68 years **Inclusion criteria of the trial** • tinea cruris or vulvovaginal candidiasis confirmed by KOH **Exclusion criteria of the trial** • not reported Randomised N = 183 Withdrawals/losses to follow-up • No drop-outs Baseline data Tinea cruris: Xianglian (52), clotrimazole (45) Candidiasis: Xianglian (40), clotrimazole (33) Other: Xianglian (8), clotrimazole (5)
Interventions	**Intervention** • Xianglian (Flos Caryophylli and Rhizoma Coptidis, mixture of Chinese herbs) lotion (5.58%), wash for 20-30 minutes, once a day, and Xianglian cream (22.32%), b.i.d. for 3 weeks in tinea cruris and vulvovaginal candidiasis treated for two weeks.

Fan 1991 *(Continued)*

	Comparator • potassium permanganate 0.02%, wash for 20-30 minutes, once a day, and clotrimazole cream (3%), b.i.d. for 4 weeks; for vulvovaginal candidiasis, wash with soda water (3%) and paint with nysfungin, once a day for two weeks
Outcomes	Assessments (3): baseline, week 1, at end of study and one week after treatment **Outcomes of the trial** (as reported) 1. Clinical evaluation of signs and symptoms 2. Clinical efficacy: 3-point Likert scale# 3. Mycological evaluation (KOH, culture and fungal identification) 4. Laboratory tests 5. Determination of minimum inhibitory concentration Denotes outcomes prespecified for this review
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote (page 170): "..randomised..". Comment: Insufficient detail was reported about the method used to generate the allocation sequence to allow a clear assessment of whether it would produce comparable groups.
Allocation concealment (selection bias)	Unclear risk	The method used to conceal the allocation sequence, that is to determine whether intervention allocations could have been foreseen in advance of, or during, enrolment, was not reported. Comment: There was insufficient information to permit a clear judgement.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote (page 170): "..single-blind..". Comment: Unclear who is blinded. The report did not provide sufficient detail about the measures used to blind study participants or personnel from knowledge of which intervention a participant received, to permit a clear judgement.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote (page 170): "..single-blind..". Comment: Uncertainty with the effectiveness of blinding of outcomes assessors (participants/healthcare providers) during the study. Insufficient information to permit a clear judgement.
Incomplete outcome data (attrition bias) All outcomes	Low risk	No drop-outs reported. Comment: We judged this as at a low risk of bias
Selective reporting (reporting bias)	Low risk	The protocol for the study was not available, but the prespecified outcomes and those mentioned in the methods section appeared to have been reported. Comment: We judged this as at a low risk of bias.
Other bias	Low risk	The study appears to be free of other forms of bias.

Fan 1994

Methods	Randomised, double-blind, active-controlled trial Setting Two hospital dermatology out-patient clinics in China Date of study Not reported. Duration of intervention 4 weeks with 1 week follow-up
Participants	N = 85 (58 male/27 female) Mean age = 37 years **Inclusion criteria of the trial** • tinea cruris/corporis or tinea versicolor confirmed by KOH **Exclusion criteria of the trial** • not reported Randomised N = 85 Withdrawals/losses to follow-up • no drop-outs Baseline data Tinea cruris: Xianglian (35), clotrimazole (12) Tinea corporis: Xianglian (15), clotrimazole (4) Tinea versicolor: Xianglian (16), clotrimazole (4)
Interventions	**Intervention** • Xianglian lotion (10%), wash for 20-30 minutes, once a day and Xianglian cream (30%), b.i.d. for 4 weeks for tinea cruris/corporis; for tinea versicolor, Xianglian spray (30%), two to three times per day, for 4 weeks (66) **Comparator** • potassium permanganate (0.02%), wash for 20-30 minutes, once a day and clotrimazole cream (3%), b.i.d. for 4 weeks for tinea cruris/corporis; for tinea versicolor, ethanol (60%), b.i.d. for 4 weeks (19)
Outcomes	Assessments (3): baseline, week 1 and at end of therapy **Outcomes of the trial** (as reported) 1. Clinical evaluation of signs and symptoms; 4-point Likert scale# 2. Clinical efficacy: 4-point Likert scale# 3. Mycological evaluation (KOH, culture and fungal identification) 4. Adverse events# Denotes outcomes prespecified for this review
Notes	

Fan 1994 *(Continued)*

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote (page 614): "..randomised.." Comment: Insufficient detail was reported about the method used to generate the allocation sequence to allow a clear assessment of whether it would produce comparable groups.
Allocation concealment (selection bias)	Unclear risk	The method used to conceal the allocation sequence, that is to determine whether intervention allocations could have been foreseen in advance of, or during, enrolment, was not reported. Comment: There was insufficient information to permit a clear judgement.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote (page 614): "..double-blind..". The report did not provide sufficient detail about the measures used to blind study participants and personnel from knowledge of which intervention a participant received, to permit a clear judgement.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote (page 614): "..double-blind..". Comment: Uncertainty with the effectiveness of blinding of outcomes assessors (participants/healthcare providers) during the study. Insufficient information to permit a clear judgement.
Incomplete outcome data (attrition bias) All outcomes	Low risk	No drop-outs reported. Intention-to-treat analysis. Comment: We judged this as at low risk of bias.
Selective reporting (reporting bias)	Low risk	The protocol for the study was not available, but the prespecified outcomes and those mentioned in the methods section appeared to have been reported. Comment: We judged this as at a low risk of bias.
Other bias	Low risk	The study appears to be free of other forms of bias.

Finzi 1986

Methods	Randomised, double-blind, active-controlled, within-patient comparison trial Setting Department of Dermatology, School of Medicine, University of Milan, Italy Date of study Not reported. Duration of intervention up to 4 weeks
Participants	N = 29 (13 male/8 female: 8 gender unreported) Age range = 20-79, average 60 years **Inclusion criteria of the trial** • dermatomycoses in symmetrical distribution or clinical comparable lesions confirmed by KOH and culture

Finzi 1986 *(Continued)*

	Exclusion criteria of the trial • antifungal treatment < 4 weeks prior to study entry • hypersensitivity to topical medications • liver disease, epilepsy or chronic disease (e.g. diabetes, hypertension) not under adequate control Randomised N = 29 Withdrawals/losses to follow-up • 8/21, reasons not reported Baseline data Diagnosis: Tinear cruris (6) Tinea corporis (2) Tinea versicolor, candidiasis, tinea pedis or other (13)
Interventions	**Intervention** • fenticonazole (2%) cream b.i.d. for up to a maximum of 4 weeks **Comparator** • clotrimazole (1%) cream b.i.d. for up to a maximum of 4 weeks
Outcomes	Assessments (5): baseline, weeks 1, 2, 3 and 4 **Outcomes of the trial** (as reported) 1. Mycological evaluation (KOH and culture) 2. Clinical evaluation of signs and symptoms (desquamation, redness, itching, vesicles, oedema) 3. Overall assessment: 3-point Likert scale# 4. Adverse events# Denotes outcomes prespecified for this review
Notes	We only included data on tinea corporis and tinea cruris. See Table 3

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote (page 41): "..were randomly assigned..". Comment: Insufficient detail was reported about the method used to generate the allocation sequence to allow a clear assessment of whether it would produce comparable groups.
Allocation concealment (selection bias)	Unclear risk	The method used to conceal the allocation sequence, that is to determine whether intervention allocations could have been foreseen in advance of, or during, enrolment, was not reported. Comment: There was insufficient information to permit a clear judgement.

Finzi 1986 *(Continued)*

Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote (page 41-42): "..double-blind.." and "The two treatments were identical in packaging and very similar as type of cream." Comment: The report provided sufficient detail about the measures used to blind study participants and personnel from knowledge of which intervention a participant received, to permit a clear judgement.
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote (page 41-42): "..double-blind.." and "The two treatments were identical in packaging and very similar as type of cream." Outcomes were investigator-assessed. Blinding of participants and key study personnel was ensured, and it is unlikely that the blinding could have been broken. Comment: We judged this as at a low risk of bias.
Incomplete outcome data (attrition bias) All outcomes	High risk	8/29 (28%) were not included in final analysis, reasons unreported. Within-patient comparison. Comment: We judged this as at a high risk of bias.
Selective reporting (reporting bias)	Low risk	Few data are reported, and although the protocol for the study was not available, the prespecified outcomes and those mentioned in the methods section appeared to have been reported. Comment: We judged this as at a low risk of bias.
Other bias	Low risk	The study appeared to be free of other forms of bias.

Fredriksson 1983

Methods	Randomised, single-blind, active-controlled trial Setting Department of Dermatology, Central Hospital, Vasteras, Sweden Date of study Not reported. Duration of intervention 14-28 days with follow-up 6 weeks after end of treatment
Participants	N = 60 (gender and age unreported) **Inclusion criteria of the trial** • participants of both sexes with clinical diagnosis of infection with Candida species, Trichophyton species, E floccosum or Malazessia furfur confirmed by KOH and culture **Exclusion criteria of the trial** • not reported Randomised N = 60 Withdrawals/losses to follow-up • no drop-outs

Fredriksson 1983 *(Continued)*

	Baseline data Fungal species reported but not the site of infections
Interventions	**Intervention** • tioconazole (1%) b.i.d. for 14-28 days (30) **Comparator** • miconazole (2%) b.i.d. for 14-28 days (30)
Outcomes	Assessments (4): baseline, weeks 2, 4 and 6 weeks after end of treatment **Outcomes of the trial** (as reported) 1. Clinical evaluation: 3-point Likert scale# 2. Mycological evaluation (KOH and culture) 3. Participants' assessment of ease of application, staining of the creams and irritation 4. Relapse 5. Adverse events# Denotes outcomes prespecified for this review
Notes	Participants with tinea cruris and corporis are likely to be included, but separate numbers not reported. See Table 1 and Table 3

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote (page 15): ".. allocated randomly.." Comment: Insufficient detail was reported about the method used to generate the allocation sequence to allow a clear assessment of whether it would produce comparable groups.
Allocation concealment (selection bias)	Unclear risk	The method used to conceal the allocation sequence, that is to determine whether intervention allocations could have been foreseen in advance of, or during, enrolment, was not reported. Comment: There was insufficient information to permit a clear judgement.
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote (page 15): "Both creams were in identical packages, marked only with a code number.." Comment: The report provided sufficient detail about the measures used to blind study participants and personnel from knowledge of which intervention a participant received, to permit a clear judgement.
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Outcomes were investigator-assessed as well as participant-assessed. Blinding of participants and key study personnel was ensured, and it is unlikely that the blinding could have been broken. Comment: We judged this as at a low risk of bias.
Incomplete outcome data (attrition bias) All outcomes	Low risk	No drop-outs reported. Comment: We judged this as at low risk of bias.

Fredriksson 1983 *(Continued)*

Selective reporting (reporting bias)	Low risk	The protocol for the study was not available, but the prespecified outcomes and those mentioned in the methods section appeared to have been reported. Comment: We judged this as at a low risk of bias.
Other bias	Low risk	The study appears to be free from other forms of bias.

Friederich 1985

Methods	Randomised, double-blind, active-controlled trial Setting Dermatology clinics (2), Germany Date of study Not reported. Duration of the intervention 4 weeks with follow-up at 8 weeks
Participants	N = 62 (36 male/21 female; 5 gender unreported) Mean age = 40 years **Inclusion criteria of the trial** • participants with inflammatory dermatomycosis **Exclusion criteria of the trial** • systemic treatment with antifungals < 4 weeks prior to study entry • topical antifungal treatment or corticosteroid < 1 week prior to study entry • pregnant women • participants with a contraindication for topical corticosteroids Randomised N = 57 Withdrawals/losses to follow-up • naftifine (3/31), econazole-triamcinolone (2/31), reasons negative culture at baseline or lost to follow-up Baseline data Location: Arms: naftifine (2), econazole-triamcinolone acetonide group (3) Trunk: naftifine (5), econazole-triamcinolone acetonide group (4) Feet: naftifine (12), econazole-triamcinolone acetonide group (10) Hands: naftifine (4), econazole-triamcinolone acetonide group (1) Groins: naftifine (8), econazole-triamcinolone acetonide group (10) Buttocks: naftifine (3), econazole-triamcinolone acetonide group (1) Other: naftifine (3), econazole-triamcinolone acetonide group (5)
Interventions	**Intervention**

Friederich 1985 *(Continued)*

- naftifine cream b.i.d. for 4 weeks (31)

Comparator

- econazole-triamcinolone acetonide cream b.i.d. for 2 weeks, followed by 2 weeks econazole alone b.i.d. (31)

Outcomes	Assessments (6): baseline, day 4, weeks 1, 2, 4 and 8 **Outcomes of the trial** (as reported) 1. Clinical evaluation of signs and symptoms (erythema, scaling, vesicles, exudation, papules, pustules, infiltration, maceration and itching): 6-point Likert scale# 2. Mycological evaluation (KOH and culture) 3. Adverse events: 4-point Likert scale# 4. Antihistaminergic/antiphlogistic properties Denotes outcomes prespecified for this review
Notes	After 2 weeks the naftifine group continued with naftifine, while the econazole-triamcinolone group continued with econazole alone. We only included data from the first 2 weeks. Only participants with tinea cruris and corporis were considered. See Table 3

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote (page 77): "..wurden randomisiert.." Comment: Insufficient detail was reported about the method used to generate the allocation sequence to allow a clear assessment of whether it would produce comparable groups.
Allocation concealment (selection bias)	Unclear risk	The method used to conceal the allocation sequence, that is to determine whether intervention allocations could have been foreseen in advance of, or during, enrolment, was not reported. Comment: There was insufficient information to permit a clear judgement.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote (page 77): "..doppelblind.." Comment: The report did not provide sufficient detail about the measures used to blind study participants and personnel from knowledge of which intervention a participant received, to permit a clear judgement.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote (page 77): "..doppelblind.." Comment: Uncertainty with the effectiveness of blinding of outcomes assessors (participants/healthcare providers) during the study. Insufficient information to permit a clear judgement.
Incomplete outcome data (attrition bias) All outcomes	Low risk	Naftifine (3/31), econazole-triamcinolone (2/31), reasons negative culture at baseline or lost to follow-up. Comment: Low and well balanced number of drop-outs and although per-protocol analysis considered to be at low risk of bias.
Selective reporting (reporting bias)	Low risk	The protocol for the study was not available, but the prespecified outcomes and those mentioned in the methods section appeared to have been reported. Comment: We judged this as at a low risk of bias.

Friederich 1985 *(Continued)*

Other bias	Low risk	The study appears to be free from other forms of bias.

Fulton 1975

Methods	Randomised, double-blind, placebo-controlled trial Setting Department of Dermatology University of Miami, Florida USA Date of study 1972. Duration of intervention 2 weeks including follow-up
Participants	N = 99 (all male) Age range 20-29 years **Inclusion criteria of the trial** • moderate to severe clinical condition compatible with dermatophyte or candida infection • fungal hyphae or budding yeast on KOH **Exclusion criteria of the trial** • nothing reported Randomised N = 99 Withdrawals/losses to follow-up • no losses to follow-up Baseline data Tinea cruris (48) Tinea corporis (5) Mixed tinea, including pedis (46)
Interventions	**Intervention** • miconazole (2%) cream b.i.d. for 2 weeks (49) **Comparator** • vehicle b.i.d. for 2 weeks (50)
Outcomes	Assessments (3): baseline, weeks 1, 2, and 4 **Outcomes of the trial** (as reported) 1. Mycological evaluation (KOH and culture) 2. Clinical evaluation (severity signs and symptoms, photo's) Denotes outcomes prespecified for this review
Notes	We only included data from participants with tinea corporis and tinea cruris. See Table 3

Fulton 1975 *(Continued)*

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote (page 596): "assigned sequential numbers that had previously been randomised". Comment: Method used to generate the sequence not reported.
Allocation concealment (selection bias)	Unclear risk	Quote (page 596): "..identified only by the corresponding patient number...". The method used to conceal the allocation sequence, that is to determine whether intervention allocations could have been foreseen in advance of, or during, enrolment, was not reported. Comment: There was insufficient information to permit a clear judgement.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote (page 596): "..identified only by the corresponding patient number...the identity of the tubes content was unknown to the investigator..". Comment: The report did not provide sufficient detail about if the tubes looked identical to blind study participants and personnel from knowledge of which intervention a participant received, to permit a clear judgement.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote (page 596) : "..identified only by the corresponding patient number...the identity of the tubes content was unknown to the investigator..". Outcomes were assessed by the investigators. Comment: The report did not provide sufficient detail about the measures used to blind study participants and personnel. It was unclear therefore, whether the outcome measurement was likely to be influenced by the lack of blinding.
Incomplete outcome data (attrition bias) All outcomes	Low risk	No losses to follow-up, intention-to-treat analysis. Comment: We judged this at a low risk of bias.
Selective reporting (reporting bias)	Low risk	The protocol for the study was not available, but the prespecified outcomes and those mentioned in the methods section appeared to have been reported. Comment: We judged this as at a low risk of bias.
Other bias	Low risk	The study appeared to be free of other forms of bias.

Ghaninejad 2009

Methods	Randomised, double-blind, active-controlled trial Setting Department of Dermatology, Razi Dermatology Hospital, Tehran, Iran Date of study June 2007 and May 2008. Duration of intervention 4 weeks with follow-up at 6 weeks
Participants	N = 100 (47 male/35 female; 18 gender unreported) Mean age = 35 years

Ghaninejad 2009 *(Continued)*

	Inclusion criteria of the trial • > 18 years with established diagnosis of cutaneous dermatophytosis confirmed by KOH and culture **Exclusion criteria of the trial** • not reported Randomised N = 100 Withdrawals/losses to follow-up • 18/100; sertaconazole 12/55, (22%), miconazole 5/45, (11%) were lost to follow-up. Sertaconazole group (1) developed contact dermatitis and dropped-out Baseline data Diagnosis: Tinea cruris: miconazole (17), sertaconazole (24) Tinea pedis: miconazole (16), sertaconazole (10) Tinea corporis: miconazole (11), sertaconazole (10) Tinea manuum:miconazole (1), sertaconazole (2)
Interventions	**Intervention** • miconazole (2%) cream b.i.d. for 4 weeks (45) **Comparator** • sertaconazole (2%) cream b.i.d. for 4 weeks (55)
Outcomes	Assessments (4): baseline, weeks 2, 4 and 6 **Outcomes of the trial** (as reported) 1. Clinical evaluation 2. Mycological evaluation (KOH and culture) 3. Adverse events# Denotes outcomes prespecified for this review
Notes	See contact with investigators Table 1. We only included data on tinea corporis and cruris, see Table 3

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote (page e837): "..were randomly allocated..". Comment: Insufficient detail was reported about the method used to generate the allocation sequence to allow a clear assessment of whether it would produce comparable groups.
Allocation concealment (selection bias)	Unclear risk	The method used to conceal the allocation sequence, that is to determine whether intervention allocations could have been foreseen in advance of, or during, enrolment, was not reported. Comment: There was insufficient information to permit a clear judgement.

Ghaninejad 2009 *(Continued)*

Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote (page e837): "..double-blind..". Comment: The report did not provide sufficient detail about the measures used to blind study participants and personnel from knowledge of which intervention a participant received, to permit a clear judgement.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote (page e837): "..double-blind..". Comment: Uncertainty with the effectiveness of blinding of outcomes assessors (participants/healthcare providers) during the study. Insufficient information to permit a clear judgement.
Incomplete outcome data (attrition bias) All outcomes	High risk	18/100 (18%) dropped out; 13/55 (24%) in sertaconazole group and 5/45 (11%) in the miconazole group. Per-protocol analysis. Comment: We judged this as at a high risk of bias.
Selective reporting (reporting bias)	Low risk	The protocol for the study was not available, but the prespecified outcomes and those mentioned in the methods section appeared to have been reported. Comment: We judged this as at a low risk of bias.
Other bias	Low risk	The study appeared to be free of other forms of bias.

Gip 1980

Methods	Randomised, double-blind, active-controlled, within-patient comparison trial Setting Department of Dermatology, Sundsvall Hospital, Sundsvall, Sweden Date of study Not reported. Duration of the intervention 2 weeks (followed by 2 weeks of isoconazole cream alone on both sites)
Participants	N = 30 (16 male/ 14 female) Age range 9-91 years **Inclusion criteria of the trial** • severe and allergic dermatomycoses **Exclusion criteria of the trial** • not reported Randomised N = 30 Withdrawals/losses to follow-up • 1/30 lost to follow-up Baseline data Location:

Gip 1980 *(Continued)*

	Inguinal:16 (7 were caused by dermatophytes, 9 by Candida albicans) Feet: 9 Under the breasts: 3 Axillae: 2
Interventions	**Intervention** • Travocort cream (isoconazole nitrate 1%, combined with diflucortolone valerate 0.1%) b.i.d. for 14 days (30) **Comparator** • Travogen cream b.i.d. for 14 days (30) After 2 weeks all sites continued for another 2 weeks with Travogen cream b.i.d.
Outcomes	Assessments (3): baseline, weeks 1 and 2 **Outcomes of the trial** (as reported) 1. Clinical evaluation: 4-point Likert scale# 2. Mycological evaluation (KOH and culture) 3. Clinical evaluation signs and symptoms (erythema, scaling and itch)# Denotes outcomes prespecified for this review
Notes	We only included data on dermatophytes infections in the inguinal folds. See Table 3

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote (page 79): "..randomized..". Comment: Insufficient detail was reported about the method used to generate the allocation sequence to allow a clear assessment of whether it would produce comparable groups.
Allocation concealment (selection bias)	Unclear risk	The method used to conceal the allocation sequence, that is to determine whether intervention allocations could have been foreseen in advance of, or during, enrolment, was not reported. Comment: There was insufficient information to permit a clear judgement.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote (page 79): "..double-blind..". Comment: The report did not provide sufficient detail about the measures used to blind study participants and personnel from knowledge of which intervention a participant received, to permit a clear judgement.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote (page 79): "..double-blind..". Comment: Uncertainty with the effectiveness of blinding of outcomes assessors (participants/healthcare providers) during the study. Insufficient information to permit a clear judgement.
Incomplete outcome data (attrition bias) All outcomes	Low risk	1/30 lost to follow-up.

Gip 1980 *(Continued)*

		Comment: Within-participant comparison, single drop-out, we judged this at a low risk of bias.
Selective reporting (reporting bias)	Low risk	The protocol for the study was not available, but the prespecified outcomes and those mentioned in the methods section appeared to have been reported. Comment: We judged this as at a low risk of bias.
Other bias	High risk	One investigator was employed by Schering AG, Berlin the manufacturer of Travogen cream. Comment: A potential risk of bias cannot be excluded.

Gip 1983

Methods	Randomised, double-blind, active-controlled trial Setting Department of Dermatology, Sundsvall Hospital, Sundsvall, Sweden Date of study Not reported. Duration of the study 3 weeks with follow-up at 9 weeks
Participants	N = 40 (23 male/17 female) Mean age = 45 years **Inclusion criteria of the trial** • tinea pedis and cruris/corporis confirmed by KOH and culture **Exclusion criteria of the trial** • tinea capitis, tinea unguium, tinea manuum Randomised N = 40 Withdrawals/losses to follow-up • 2/20 sulconazole group: adverse event (1), and the visit took place beyond the required time range (1) • 12/40 Week 9: positive culture (6); at end of treatment (3); inadequate clinical improvement (1), earlier than planned follow-up visit (4), loss to follow-up on first day (1) Baseline data Diagnosis: Tinea pedis: 75% Tinea cruris: 15% Tinea corporis: 10%
Interventions	**Intervention** • sulconazole (1%) cream b.i.d. for 3 weeks (20) **Comparator**

Gip 1983 *(Continued)*

	• miconazole (2%) cream b.i.d. for 3 weeks (20) Participants were asked to stop all other antifungal treatment
Outcomes	Assessments (4): baseline weeks 2, 3 and 9 **Outcomes of the trial** (as reported) 1. Clinical evaluation of signs and symptoms (erythema, scaling, itching, fissuring and maceration) 2. Mycological evaluation 3. Overal clinical assessment: 5-point Likert scale# 4. Acceptability of medication's cosmetic qualities Denotes outcomes prespecified for this review
Notes	No separate data for tinea cruris and corporis. See Table 3

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote (page 233): "..were randomised..". Comment: Insufficient detail was reported about the method used to generate the allocation sequence to allow a clear assessment of whether it would produce comparable groups.
Allocation concealment (selection bias)	Unclear risk	The method used to conceal the allocation sequence, that is to determine whether intervention allocations could have been foreseen in advance of, or during, enrolment, was not reported. Comment: There was insufficient information to permit a clear judgement.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote (page 232): "..double-blind..". Comment: The report did not provide sufficient detail about the measures used to blind study participants and personnel from knowledge of which intervention a participant received, to permit a clear judgement.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote (page 232): "..double-blind..". Comment: Uncertainty with the effectiveness of blinding of outcomes assessors (participants/healthcare providers) during the study. Insufficient information to permit a clear judgement.
Incomplete outcome data (attrition bias) All outcomes	High risk	Week 3 losses (2/20) sulconazole group and additional losses (12/40) at Week 9. Per-protocol analysis. Comment: Large losses to follow-up combined with per-protocol analysis, we judged this as at a high risk of bias.
Selective reporting (reporting bias)	Low risk	The protocol for the study was not available, but the prespecified outcomes and those mentioned in the methods section appeared to have been reported. Comment: We judged this as at a low risk of bias.
Other bias	High risk	One investigator was employed by Asta Syntex Scandinavia AB, the developer of sulconazole. Comment: A potential risk of bias cannot be excluded.

Gip 1984

Methods	Randomised, double-blind, active-controlled trial Setting Department of Dermatology, Sundsvall Hospital, Sundsvall, Sweden Date of study Not reported. Duration of the intervention 3-6 weeks with 2-3 weeks follow-up
Participants	N = 120 (57 male/63 female) Mean age = 45, age range 10-84 years **Inclusion criteria of the trial** • cutaneous candidiasis, dermatophytosis or pityriasis versicolor confirmed by KOH and culture **Exclusion criteria of the trial** • antimycotics < 2 weeks prior to study entry • hypersensitivity to antimycotics of the imidazole group • secondary bacterial infections • mycotic disorders of the appendages of the skin or deep forms of mycosis Randomised N = 120 Withdrawals/losses to follow-up • 2/60 econazole group: lost to follow-up (1), adverse event (1) Baseline data Diagnosis: Candidiasis: oxiconazole (20), econazole (20) Dermatophytosis: Inguinal: oxiconazole (4), econazole (6) Trunk: oxiconazole (1), econazole (1) Feet: oxiconazole (15), econazole (14)
Interventions	**Intervention** • oxiconazole (1%) cream b.i.d. for 3-6 weeks (60) **Comparator** • econazole (1%) cream b.i.d. for 3-6 weeks (60)
Outcomes	Assessments (4): baseline, weeks 2, 3 and 2/3 weeks after discontinuation **Outcomes of the trial** (as reported) 1. Clinicial evaluation of signs and symptoms (redness, scaling, weeping, blistering, pustulation, incrustation, itching): 4-point Likert scale# 2. Mycological evaluation (KOH and culture)

Gip 1984 *(Continued)*

3. Overall clinical evaluation: 3-point Likert scale#
4. Tolerance/adverse events#

Denotes outcomes prespecified for this review

Notes	No separate data for tinea cruris and corporis were reported. See Table 3

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote (page 298): " Patients were assigned to either one of the two treatments according to a double-blind randomized schedule". Comment: Insufficient detail was reported about the method used to generate the allocation sequence to allow a clear assessment of whether it would produce comparable groups.
Allocation concealment (selection bias)	Unclear risk	The method used to conceal the allocation sequence, that is to determine whether intervention allocations could have been foreseen in advance of, or during, enrolment, was not reported. Comment: There was insufficient information to permit a clear judgement.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote (page 298): "..double-blind..". Comment: The report did not provide sufficient detail about the measures used to blind study participants and personnel from knowledge of which intervention a participant received, to permit a clear judgement.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote (page 298): "..double-blind..". Comment: Uncertainty with the effectiveness of blinding of outcomes assessors (participants/healthcare providers) during the study. Insufficient information to permit a clear judgement.
Incomplete outcome data (attrition bias) All outcomes	Low risk	2/60 in econazole group: lost to follow-up (1), adverse event (1). Per-protocol analysis. Comment: Although per-protocol analysis, only 2 participants dropped out and we judged this as at a low risk of bias.
Selective reporting (reporting bias)	Low risk	The protocol for the study was not available, but the prespecified outcomes and those mentioned in the methods section appeared to have been reported. Comment: We judged this as at a low risk of bias.
Other bias	Low risk	The study appeared to be free of other forms of bias.

Gip 1987

Methods	Randomised, double-blind, placebo-controlled trial Setting Dermatology department, Hospital of Sundsvall, Sweden Date of study Not reported. Duration of intervention 2 weeks with follow-up at 6 weeks

Gip 1987 *(Continued)*

Participants	N = 63 (58 male/5 female) Mean age = 31, range 16-65 years **Inclusion criteria of the trial** • tinea cruris confirmed by KOH and culture **Exclusion criteria of the trial** • < 2 weeks antimycotic therapy prior to study entry Randomised N = 63 Withdrawals/losses to follow-up • none reported Baseline data Nothing reported
Interventions	**Intervention** • naftifine (1%) cream b.i.d. for 2 week (32) **Comparator** • placebo b.i.d. for 2 weeks (31)
Outcomes	**Outcomes of the trial** (as reported) 1. Clinical evaluation of sign and symptoms (erythema, scaling, vesiculation, pustulation, exudation, pruritus): 7-point Likert scale# 2. Mycological evaluation (KOH and culture) 3. Overall assessment 4. Tolerance/adverse events: 7-point Likert scale# Denotes outcomes prespecified for this review
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote (page 38): " were assigned...randomized schedule.." Comment: Insufficient detail was reported about the method used to generate the allocation sequence to allow a clear assessment of whether it would produce comparable groups.
Allocation concealment (selection bias)	Unclear risk	The method used to conceal the allocation sequence, that is to determine whether intervention allocations could have been foreseen in advance of, or during, enrolment, was not reported. Comment: There was insufficient information to permit a clear judgement.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote (page 38): "..double-blind..".

Gip 1987 *(Continued)*

		Comment: The report did not provide sufficient detail about the measures used to blind study participants and personnel from knowledge of which intervention a participant received, to permit a clear judgement.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote (page 38): "..double-blind..". Comment: Uncertainty with the effectiveness of blinding of outcomes assessors (participants/healthcare providers) during the study. Insufficient information to permit a clear judgement.
Incomplete outcome data (attrition bias) All outcomes	Low risk	No drop-outs reported. Intention-to-treat analysis. Comment: We judged this as at a low risk of bias.
Selective reporting (reporting bias)	Low risk	The protocol for the study was not available, but the prespecified outcomes and those mentioned in the methods section appeared to have been reported. Comment: We judged this as at a low risk of bias.
Other bias	Low risk	The study appears to be free of other forms of bias.

Gong 1991

Methods	Randomised, double-blind, active-controlled trial Setting Wugang 1st Workers' hospital, China Date of study Not reported. Duration of intervention 4 weeks
Participants	N = 140 (94 male/46 female) Age range 17-64 years **Inclusion criteria of the trial** • tinea corporis, tinea cruris 'and' or 'or' tinea pedis confirmed by KOH **Exclusion criteria of the trial** • not reported Randomised N = 140 Withdrawals/losses to follow-up • no drop-outs Baseline data Tinea corporis: ketoconazole (17), clotrimazole (10) Tinea cruris: ketoconazole (18), clotrimazole (14) Tinea pedis: ketoconazole (45), clotrimazole (36)

Gong 1991 *(Continued)*

Interventions	**Intervention** • ketoconazole (2%) cream b.i.d. for 4 weeks (80) **Comparator** • clotrimazole (1%) cream b.i.d. for 4 weeks (60)
Outcomes	**Outcomes of the trial** (as reported) 1. Clinical efficacy: 4-point Likert scale# Denotes outcomes prespecified for this review
Notes	No separate data for tinea cruris and corporis were reported. See Table 3

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote (page 253): "randomised" Comment: Insufficient detail was reported about the method used to generate the allocation sequence to allow a clear assessment of whether it would produce comparable groups.
Allocation concealment (selection bias)	Unclear risk	The method used to conceal the allocation sequence, that is to determine whether intervention allocations could have been foreseen in advance of, or during, enrolment, was not reported. Comment: There was insufficient information to permit a clear judgement.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote (page 253): "double-blind". The report did not provide sufficient detail about the measures used to blind study participants and personnel from knowledge of which intervention a participant received, to permit a clear judgement.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote (page 253): "double-blind". Comment: Uncertainty with the effectiveness of blinding of outcomes assessors (participants/healthcare providers) during the study. Insufficient information to permit a clear judgement.
Incomplete outcome data (attrition bias) All outcomes	Low risk	No drop-outs reported. Intention-to-treat analysis. Comment: We judged this as at a low risk of bias
Selective reporting (reporting bias)	Low risk	The protocol for the study was not available, but the prespecified outcomes and those mentioned in the methods section appeared to have been reported. Comment: We judged this as at a low risk of bias.
Other bias	Low risk	The study appears to be free of other forms of bias.

Greer 1990

Methods	Randomised, double-blind, placebo-controlled trial

Greer 1990 *(Continued)*

	Setting Unreported, USA Date of study Not reported. Duration of intervention two weeks, to follow-up at 4 weeks
Participants	N = 23 (male) Age range 22-64, mean 38 years **Inclusion criteria of the trial** • tinea cruris confirmed by positive KOH microscopy • 18 and 65 years of age **Exclusion criteria of the trial** • concomitant yeast or bacterial infections of the skin • systemic antifungals prior 4 weeks • topical antifungal therapy prior 2 weeks Concomitant therapy for chronic diseases e.g. diabetes or hypertension, permitted Randomised N = 23 Delayed exclusions/Withdrawals/losses to follow-up 3/23 • terbinafine group (1) delayed exclusion (negative baseline culture) • failed follow-up (2); terbinafine (1) vehicle (1) Baseline data Both groups were similar in age, gender, duration of disease, prior therapy, size and location of lesion, infecting organism, and predisposing factors.
Interventions	**Intervention** • terbinafine (1%) cream b.i.d. for 2 weeks (9) **Comparator** • vehicle b.i.d. for 2 weeks (11)
Outcomes	Assessments (4): baseline weeks 1, 2 and 4 **Outcomes of the trial** (as reported) 1. Mycological evaluation (KOH and culture) 2. Clinical evaluation (erythema, pustules, desquamation, incrustation, vesiculation, and pruritus): 4-point Likert scale# 3. Haematologic and biochemical tests 4. Adverse events: 3-point Likert scale# 5. Therapeutic response Denotes outcomes prespecified for this review
Notes	

Greer 1990 *(Continued)*

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote (page 800): "..randomly assigned to treatment with either..". Comment: Insufficient detail was reported about the method used to generate the allocation sequence to allow a clear assessment of whether it would produce comparable groups.
Allocation concealment (selection bias)	Unclear risk	The method used to conceal the allocation sequence, that is to determine whether intervention allocations could have been foreseen in advance of, or during, enrolment, was not reported. Comment: There was insufficient information to permit a clear judgement.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote (page 800): "..double-blind..". Comment: The report did not provide sufficient detail about the measures used to blind study participants and personnel from knowledge of which intervention a participant received, to permit a clear judgement.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote (page 800): "..double-blind..". Comment: Uncertainty with the effectiveness of blinding of outcomes assessors (participants/healthcare providers) during the study. Insufficient information to permit a clear judgement.
Incomplete outcome data (attrition bias) All outcomes	Low risk	Lost to follow-up 3/23 (13%). Delayed exclusion after randomisation due to negative mycology (1) Reasons stated. Per-protocol analysis. Comment: Although per-protocol analysis, low and balanced number of drop-outs across the groups considered to be at a low risk of bias.
Selective reporting (reporting bias)	Low risk	The protocol for the study was not available, but the prespecified outcomes and those mentioned in the methods section appeared to have been reported. Comment: We judged this as at a low risk of bias.
Other bias	High risk	Supported in part by an educational grant from Sandoz Pharmaceuticals Corp, East Hanover, N.J. Comment: Although the investigators did not clarify precisely what support was provided, a potential risk of bias cannot be excluded.

Greer 1997

Methods	Randomised, double-blind, placebo-controlled trial Setting Five study sites, USA Date of study Not reported. Duration of intervention daily for 14 days and follow-up to 6 weeks
Participants	N = 91 (gender unreported)

Greer 1997 *(Continued)*

Age unreported other than older than 12 years

Inclusion criteria of the trial

- two of three major signs and symptoms of tinea corporis (erythema, scaling, and pruritus), with a minimum combined score of 5 (scored; 0 = absent, 1 = mild, 2 = moderate, 3 = severe)
- positive KOH) and positive culture for a fungal pathogen other than yeast
- females; postmenopausal, surgically sterilized, or using a medically acceptable form of contraception

Exclusion criteria of the trial

- unreported

Randomised

N = 91

Delayed exclusions

- 11/91 excluded (negative baseline cultures); 5/47 in butenafine group and 6/44 in vehicle group

Withdrawals/losses to follow-up

- 2/44 in vehicle group failed to return for any follow-up and were excluded from the analysis

Baseline data

Not reported

Interventions	**Intervention** • butenafine (1%) cream for 2 weeks (47) **Comparator** • vehicle for 2 weeks (42)
Outcomes	Assessments (4): baseline, days 7, 14 and 42 **Outcomes of the trial** (as reported) 1. Clinical evaluation of erythema, scaling, maceration, papules, vesiculation, and pruritus: 4-point Likert scale# 2. Global response assessment of signs and symptoms relative to baseline: 7-point Likert scale# 3. Participant's assessment: 5-point Likert scale# 4. Mycological evaluation (KOH and culture) 5. Adverse events# Denotes outcomes prespecified for this review
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote (page 232): "..randomly selected..". Comment: Insufficient detail was reported about the method used to generate the allocation sequence to allow a clear assessment of whether it would produce comparable groups.

Greer 1997 *(Continued)*

Allocation concealment (selection bias)	Unclear risk	The method used to conceal the allocation sequence, that is to determine whether intervention allocations could have been foreseen in advance of, or during, enrolment, was not reported. Comment: There was insufficient information to permit a clear judgement.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote (page 231): "..double-blind..". Comment: The report did not provide sufficient detail about the measures used to blind study participants and personnel from knowledge of which intervention a participant received, to permit a clear judgement.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote: (page 231): "..double-blind evaluation.." Comment: Uncertainty with the effectiveness of blinding of outcomes assessors (participants/healthcare providers) during the study. Insufficient information to permit a clear judgement.
Incomplete outcome data (attrition bias) All outcomes	Low risk	Losses after randomisation due to negative baseline culture: butenafine group (5/47), vehicle group (6/44). Failed to attend at any follow-up: vehicle group (2/44). Per-protocol analysis. Comment: Entry criterion (culture specimen) measured prior to randomisation. The delayed exclusions well-balanced between groups, no attrition bias between groups. See ICH Expert Working Group 1998. Low number of drop-outs at follow-up, only in vehicle group. Per-protocol analysis but we considered this to be at a low risk of bias.
Selective reporting (reporting bias)	Low risk	The protocol for the study was not available, but the prespecified outcomes and those mentioned in the methods section appeared to have been reported. Comment: We judged this as at a low risk of bias.
Other bias	Unclear risk	Supported by Penederm Inc, Foster City, Calif which marketed patented topically administered prescription products. Comment: Although the investigators did not clarify precisely what support was provided, a potential risk of bias cannot be excluded.

Grigoriu 1983

Methods	Randomised, double-blind, active-controlled trial Setting Dermatology and Venerology Department, Centre hospitalier universitaire Vaudois, Lausanne, Switzerland Date of study Not reported. Duration of intervention mean 4 weeks with follow-up 6 weeks after end of treatment
Participants	N = 61 (40 male/21 female) Mean age = 40 years **Inclusion criteria of the trial** • fungal infection of the skin or erythrasma

Grigoriu 1983 *(Continued)*

	Exclusion criteria of the trial • tinea capitis and onychomycosis • antifungal treatment < 1 week prior to study entry • use of another test drug Randomised N = 61 Withdrawals/losses to follow-up • tioconazole (1/30) Baseline data Location of the infection: Trunk: tioconazole (10), econazole (14) Groins: tioconazole (13), econazole (7) Hands: tioconazole (3), econazole (4) Feet: tioconazole (4), econazole (5) Toe-cleft: tioconazole (6), econazole (4)
Interventions	**Intervention** • tioconazole (1%) cream b.i.d. up to a mean of 4 weeks (30) **Comparator** • econazole (1%) cream b.i.d. up to a mean of 4 weeks (31)
Outcomes	Assessments: baseline, weekly and after 4 weeks 2-weekly **Outcomes of the trial** (as reported) 1. Clinical evaluation: 3-point Likert scale# 2. Mycological evaluation (KOH and culture) 3. Relapse Denotes outcomes prespecified for this review
Notes	We only included participants with tinea corporis and cruris. See Table 3

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote (page 9): "..were allocated from a previously prepared randomization table..". Comment: Probably done.
Allocation concealment (selection bias)	Unclear risk	The method used to conceal the allocation sequence, that is to determine whether intervention allocations could have been foreseen in advance of, or during, enrolment, was not reported. Comment: There was insufficient information to permit a clear judgement.

Grigoriu 1983 *(Continued)*

Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote (page 8): "..double-blind..". Comment: The report did not provide sufficient detail about the measures used to blind study participants and personnel from knowledge of which intervention a participant received, to permit a clear judgement.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote (page 8): "..double-blind..". Comment: Uncertainty with the effectiveness of blinding of outcomes assessors (participants/healthcare providers) during the study. Insufficient information to permit a clear judgement.
Incomplete outcome data (attrition bias) All outcomes	Low risk	Lost to follow-up 1/61. Per-protocol analysis. Comment: Low number of drop-outs and although per-protocol analysis considered to be at a low risk of bias.
Selective reporting (reporting bias)	Low risk	The protocol for the study was not available, but the prespecified outcomes and those mentioned in the methods section appeared to have been reported. Comment: We judged this as at a low risk of bias.
Other bias	Low risk	The study appears to be free from other forms of bias.

Guillano 2005

Methods	Randomised, double-blind, active-controlled trial Setting Department of Dermatology, Davao Medical Center, Davao Phillipines Date of study August to October 2004. Duration of intervention 21 days and follow-up to 4 weeks
Participants	N = 40 (26 male/14 female) Age mean 32 years ± 14 **Inclusion criteria of the trial** • age range 7–79 years • diagnosis of tinea corporis 'and' or 'or' tinea cruris confirmed KOH **Exclusion criteria of the trial** • topical antifungals prior 2 weeks • topical keratolytics prior week • systemic antifungals prior 30 days • pregnant and lactating women • diabetes • disseminated tinea corporis involving > 30% body • hypersensitivity to either intervention Randomised N = 40

Guillano 2005 *(Continued)*

Withdrawals/losses to follow-up

- kakawate (7/19, 37%), miconazole (3/21,14%)
- reasons include perception of cure and inability to follow-up in the centre.

Baseline data

Tinea corporis: kakawate (9), miconazole (6)

Tinea cruris: kakawate (6), miconazole (10)

Both: kakawate (4), miconazole (5)

Interventions	**Intervention** • kakawate/madre de cacao (50%) ointment *Gliricidia septicum* b.i.d. for 21 days (19) **Comparator** • miconazole (2%) ointment b.i.d. for 21 days (21)
Outcomes	Assessments (4): baseline, weeks 1, 2 and 3 **Outcomes of the trial** (as reported) 1. Mycological evaluation (KOH)# 2. Clinical evaluation (investigator global response): 7-point Likert scale# 3. Adverse events# 4. Total of signs and symptoms: 4-point Likert scale# 5. Participant's assessment: 5-point Likert scale# Denotes outcomes prespecified for this review
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote (page 17): "..the patients were randomly allocated to receive either 50% kakawate ointment or miconazole ointment using a table of random numbers by "coin tossing" method. Comment: Probably done.
Allocation concealment (selection bias)	Low risk	Quote (page 17): "test drugs were assigned code A and B, by another staff in the department. The investigators and the subjects were not aware of which test drug was given. " Comment: This was probably done.
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote (page 17): "Both products were placed in identical white containers and the test drugs were assigned code A and B by another staff in the department." Comment: The report provided sufficient detail about the measures used to blind study participants and personnel from knowledge of which intervention a participant received, to permit a clear judgement.
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Outcomes were participant- and investigator-assessed. Blinding of participants and key study personnel was ensured, and it is unlikely that the blinding could have been broken.

Guillano 2005 *(Continued)*

		Comment: We judged this as at a low risk of bias.
Incomplete outcome data (attrition bias) All outcomes	Low risk	Kakawate (7/19, 37%), miconazole (3/21,14%) were lost to follow-up. Quote (page 18): "There were a greater number of drop-outs among patients receiving kakawate ointment.... though most drop-outs in both groups were not attributed by the patients to failure or adverse effects by either drug". Comment: Missing data appear to have been imputed using appropriate methods, and comparisons made between intention-to-treat analysis and per-protocol analyses were reported together with corresponding P values. We judged this as at a low risk of bias.
Selective reporting (reporting bias)	Low risk	The protocol for the study was not available, but the prespecified outcomes and those mentioned in the methods section appeared to have been reported. Comment: We judged this as at a low risk of bias.
Other bias	Low risk	The study appears to be free from other forms of bias.

Hall-Smith 1974

Methods	Randomised, double-blind, active-controlled trial Setting Dermatology clinic of Brighton, Lewes and Mid-Sussex Groups of Hospitals, UK Date of study Not reported. Duration of intervention 4 weeks
Participants	N = 60 (30 male/13 female; 17 gender unreported) Average age 40 years **Inclusion criteria of the trial** • clinical diagnosis of ringworm **Exclusion criteria of the trial** • diagnosis not confirmed by microscopy (KOH) and culture Randomised N = 60 Withdrawals/losses to follow-up 17/60 (28%) • clotrimazole group (9), tolnaftate group (8) lost to follow-up at 2 weeks of treatment Baseline data clotrimazole group (41 infected sites), tolnaftate group (21 infected sites)
Interventions	**Intervention** • clotrimazole (1%) b.i.d. over 4 weeks (35) **Comparator**

Hall-Smith 1974 *(Continued)*

- tolnaftate (1%) b.i.d. over 4 weeks (25)

Outcomes	Assessments (3): baseline, weeks 2 and 4 **Outcomes of the trial** (as reported) 1. Clinical assessment: 4-point Likert scale# 2. Mycological evaluation (KOH and culture): 3-point Likert scale# 3. Adverse events# Denotes outcomes prespecified for this review
Notes	No separate data for tinea cruris and corporis were reported. See Table 3. Some had more than one infected site on the body.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote (page 71): "..randomly allocated...". Comment: Insufficient detail was reported about the method used to generate the allocation sequence to allow a clear assessment of whether it would produce comparable groups.
Allocation concealment (selection bias)	Unclear risk	The method used to conceal the allocation sequence, that is to determine whether intervention allocations could have been foreseen in advance of, or during, enrolment, was not reported. Comment: There was insufficient information to permit a clear judgement.
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote (page 70-1): "double-blind" and "The creams are practically indistinguishable and are dispensed in plain, numbered, sealed containers". Comment: The report provided sufficient detail about the measures used to blind study participants and personnel from knowledge of which intervention a participant received, to permit a clear judgement.
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Outcomes were investigator-assessed. Blinding of participants and key study personnel was ensured, and it is unlikely that the blinding could have been broken. Comment: We judged this as at a low risk of bias.
Incomplete outcome data (attrition bias) All outcomes	High risk	Lost to follow-up, 17/60 reasons not stated, balanced across the groups. Per-protocol-analysis. Comment: We judged this as at a high risk of bias.
Selective reporting (reporting bias)	Low risk	The protocol for the study was not available, but the prespecified outcomes and those mentioned in the methods section appeared to have been reported. Comment: We judged this as at a low risk of bias.
Other bias	High risk	Baseline imbalance, greater number of affected sites in the clotrimazole group. Bayer Pharmaceuticals is acknowledged for collating the results. Comment: Although the impact of Bayer Pharmaceuticals on the results is not clarified precisely a potential risk of bias cannot be excluded. But together with the baseline imbalance we judged this as at high risk of bias.

Hantschke 1980

Methods	Randomised, double-blind, active-controlled trial Setting Dermatology Department, University Clinic, Essen, Germany Date of study Not reported. Duration of the intervention up to 12 weeks with 2 weeks follow-up
Participants	N = 30 (20 male/10 female) Age range 9-81 years **Inclusion criteria of the trial** • participants with serious mycoses confirmed by KOH and culture **Exclusion criteria of the trial** • not reported Randomised N = 30 Withdrawals/losses to follow-up • no losses to follow-up reported Baseline data Diagnosis: Tinea corporis: clotrimazole (1), tolnaftate (1), naftifine (5) Tinea cruris: clotrimazole (2), tolnaftate (2), naftifine (2) Other mycoses: clotrimazole (8), tolnaftate (8), naftifine (4)
Interventions	**Intervention** • clotrimazole cream (1%) b.i.d. until clinical cure was observed (10) **Comparator 1** • tolnaftate cream (1%) b.i.d. until clinical cure was observed (10) **Comparator 2** • naftifine cream (1%) b.i.d. until clinical cure was observed (10)
Outcomes	Assessments: baseline, weekly until clinical cure was observed and 2 weeks after discontinuation **Outcomes of the trial** (as reported) 1. Clinical evaluation (erythema, scaling, vesicles, exudation, crusts, itch: 4-point Likert scale# 2. Mycological evaluation (KOH and culture) Denotes outcomes prespecified for this review
Notes	Individual patient data were reported.

Hantschke 1980 *(Continued)*

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote (page 657): "..randomized..". Comment: Insufficient detail was reported about the method used to generate the allocation sequence to allow a clear assessment of whether it would produce comparable groups.
Allocation concealment (selection bias)	Unclear risk	The method used to conceal the allocation sequence, that is to determine whether intervention allocations could have been foreseen in advance of, or during, enrolment, was not reported. Comment: There was insufficient information to permit a clear judgement.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote (page 657): "..double-blind..". Comment: The report did not provide sufficient detail about the measures used to blind study participants and personnel from knowledge of which intervention a participant received, to permit a clear judgement.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote (page 657): "..double-blind..". Comment: Uncertainty with the effectiveness of blinding of outcomes assessors (participants/healthcare providers) during the study. Insufficient information to permit a clear judgement.
Incomplete outcome data (attrition bias) All outcomes	Low risk	No apparent losses to follow-up. Individual patient data reported Comment: We judged this as at a low risk of bias.
Selective reporting (reporting bias)	Low risk	The protocol for the study was not available, but the prespecified outcomes and those mentioned in the methods section appeared to have been reported. Comment: We judged this as at a low risk of bias.
Other bias	Low risk	The study appears to be free from other forms of bias.

Haroon 1996

Methods	Randomised, open, active-controlled study Setting Department of Mycology, King Edward Hospital Medical College/Hospital Lahore, Pakistan Date of study April to September 1993. Duration of intervention 4 weeks with follow-up 4 weeks
Participants	N = 42 (30 male/3 female; gender unreported 9) Age range 19-70 years **Inclusion criteria of the trial** • adults with clinical and mycological evidence of tinea cruris **Exclusion criteria of the trial**

Haroon 1996 *(Continued)*

- pregnancy
- onychomycosis
- infection of skin by bacteria or yeast
- topical or systemic antimycotics or antibiotics in prior 2 weeks
- hypersensitivity to either intervention

Randomised

N = 42

Withdrawals/losses to follow-up

- 9/42 (21%) which group, when and reasons not reported

Baseline data

Disease duration in weeks: naftifine group (24.4), tioconazole group (27.1)

Interventions	**Intervention** • naftifine cream (1%) once daily 4 weeks (n = 15 available case) **Comparator** • tioconazole cream (1%) b.i.d. 4 weeks (n = 18 available case)
Outcomes	Assessments (4): baseline, weeks 2, 4 and 8 **Outcomes of the trial** (as reported) 1. Clinical evaluation, signs and symptoms (erythema, scaling, vesiculation, pustulation): 4-point Likert scale# 2. Pruritus assessment: 4-point Likert scale 3. Mycological evaluation (KOH and culture) 4. Adverse events: 4-point Likert scale# Denotes outcomes prespecified for this review
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote (page 182): "..randomized into two groups..". Comment: Insufficient detail was reported about the method used to generate the allocation sequence to allow a clear assessment of whether it would produce comparable groups.
Allocation concealment (selection bias)	Unclear risk	The method used to conceal the allocation sequence, that is to determine whether intervention allocations could have been foreseen in advance of, or during, enrolment, was not reported. Comment: There was insufficient information to permit a clear judgement.
Blinding of participants and personnel (performance bias) All outcomes	High risk	Quote (page 182): "..open randomized therapeutic trial..". Comment: The outcome was likely to be influenced by the lack of blinding.

Haroon 1996 *(Continued)*

Blinding of outcome assessment (detection bias) All outcomes	High risk	Quote (page182): "..open randomized therapeutic trial..". Assessments in this 'open' study were made by investigators and laboratory personnel, it is not possible to exclude the potential impact on outcome assessment.
Incomplete outcome data (attrition bias) All outcomes	High risk	Missing data 9/42 (21%). Per-protocol analysis. Comment: We judged this as at a high risk of bias.
Selective reporting (reporting bias)	Low risk	Although the protocol for the study was not available and minimal data were reported, the prespecified outcomes and those mentioned in the methods section appear to have been reported. Comment: We judged this as at a low risk of bias.
Other bias	Unclear risk	Sandoz (Pakistan) provide the medication. Comment: At least one of the interventions was manufactured by Sandoz, a potential risk of bias cannot be excluded.

Holti 1970

Methods	Randomised, double-blind, cross-over trial Setting Department of Dermatology, Newcastle University, UK Date of study Not reported. Duration of intervention 8 weeks and cross-over further 8 weeks with follow-up 12 weeks
Participants	N = 14 Mean age = adults nothing further reported **Inclusion criteria of the trial** • tinea infections **Exclusion criteria of the trial** • nothing reported Randomised N = 14 Withdrawals/losses to follow-up • nothing reported Baseline data 2/14 with tinea corporis, 12/14 tinea pedis
Interventions	**Intervention** • Whitfield's ointment (benzoic acid compound ointment) daily for 8 weeks **Comparator**

Holti 1970 *(Continued)*

	• pecilocin (Variotin, Leo Laboratories) daily for 8 weeks Cross-over for further 8 weeks only if persistent infection
Outcomes	Assessment (3): baseline, 3 months, then cross-over **Outcomes of the trial** (as reported) 1. Clinical evaluation 2. Mycological evaluation (culture) Denotes outcomes prespecified for this review
Notes	We only included participants (2) with tinea corporis.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote (page 229): "..in a randomised double-blind trial arrangement....drawn up by the Dept of Medical Statistics". Comment: Probably done.
Allocation concealment (selection bias)	Low risk	Quote (page 229): "..were supplied coded by Leo Laboratories..". Comment: Form of central allocation, reasonable attempts to ensure that the intervention allocations could not have been foreseen in advance of, or during enrolment.
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote (page 229): "..double-blind trial..identical tubes and issued by the hospital pharmacy..." Comment: Probably done.
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Outcomes were investigator assessed. Blinding of key study personnel was ensured, and it was unlikely that the blinding could have been broken. Comment: We judged this as at a low risk of bias.
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Very limited data reported to enable a clear judgement of the risk of bias.
Selective reporting (reporting bias)	Low risk	The protocol for the study was not available, but the few prespecified outcomes mentioned in the methods section appeared to have been reported. Comment: We judged this as at a low risk of bias.
Other bias	Low risk	The study appeared to be free of other forms of bias.

Jerajani 2013

Methods	Randomised, open-label, active-controlled, 3-arm trial Setting Multi-centre, India

Jerajani 2013 *(Continued)*

	Date of study Not reported. Duration of intervention 4 weeks with follow-up at 6 weeks
Participants	N = 83 (54 male/29 female) Mean age = 28-33 years **Inclusion criteria of the trial** • 18-70 years with clinical diagnosis of tinea corporis or cruris confirmed by KOH **Exclusion criteria of the trial** • tinea pedis/manuum • topical antifungal <1 week prior to study entry, oral antifungal < 4 weeks prior to study entry • history of hypersensitivity to study drugs • immunocompromised • additional bacterial infection • pregnant 'and' or 'or' lactating women Randomised N = 83 Withdrawals/losses to follow-up • 21/83 (25%) • sertaconazole: lost to follow-up (6), suspected contact dermatitis (1) • terbinafine: lost to follow-up (7) • luliconazole: lost to follow-up (7) Baseline data Number of participants/infection site unreported
Interventions	**Intervention** • sertaconazole (2%) cream b.i.d. for 4 weeks (27) **Comparator 1** • terbinafine (15) cream once daily for 2 weeks (29) **Comparator 2** • luliconazole (1%) cream once daily for 2 weeks (27)
Outcomes	Assessments (3): baseline, end of treatment, 2 weeks after treatment **Outcomes of the trial** (as reported) 1. Clinical evaluation of signs and symptoms (erythema, pruritus, vesicle, desquamation): 4-point Likert scale# 2. Mycological evaluation (KOH)# 3. Adverse events# Denotes outcomes prespecified for this review
Notes	Treatment periods vary between interventions but correspond to standard regimen

Risk of bias

Bias	Authors' judgement	Support for judgement

Jerajani 2013 *(Continued)*

Random sequence generation (selection bias)	Unclear risk	Quote (page 35): "..were randomized to receive trial drugs supplied by Sponsor as per randomization schedule in 1:1:1 ratio involving three study groups.." Comment: Insufficient detail was reported about the method used to generate the allocation sequence to allow a clear assessment of whether it would produce comparable groups.
Allocation concealment (selection bias)	Unclear risk	The method used to conceal the allocation sequence, that is to determine whether intervention allocations could have been foreseen in advance of, or during, enrolment, was not reported. Comment: There was insufficient information to permit a clear judgement.
Blinding of participants and personnel (performance bias) All outcomes	High risk	Quote (page 34): "..open-label.." Comment: The outcome was likely to be influenced by the lack of blinding.
Blinding of outcome assessment (detection bias) All outcomes	High risk	Quote (page 34): "..open-label.." Comment: The outcome measurement was likely to be influenced by the lack of blinding.
Incomplete outcome data (attrition bias) All outcomes	High risk	21/83 (25%), balanced between the groups, reasons reported. Per-protocol analysis. Comment: We judged this as at a high risk of bias.
Selective reporting (reporting bias)	Low risk	The protocol for the study was not available, but the prespecified outcomes and those mentioned in the methods section appeared to have been reported. Comment: We judged this as at a low risk of bias.
Other bias	Low risk	The study appeared to be free of other forms of bias.

Jordon 1990

Methods	Randomised, double-blind, placebo-controlled trial Setting Multi-centre USA Date of study Not reported. Duration of intervention 4 weeks with follow-up to 6 weeks
Participants	N = 70 (57 male/13 female) Age range 14-67, mean 40.6 years **Inclusion criteria of the trial** • tinea cruris or tinea corporis confirmed by KOH and culture **Exclusion criteria of the trial** • not reported Randomised

Jordon 1990 *(Continued)*

N = 70

Withdrawals/losses to follow-up

- withdrawal vehicle group (2) due to side effects vehicle (1) severe oedema and erythema, severe pruritus (1)
- 29 in naftifine group attended for week 4 visit, 33 in vehicle group

Baseline data

Nothing reported

Interventions	**Intervention** • naftifine cream (1%) once daily 4 weeks (33) **Comparator** • vehicle cream once daily 4 weeks (37)
Outcomes	Assessments (4): baseline, weeks 2, 4 and 6 **Outcomes of the trial** (as reported) 1. Clinical evaluations, signs and symptoms (erythema, scaling, and pruritus) 2. Mycological evaluation (KOH and culture) 3. Adverse events# Denotes outcomes prespecified for this review
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote (page 441): "..were randomly assigned....". Comment: Insufficient detail was reported about the method used to generate the allocation sequence to allow a clear assessment of whether it would produce comparable groups.
Allocation concealment (selection bias)	Unclear risk	The method used to conceal the allocation sequence, that is to determine whether intervention allocations could have been foreseen in advance of, or during, enrolment, was not reported. Comment: There was insufficient information to permit a clear judgement.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote (page 441): "..double-blind.. ". Comment: The report did not provide sufficient detail about the measures used to blind study participants and personnel from knowledge of which intervention a participant received, to permit a clear judgement.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote (page 441): "..double-blind.. ". Comment: Uncertainty with the effectiveness of blinding of outcomes assessors (participants/healthcare providers) during the study. Insufficient information to permit a clear judgement.
Incomplete outcome data (attrition bias) All outcomes	Low risk	Although the report presented minimal data, no drop-outs, withdrawals, or missing outcome data were reported

Jordon 1990 *(Continued)*

		Comment: We judged this as at a low risk of bias.
Selective reporting (reporting bias)	Low risk	The protocol for the study was not available, but the prespecified outcomes and those mentioned in the methods section appeared to have been reported. Comment: We judged this as at a low risk of bias.
Other bias	Low risk	The study appeared to be free of other forms of bias.

Jung 1988

Methods	Randomised, double-blind, active-controlled trial Setting Hautklinik der Facultät für Klinischen Medizin Mannheim der Universität Heidelberg, Germany Date of study Not reported. Duration of the intervention 4 weeks with follow-up at 7-8 weeks
Participants	N = 41 (28 male/13 female) Mean age = 53, range 26-80 years **Inclusion criteria of the trial** • dermatophytes infection confirmed by KOH and culture **Exclusion criteria of the trial** • onychomycosis • severe systemic disease or immunodeficiency • known hypersensitivity to imidazole derivatives • pregnant or lactating women • participants using other antifungal treatments Randomised N = 41 Withdrawals/losses to follow-up • no drop-outs Baseline data Diagnosis: Tinea inguinalis: fenticonazole (1), bifonazole (4) Mycosis plantaris: fenticonazole (7), bifonazole (5) Mycosis interdigitalis: fenticonazole (11), bifonazole (9) Tinea pedis: fenticonazole (2), bifonazole (1) Mycosis palmoplantaris: fenticonazole (1), bifonazole (1) Tinea corporis: fenticonazole (0), bifonazole (1)
Interventions	**Intervention**

Jung 1988 *(Continued)*

	• fenticonazole (2%) cream once daily for up to 4 weeks (21) **Comparator** • bifonazole (1%) cream once a day for up to 4 weeks (20)
Outcomes	Assessments (6): baseline, weeks 1, 2, 3, 4 and 7-8 **Outcomes of the trial** (as reported) 1. Clinical evaluation of signs and symptoms (itching, erythema, oedema, desquamation): 4-point Likert scale# 2. Mycological evaluation (KOH and culture) 3. Overal judgment of investigator based on clinical and mycological evaluation: 5-point Likert scale# 4. Laboratory tests 5. Adverse events# 6. Relapse rate# Denotes outcomes prespecified for this review
Notes	We only included data on tinea corporis and tinea cruris. See Table 3

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote (page 105): "..were randomly allocated..". Comment: Insufficient detail was reported about the method used to generate the allocation sequence to allow a clear assessment of whether it would produce comparable groups.
Allocation concealment (selection bias)	Unclear risk	The method used to conceal the allocation sequence, that is to determine whether intervention allocations could have been foreseen in advance of, or during, enrolment, was not reported. Comment: There was insufficient information to permit a clear judgement.
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote (page 105): "Both were supplied in identical anonymous tubes and the creams were undistinguishable" Comment: The report provided sufficient detail about the measures used to blind study participants and personnel from knowledge of which intervention a participant received, to permit a clear judgement.
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Outcomes were investigator-assessed. Blinding of participants and key study personnel was ensured, and it is unlikely that the blinding could have been broken. Comment: We judged this as at a low risk of bias.
Incomplete outcome data (attrition bias) All outcomes	Low risk	No drop-outs. Comment: We judged this as at a low risk of bias.
Selective reporting (reporting bias)	Low risk	The protocol for the study was not available, but the prespecified outcomes and those mentioned in the methods section appeared to have been reported. Comment: We judged this as at a low risk of bias.

Jung 1988 *(Continued)*

Other bias	High risk	Quote (page 105): "fenticonazole was supplied by Recordati S.p.A. Milan". One of the investigators is employed by the company. Comment: A potential risk of bias cannot be excluded.

Kagawa 1987

Methods	Randomised, double-blind, active-controlled trial Setting Tokyo Medical and Dental University, Japan Date of study Not reported. Duration of intervention 2 (tinea corporis/cruris) and 5 weeks (tinea pedis)
Participants	N = 393 (231 male/148 female; 14 gender unreported) Mean age = 42 years **Inclusion criteria of the trial** • tinea pedum, tinea cruris, tinea corporis confirmed by KOH and culture **Exclusion criteria of the trial** • pregnant women • hyperkeratotic type of tinea pedis • contact dermatitis or secondarily infected area • serious concurrent diseases • systemic antimycotic agents < 1 month or topical antimycotics < 1 week prior to study entry • treatment with oral corticosteroids Randomised N = 393 Withdrawals/losses to follow-up • naftifine (10), clotrimazole (4) due to protocol violation [Unclear if losses and withdrawals were double counted]. • naftifine (19), clotrimazole (35) dropped out for the utility evaluation • naftifine (19), clotrimazole (37) were not included in the evaluation of global efficacy • naftifine (19), clotrimazole (36) were not included from the evaluation of mycological evaluation as visits were outside the acceptable range or treatment was interrupted by adverse events Baseline data Diagnosis: Tinea pedis: naftifine (78), clotrimazole (77) Tinea cruris: naftifine (51), clotrimazole (55) Tinea corporis: naftifine (56), clotrimazole (62)
Interventions	**Intervention**

Kagawa 1987 *(Continued)*

- naftifine (1%) cream b.i.d. for 2 weeks (tinea corporis/cruris) or 5 weeks (tinea pedis) (195)

Comparator

- clotrimazole (1%) b.i.d. for 2 weeks (tinea corporis/cruris) or 5 weeks (tinea pedis)(198)

Outcomes	Assessments (4): baseline, weeks 1, 3 and 5 **Outcomes of the trial** (as reported) 1. Clinical evaluation of signs and symptoms (itching, erythema, papules, vesicles, erosion, scaling): 4-point Likert scale# 2. Mycological evaluation (KOH and culture) 3. Global efficacy: 5-point Likert scale# 4. Usefulness: 3-point Likert scale 5. Adverse reactions Denotes outcomes prespecified for this review
Notes	We only included data on participants with tinea cruris and corporis. Withdrawals and losses in the report were double counted during the evaluations.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote (page 64): ".. were randomly allocated.." Comment: Insufficient detail was reported about the method used to generate the allocation sequence to allow a clear assessment of whether it would produce comparable groups.
Allocation concealment (selection bias)	Unclear risk	The method used to conceal the allocation sequence, that is to determine whether intervention allocations could have been foreseen in advance of, or during, enrolment, was not reported. Comment: There was insufficient information to permit a clear judgement.
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote (page 64): ".. were presented in tubes of identical appearance.." Comment: The report provided sufficient detail about the measures used to blind study participants and personnel from knowledge of which intervention a participant received, to permit a clear judgement.
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Outcomes were investigator- and participant-assessed. Blinding of participants and key study personnel was ensured, and it is unlikely that the blinding could have been broken. Comment: We judged this as at a low risk of bias.
Incomplete outcome data (attrition bias) All outcomes	High risk	Naftifine (10), clotrimazole (4) losses due to protocol violation, and naftifine (19), clotrimazole (36) were not included in most analyses. Per-protocol analysis. Comment: Between15% to 20% per group not included in the analysis; we judged this as at a high risk of bias.
Selective reporting (reporting bias)	Low risk	The protocol for the study was not available, but the prespecified outcomes and those mentioned in the methods section appeared to have been reported.

Kagawa 1987 *(Continued)*

		Comment: We judged this as at a low risk of bias.
Other bias	Low risk	The study appears to be free from other bias.

Kalis 1996

Methods	Randomised, double-blind, active-controlled trial Setting Multi-centre, 8 dermatology departments in France Date of study Not reported. Duration of intervention 2-3 weeks
Participants	N = 79 (age and gender unreported) **Inclusion criteria of the trial** • tinea cruris diagnosed clinically and confirmed by KOH and culture **Exclusion criteria of the trial** • topical or systemic antifungal treatment in prior 2 weeks Randomised N = 79 Delayed exclusions: • oxiconazole (3/42), ketoconazole (1/37), negative culture Withdrawals/losses to follow-up • oxiconazole (3/42), loss to follow-up (3), • ketoconazole (6/37), adverse event (4), loss to follow-up (2) Baseline data Nothing reported
Interventions	**Intervention** • oxiconazole (1%) once daily for 2-3 weeks (42) **Comparator** • ketoconazole (2%) once daily for 2-3 weeks (37)
Outcomes	Assessments (3): baseline, weeks 2 and 3 **Outcomes of the trial** (as reported) 1. Clinical evaluation 2. Mycological evaluation (KOH and culture) 3. Time to cure 4. Adverse events (tolerance) Denotes outcomes prespecified for this review

Kalis 1996 *(Continued)*

Notes

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote (page 448): "...randomisé..." "ont eté administrés après tirage au sort". Comment: Insufficient detail was reported about the method used to generate the allocation sequence to allow a clear assessment of whether it would produce comparable groups.
Allocation concealment (selection bias)	Unclear risk	The method used to conceal the allocation sequence, that is to determine whether intervention allocations could have been foreseen in advance of, or during, enrolment, was not reported. Comment: There was insufficient information to permit a clear judgement.
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote (page 448): "en double-insu"..."sous forme de préparations de composition différente, mais d' aspect identique et selon de mêmes modalités..". Comment: The report provided sufficient detail about the measures used to blind study participants and personnel from knowledge of which intervention a participant received, to permit a clear judgement.
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Outcomes were investigator-assessed. Blinding of participants and key study personnel was ensured, and it is unlikely that the blinding could have been broken. Comment: We judged this as at a low risk of bias.
Incomplete outcome data (attrition bias) All outcomes	High risk	Losses after randomisation due to negative baseline culture: oxiconazole (3/42), ketoconazole group (1/37) = 4/79 (5%). Failed to attend for follow-up : oxiconazole (3/42, 7%), ketoconazole group (6/37, 16%) = 9/79 (11%). Comment: Entry criterion (culture specimen) measured prior to randomisation. The delayed exclusions are balanced between groups, no attrition bias between the groups. See ICH Expert Working Group 1998. Per-protocol analysis. Comment: Although the total percentage of loss to follow-up was low, losses in the ketoconazole group were double. Combined with the per-protocol analysis we judged this at a high risk of bias.
Selective reporting (reporting bias)	Low risk	The protocol for the study was not available, but the prespecified outcomes and those mentioned in the methods section appeared to have been reported. Comment: We judged this as at a low risk of bias.
Other bias	Low risk	The study appeared to be free of other forms of bias.

Kashin 1985

Methods	Randomised, open, active-controlled trial Setting

Kashin 1985 *(Continued)*

	Multi-centre, 4 centres in Europe Date of study Not reported. Duration of intervention 2-4 weeks with follow-up to 8 weeks
Participants	N = 100 (66 male/34 female) Mean age = 36.2 years (tioconazole once daily group), 30.6 years (twice daily group) **Inclusion criteria of the trial** • clinical and mycological (KOH and culture) evidence of cutaneous fungal infection • tinea pedis (except deep infections of the sole), tinea cruris, tinea corporis, tinea versicolor and cutaneous candidosis **Exclusion criteria of the trial** • nothing reported Randomised N = 100 Withdrawals/losses to follow-up • once daily group (0/48), twice daily group (3/52), due to protocol violations Baseline data Tinea corporis: once daily group (8), twice daily group (11) Tinea cruris: once daily group (6), twice daily group (7) Tinea pedis: once daily group (18), twice daily group (21) Tinea versicolor: once daily group (10), twice daily group (10) Candidiasis: once daily group (10), twice daily group (10) Once daily group (2) with 2 diagnoses and (1) with 3 diagnoses. In the twice daily group (5) with 2 diagnoses and (1) with 3 diagnoses
Interventions	**Intervention** • tioconazole (1%) cream once daily for 2-4 weeks (48) **Comparator** • tioconazole (1%) cream b.i.d. for 2-4 weeks (52)
Outcomes	**Outcomes of the trial** (as reported) 1. Clinical evaluation of sign and symptoms (itching, rash, burning/pain, erythema, fissuring, scaling maceration, cellulitis, vesicles etc: 4-point Likert scale # 2. Overall clinical response: 3-point Likert scale# 3. Mycological response (KOH and culture) 4. Relapse/reinfection Denotes outcomes prespecified for this review
Notes	Two studies, only Study I is a comparative study. We only included participants which had tinea corporis or cruris. See Table 3

Kashin 1985 *(Continued)*

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote (page 89): "...were randomly assigned.." Comment: Insufficient detail was reported about the method used to generate the allocation sequence to allow a clear assessment of whether it would produce comparable groups.
Allocation concealment (selection bias)	Unclear risk	The method used to conceal the allocation sequence, that is to determine whether intervention allocations could have been foreseen in advance of, or during, enrolment, was not reported. Comment: There was insufficient information to permit a clear judgement.
Blinding of participants and personnel (performance bias) All outcomes	High risk	Quote (page 89): "open-comparative multicentre trial..". Comment: The outcome was likely to be influenced by the lack of blinding.
Blinding of outcome assessment (detection bias) All outcomes	High risk	Quote (page 89): "open-comparative multicentre trial..". Comment: The outcome measurement was likely to be influenced by the lack of blinding.
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Protocol violations: (0/48) once daily group; (3/52) of the twice daily group, dropped out. Per-protocol analysis. Comment: Low number of losses all in twice daily group; an unclear risk of bias.
Selective reporting (reporting bias)	Low risk	The protocol for the study was not available, but the prespecified outcomes and those mentioned in the methods section appeared to have been reported. Comment: We judged this as at a low risk of bias.
Other bias	Unclear risk	Quote (page 95): "We wish to thank the investigators and the Pfizer Medical Departments in the various countries for their assistance, cooperation and participation in the carrying out of these studies." Comment: Although the investigators did not clarify precisely what support was provided, a potential risk of bias cannot be excluded.

Katz 1972

Methods	Randomised, double-blind, active and placebo-controlled trial Setting Dermatology Clinic at Fort Bragg, NC, US Date of study Not reported. Duration of intervention 2-4 weeks
Participants	N = 74 (age and gender unreported, adult soldiers, probably male) **Inclusion criteria of the trial**

Katz 1972 *(Continued)*

- clinical diagnosis of dermatophytes infection confirmed by KOH

Exclusion criteria of the trial

- not reported

Randomised

N = 74

Withdrawals/losses to follow-up

- haloprogin (1/27), tolnaftate (0/20), placebo (1/27), reasons unreported

Baseline data

27 received a haloprogin treatment, 20 a tolnaftate treatment and 27 a placebo treatment

Tinea pedis: haloprogin (15), tolnaftate (11), placebo (17)

Tinea corporis: haloprogin (11), tolnaftate (9), placebo (9)

Interventions	**Intervention** • haloprogin (1%) cream b.i.d. for 14-28 days **Comparator 1** • haloprogin (1%) solution b.i.d. for 14-28 days **Comparator 2** • tolnaftate (1%) cream b.i.d. for 14-28 days **Comparator 3** • tolnaftate (1%) solution b.i.d. for 14-28 days **Comparator 4** • haloprogin vehicle cream b.i.d. for 14-28 days **Comparator 5** • haloprogin vehicle solution b.i.d. for 14-28 days No other topical or systemic antifungal agent was used during the study.
Outcomes	Assessments (3): baseline, weeks 2 and 4 **Outcomes of the trial** (as reported) 1. Improvement of clinical severity of lesions: 4-point Likert scale# 2. Mycological evaluation (KOH)# Denotes outcomes prespecified for this review
Notes	Data for haloprogin cream and solution are reported combined, as well as tolnaftate cream and solution and the two vehicles. We only included the data on participants with tinea corporis. See Table 3

Risk of bias

Bias	Authors' judgement	Support for judgement

Katz 1972 *(Continued)*

Random sequence generation (selection bias)	Unclear risk	Quote (page 837): "Each patient was randomly assigned to one of the formulations." Comment: Insufficient detail was reported about the method used to generate the allocation sequence to allow a clear assessment of whether it would produce comparable groups.
Allocation concealment (selection bias)	Unclear risk	The method used to conceal the allocation sequence, that is to determine whether intervention allocations could have been foreseen in advance of, or during, enrolment, was not reported. Comment: There was insufficient information to permit a clear judgement.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote (page 837): "..double-blind..." and "Neither the physician nor the patient knew the identity of the medication used.." Comment: The report did not provide sufficient detail about the measures used to blind study participants and personnel from knowledge of which intervention a participant received, to permit a clear judgement.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote (page 837): "..double-blind.." and "Neither the physician nor the patient knew the identity of the medication used.." Comment: Uncertainty with the effectiveness of blinding of outcomes assessors (participants/healthcare providers) during the study. Insufficient information to permit a clear judgement.
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Limited data reported, haloprogin group (1/27), tolnaftate group (0/20), and placebo group (1/27) dropped out, reasons unreported. Comment: Low numbers and inadequate reporting of attrition/exclusions to permit a clear judgement.
Selective reporting (reporting bias)	Low risk	The protocol for the study was not available, but the prespecified outcomes and those mentioned in the methods section appeared to have been reported. Comment: We judged this as at a low risk of bias.
Other bias	Unclear risk	Quote (page 838): "The preparations used in this study were supplied by Harold W. Hermann, MD, Mead Johnson Research Center, Evansville, Ind" Comment: Unclear to what extent this represents a potential risk of bias.

Katz 1984

Methods	Randomised, double-blind, active-controlled trial Setting Multi-centre, USA Date of study Not reported. Duration of intervention 2 weeks to follow-up at 4 weeks
Participants	N = 331 (241 male/90 female) Age range 38-42 , mean 40 years **Inclusion criteria of the trial**

Katz 1984 *(Continued)*

- clinical diagnosis tinea cruris or corporis confirmed KOH, and positive culture scraping
- clinical signs/symptoms (erythema, maceration, scaling, pruritus, vesicles, papules, pustules). Total score > 6. Rated (0 = none, to 3 = marked severe, intense) with erythema > 2

Exclusion criteria of the trial

- pregnancy
- topical steroids in prior week
- systemic steroid therapy in prior 2 weeks
- hypersensitivity to any of the interventions
- any concomitant therapy that might effect the study outcome

Randomised

N = 331

Withdrawals/losses to follow-up

93 treatment failure

- combined therapy (9)
- clotrimazole (32)
- betamethasone propionate(52)

Baseline data

Tinea cruris (179)

Tinea corporis (152)

Interventions

Intervention

- clotrimazole (1%) combined with betamethasone dipropionate (0.05%) cream b.i.d. for 2 weeks (112)

Comparator

- clotrimazole (1%) cream b.i.d. for 2 weeks (112)
- betamethasone dipropionate (0.05%) cream b.i.d. for 2 weeks (106)

Outcomes

Assessments (5): baseline, once in first week, weeks 1, 2, and 4

Outcomes of the trial (as reported)

1. Total signs and symptoms score as described under inclusion criteria
2. Clinical response rating: 6-point Likert scale#
3. Mycological response (KOH and culture)
4. Adverse events: 3-point Likert scale#

Denotes outcomes prespecified for this review

Notes

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote (page 184): " randomized....". Comment: Insufficient detail was reported about the method used to generate the allocation sequence to allow a clear assessment of whether it would produce comparable groups.

Katz 1984 *(Continued)*

Allocation concealment (selection bias)	Unclear risk	The method used to conceal the allocation sequence, that is to determine whether intervention allocations could have been foreseen in advance of, or during, enrolment, was not reported. Comment: There was insufficient information to permit a clear judgement.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote (page 183): "..double- blind....". Comment: The report did not provide sufficient detail about the measures used to blind study participants and personnel from knowledge of which intervention a participant received, to permit a clear judgement.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote (page 183): "..double- blind....". Comment: Uncertainty with the effectiveness of blinding of outcomes assessors (participants/healthcare providers) during the study. Insufficient information to permit a clear judgement.
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Lost to follow-up 93/331 (28%). Numbers are not balanced across groups. Intention-to treat-analysis. Comment: Intention-to-treat analysis, but large and imbalanced losses to follow-up. We judged this as at unclear risk of bias.
Selective reporting (reporting bias)	Low risk	The protocol for the study was not available, but the prespecified outcomes and those mentioned in the methods section appeared to have been reported. Comment: We judged this as at a low risk of bias.
Other bias	Unclear risk	Schering Corporation, Kenilworth, New Jersey supplied the medication and funds to support this study. Comment: A potential risk of bias cannot be excluded.

Keczkes 1975

Methods	Randomised, double-blind, active-controlled trial Setting Department of Dermatology, Hull Royal Infirmary, UK Date of study March 1973 - March 1974. Duration of intervention 4 weeks with follow-up at 8 weeks
Participants	N = 70 (35 male/35 female) Mean age = 39 years for dermatophytes infections, 48 years for Candida infections **Inclusion criteria of the trial** • clinical diagnosis of dermatophytes or Candida infection confirmed by KOH and culture **Exclusion criteria of the trial** • not reported Randomised N = 70

Keczkes 1975 *(Continued)*

	Withdrawals/losses to follow-up • dermatophytes infections: clotrimazole (0/22), tolnaftate (2/21) due to eczematous reaction • Candida infections: clotrimazole (1/13), nystatin (1/14) due to irritation Baseline data Species are reported but not sites of infections.
Interventions	**Intervention** • clotrimazole (1%) cream b.i.d. for 4 weeks (35) **Comparator** • tolnaftate (1%) cream (for the candida infections nystatin cream was used) b.i.d. for 4 weeks (35)
Outcomes	Assessments (4): baseline, weeks 2, 4 and 8 **Outcomes of the trial** (as reported) 1. Clinical evaluation 2. Mycological evaluation (KOH and culture) 3. Adverse events# 4. Relapse Denotes outcomes prespecified for this review
Notes	Participants with tinea cruris and corporis are likely to be included, but separate data are not reported. Old study no contact details available. See Table 3

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote (page 413): "..being randomized according to treatment.." Comment: Insufficient detail was reported about the method used to generate the allocation sequence to allow a clear assessment of whether it would produce comparable groups.
Allocation concealment (selection bias)	Unclear risk	The method used to conceal the allocation sequence, that is to determine whether intervention allocations could have been foreseen in advance of, or during, enrolment, was not reported. Comment: There was insufficient information to permit a clear judgement.
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote (page 413): "..double-blind.." and "Supplies were dispensed in identical, plain, sealed, numbered containers.." Comment: The report provided sufficient detail about the measures used to blind study participants and personnel from knowledge of which intervention a participant received, to permit a clear judgement.
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Outcomes were investigator-assessed as well as participant-assessed. Blinding of participants and key study personnel was ensured, and it is unlikely that the blinding could have been broken. Comment: We judged this as at a low risk of bias.

Keczkes 1975 *(Continued)*

Incomplete outcome data (attrition bias) All outcomes	Low risk	Total 4/70 (6%). Drop-outs in the dermatophytes infections: clotrimazole (0/22), tolnaftate (2/21) due to eczematous reaction and in the Candida infections: clotrimazole (1/13), nystatin (1/14) due to irritation. Comment: Low and balanced number of drop-outs, we judged this as at a low risk of bias.
Selective reporting (reporting bias)	Low risk	The protocol for the study was not available, but the prespecified outcomes and those mentioned in the methods section appeared to have been reported. Comment: We judged this as at a low risk of bias.
Other bias	Low risk	The study appears to be free from other forms of bias.

Kokoschka 1986

Methods	Randomised, double-blind, active-controlled trial Setting Universitäts-Hautklinik, Viena, Austria Date of study Unreported. Duration of intervention 4 weeks
Participants	N = 52 (27 male/25 female) Age range 5-89, mean age = 50 years **Inclusion criteria of the trial** • acute recurrent dermatomycoses or pityriasis versicolor confirmed by KOH and culture **Exclusion criteria of the trial** • severe hypertension, liver disease, severe renal or heart failure or chronic disease not therapeutically controlled • antifungal treatments < 4 weeks prior to study entry • hypersensitivity to topical preparations Randomised N = 52 Withdrawals/losses to follow-up • no losses reported Baseline data Location of dermatomycosis: Feet: fenticonazole (9), econazole (10) Hands: fenticonazole (3), econazole (3) Genitofemoral: fenticonazole (5), econazole (6) Intergluteal region: fenticonazole (1), econazole (1) Head: fenticonazole (2), econazole (1)

Kokoschka 1986 *(Continued)*

	Tibial region: fenticonazole (2), econazole (1) Trunk: fenticonazole (4), econazole (0) Submammary region: fenticonazole (2), econazole (1)
Interventions	**Intervention** • fenticonazole (2%) cream b.i.d. for 4 weeks (28) **Comparator** • econazole (1%) cream b.i.d. for 4 weeks (24) Other topical or systemic antifungal therapies were not allowed during the study
Outcomes	Assesments (5): baseline, weeks 1, 2, 3, and 4 **Outcomes of the trial** (as reported) 1. Mycological evaluation (KOH and culture) 2. Clinical evaluation of symptoms (desquamation, redness, itching, vesicles, oedema): 6-point Likert scale# 3. Complete clinical assessment: 4-point Likert scale# 4. Laboratory investigations Denotes outcomes prespecified for this review
Notes	23 infections were caused by Candida Albicans, unclear how many exactly were matching our inclusion criteria. See Table 3

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote (page 46): " ..randomly assigned..". Comment: Insufficient detail was reported about the method used to generate the allocation sequence to allow a clear assessment of whether it would produce comparable groups.
Allocation concealment (selection bias)	Unclear risk	The method used to conceal the allocation sequence, that is to determine whether intervention allocations could have been foreseen in advance of, or during, enrolment, was not reported. Comment: There was insufficient information to permit a clear judgement.
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote (page 46): "..were identical in packaging and type of cream.." Comment: Blinding was ensured we judged this as at a low risk of bias.
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Blinding of the outcomes assessors, key personnel, was ensured, and it was unlikely that the blinding could have been broken. Comment: We judged this as at a low risk of bias.
Incomplete outcome data (attrition bias) All outcomes	Low risk	No losses to follow-up. Comment: We judged this as at a low risk of bias.

Kokoschka 1986 *(Continued)*

Selective reporting (reporting bias)	Low risk	The protocol for the study was not available, but the prespecified outcomes and those mentioned in the methods section appeared to have been reported. Comment: We judged this as at a low risk of bias.
Other bias	Low risk	The study appeared to be free of other forms of bias.

Kuhlwein 1990

Methods	Randomised, double-blind, active-controlled trial Setting Not reported, Germany Date of study Not reported. Duration of intervention 3 weeks with follow-up at 5 weeks
Participants	N = 60 (53 male/7 female) Mean age = 29 years **Inclusion criteria of the trial** • tinea pedis and cruris confirmed by KOH and culture **Exclusion criteria of the trial** • breastfeeding and pregnant women and women of childbearing age • treatment with other topical or systemic antifungal treatment • other local treatment • hypersensitivity for bifonazole or other imidazole derivatives Randomised N = 60 Withdrawals/losses to follow-up • no drop-outs or losses to follow-up Baseline data Diagnosis: Tinea pedis: bifonazole (17), croconazole (19) Tinea inguinalis: bifonazole (13), croconazole (11)
Interventions	**Intervention** • bifonazole (1%) cream once a day for 3 weeks (30) **Comparator** • croconazole (1%) cream once a day for 3 weeks (30)
Outcomes	Assessments (5): baseline, weeks 1, 2, 3 and 5 **Outcomes of the trial** (as reported)

Kuhlwein 1990 *(Continued)*

1. Clinical evaluation of signs and symptoms (itching, burning, pain, erythema, exudation, maceration, vesiculation, scaling, rhagades and keratoses)
2. Mycological evaluation (KOH and culture)
3. Efficacy: 3-point Likert scale#
4. Tolerance: 3-point Likert scale
5. Adverse events#
6. Relapse

Denotes outcomes prespecified for this review

Notes	We only included data from participants with tinea cruris. See Table 3

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote (page 1644): "..entsprechend einer Randomisierungsliste.." Comment: Probably done.
Allocation concealment (selection bias)	Unclear risk	The method used to conceal the allocation sequence, that is to determine whether intervention allocations could have been foreseen in advance of, or during, enrolment, was not reported. Comment: There was insufficient information to permit a clear judgement.
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote (page 1643-44): "double-blind" and "..in neutraler Verpackung.." Comment: Blinding was ensured we judged this as at a low risk of bias.
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Blinding of the outcomes assessors, key personnel, was ensured, and it was unlikely that the blinding could have been broken. Comment: We judged this as at a low risk of bias.
Incomplete outcome data (attrition bias) All outcomes	Low risk	No drop-outs reported. Comment: We judged this as at a low risk of bias.
Selective reporting (reporting bias)	Low risk	The protocol for the study was not available, but the prespecified outcomes and those mentioned in the methods section appeared to have been reported. Comment: We judged this as at a low risk of bias.
Other bias	High risk	One investigator was employed by Merz and Co. Comment: Merz and Co is the manufacturer of croconazole. A potential risk of bias cannot be excluded.

Lassus 1983

Methods	Randomised, double-blind, active-controlled trial Setting Department of Dermatology, University Central Hospital, Helsinki, Finland Date of study

Lassus 1983 *(Continued)*

	Not reported. Duration of intervention 4 weeks with follow-up at 6 and 12 weeks
Participants	N = 40 (31 male/9 female) Mean age = 43 years **Inclusion criteria of the trial** • dermatophytosis, confirmed by KOH and culture **Exclusion criteria of the trial** • not reported Randomised N = 40 Withdrawals/losses to follow-up • sulconazole: 1/20 adverse reaction • clotrimazole: 1/20 delayed visit, 1/20 adverse reaction Baseline data Site of infection: Toe webs: sulconazole (15), clotrimazole (13) Groin: sulconazole (5), clotrimazole (6) Plantar surface: sulconazole (0), clotrimazole (1)
Interventions	**Intervention** • sulconazole (1%) cream b.i.d. for 4 weeks (20) **Comparator** • clotrimazole (1%) cream b.i.d. for 4 weeks (20) No other topical or systemic treatments were allowed during the whole study period
Outcomes	Assessments (6): baseline, weeks 2, 3, 4, 6 and 12 **Outcomes of the trial** (as reported) 1. Clinical evaluation of signs and symptoms (erythema, itching, scaling, maceration, fissuring and vesiculation): 4-point Likert scale# 2. Mycological evaluation (KOH and culture) 3. Overall clinical improvement: 6-point Likert scale# 4. Relapse 5. Adverse events# Denotes outcomes prespecified for this review
Notes	We only included data on participants with tinea cruris. See Table 3

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote (page 196)""..were randomly allocated.."

Lassus 1983 *(Continued)*

		Comment: Insufficient detail was reported about the method used to generate the allocation sequence to allow a clear assessment of whether it would produce comparable groups.
Allocation concealment (selection bias)	Unclear risk	The method used to conceal the allocation sequence, that is to determine whether intervention allocations could have been foreseen in advance of, or during, enrolment, was not reported. Comment: There was insufficient information to permit a clear judgement.
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote (page 196): "The two test preparations were presented in tubes of identical appearance.." Comment: Blinding was ensured we judged this as at a low risk of bias.
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Blinding of the outcomes assessors, key personnel, was ensured, and it was unlikely that the blinding could have been broken. Comment: We judged this as at a low risk of bias.
Incomplete outcome data (attrition bias) All outcomes	Low risk	3/40 (1 sulconazole; 2 clotrimazole) not included in the analysis. Per-protocol analysis. Comment: Low and balanced number of drop-outs and although per-protocol analysis we judged this as at low risk of bias.
Selective reporting (reporting bias)	Low risk	The protocol for the study was not available, but the prespecified outcomes and those mentioned in the methods section appeared to have been reported. Comment: We judged this as at a low risk of bias.
Other bias	High risk	Quote (page 198): "The trial preparations were kindly provided by Syntex Research and the statistical analyses were performed by Lynn Shemanski, Dept of Biostatistics, Syntex Research" Comment: Syntex Research is the manufacturer of sulconazole and a potential risk of bias cannot be excluded.

Lassus 1984

Methods	Randomised, double-blind, active-controlled trial Setting Department of Dermatology and Venereology, University Central Hospital, Helsinki, Finland Date of study Not reported. Duration of intervention 4 weeks with follow-up at 10 weeks
Participants	N = 40 (30 male/10 female) Mean age = 38 years **Inclusion criteria of the trial** • participants with dermatophytoses, confirmed by KOH and culture **Exclusion criteria of the trial** • not reported

Lassus 1984 *(Continued)*

	Randomised N = 40 Withdrawals/losses to follow-up • 2/40; allergic reaction to econazole (1) and concomitant therapy for eczema in the sulconazole group (1) Baseline data Diagnosis: Tinea pedis: sulconazole (16), econazole (17) Tinea cruris: sulconazole (4), econazole (3)
Interventions	**Intervention** • sulconazole (1%) cream b.i.d. for 4 weeks **Comparator** • econazole (1%) cream b.i.d. for 4 weeks No other topical or systemic antifungal therapy was permitted during the study
Outcomes	Assessments (4): baseline, weeks 2, 4 and 10 **Outcomes of the trial** (as reported) 1. Mycological evaluation (KOH and culture) 2. Clinical evaluation of signs and symptoms (erythema, itching, scaling, maceration, vesiculation, and fissuring): 4-point Likert scale# 3. Overall clinical improvement 4. Relapse rate# Denotes outcomes prespecified for this review
Notes	We only include and report data on participants with tinea cruris. See Table 3

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote (page 595): "..was based on a predetermined randomization schedule.." Comment: Probably done.
Allocation concealment (selection bias)	Unclear risk	The method used to conceal the allocation sequence, that is to determine whether intervention allocations could have been foreseen in advance of, or during, enrolment, was not reported. Comment: There was insufficient information to permit a clear judgement.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote (page 595): "..double-blind.." Comment: The report did not provide sufficient detail about the measures used to blind study participants and personnel from knowledge of which intervention a participant received, to permit a clear judgement.
Blinding of outcome assessment (detection bias)	Unclear risk	Quote (page 595): "..double-blind.."

Lassus 1984 *(Continued)*

All outcomes		Comment: Uncertainty with the effectiveness of blinding of outcomes assessors (healthcare providers) during the study. Insufficient information to permit a clear judgement.
Incomplete outcome data (attrition bias) All outcomes	Low risk	2/40 were not included in the analysis, one from each group. Per-protocol analysis. Comment: Low and balanced number of drop-outs and although per-protocol analysis we judged this as at a low risk of bias.
Selective reporting (reporting bias)	Low risk	The protocol for the study was not available, but the prespecified outcomes and those mentioned in the methods section appeared to have been reported. Comment: We judged this as at a low risk of bias.
Other bias	High risk	One of the investigators was employed by Astra Syntex, the manufacturer and the trial preparations are provided by Syntex Research. Comment: A potential risk of bias cannot be excluded.

Lassus 1988

Methods	Randomised, double-blind, active-controlled study Setting Two centres, University Central Hospital, Helsinki, Finland and University Skin Clinic of the Westfälian Wilhelms University, Münster, Germany Date of study Not reported. Duration of intervention 21 days to follow-up at 28 days
Participants	N = 140 (102 male/36 female; 2 gender unreported) Mean age = 44, range 16-80 years **Inclusion criteria of the trial** • inflamed mycotic infections confirmed by culture examinations **Exclusion criteria of the trial** • concomitant therapy that might interfere with study results • concurrent medical condition that could complicate participation • topical antibiotic/antimycotic 2 weeks prior to study Randomised N = 140 Withdrawals/losses to follow-up • ciclopirox group (1/70), ciclopirox combination (1/70), not matching inclusion criteria • ciclopirox group (1/70) withdrew after 3 days Baseline data Causative pathogen: Candida (44), dermatophytes (94), unidentified (2)

Lassus 1988 *(Continued)*

	Affected areas: inguinal (31), anogenital (53), feet (77), hands (20), other (17) (some participants with several affected areas)
Interventions	**Intervention** • ciclopirox olamine (1%) cream b.i.d. for 21 days (70) **Comparator** • ciclopirox olamine (1%) - hydrocortisone acetate (1%) cream b.i.d. for 21 days (70)
Outcomes	Assessments (6): baseline, days 4, 7, 14, 21, 28 **Outcomes of the trial** (as reported) 1. Signs and symptoms (redness, swelling, scaling, pruritus): 5-point Likert scale# 2. Mean improvement 3. Culture 4. Adverse events# Denotes outcomes prespecified for this review
Notes	We only included data from participants with tinea corporis or cruris. Unclear how many inguinal were caused by dermatophytes or by other pathogens. See Table 3

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote (page 595): "..were randomly assigned..". Comment: Insufficient detail was reported about the method used to generate the allocation sequence to allow a clear assessment of whether it would produce comparable groups.
Allocation concealment (selection bias)	Unclear risk	The method used to conceal the allocation sequence, that is to determine whether intervention allocations could have been foreseen in advance of, or during, enrolment, was not reported. Comment: There was insufficient information to permit a clear judgement.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote (page 595): "..double-blind..". Comment: The report did not provide sufficient detail about the measures used to blind study participants and personnel from knowledge of which intervention a participant received, to permit a clear judgement.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote (page 595): "..double-blind..". Comment: Uncertainty with the effectiveness of blinding of outcomes assessors (participants/healthcare providers) during the study. Insufficient information to permit a clear judgement.
Incomplete outcome data (attrition bias) All outcomes	Low risk	Excluded from analysis (3/140): did not match the inclusion criteria (1) in each group; ciclopirox olamine group (1) withdrew after 3 treatment days. Per-protocol analysis. Comment: Although a per-protocol analysis, well balanced and low number of drop-outs judged at low risk of bias.
Selective reporting (reporting bias)	Low risk	The protocol for the study was not available, but the prespecified outcomes and those mentioned in the methods section appeared to have been reported.

Lassus 1988 *(Continued)*

		Comment: We judged this as at a low risk of bias.
Other bias	Low risk	The study appeared to be free of other forms of bias.

Lebwohl 1998

Methods	6 randomised, double-blind, vehicle-controlled trials Setting Multi-centre US and Europe Date of study Not reported. Duration of intervention 1 week
Participants	N = not reported Mean age = not reported **Inclusion criteria of the trial** • participants with tinea pedis and with tinea corporis/cruris **Exclusion criteria of the trial** • not reported Randomised N = unreported Withdrawals/losses to follow-up • not reported Baseline data Not reported
Interventions	**Intervention** • terbinafine (1%) solution or terbinafine (1%) gel for 1 week (unclear how many applications per day) **Comparator** • vehicle
Outcomes	Assessments: unclear **Outcomes of the trial** (as reported) 1. Clinical evaluation of signs and symptoms 2. Mycological evaluation (KOH and culture) 3. Adverse events# Denotes outcomes prespecified for this review
Notes	Poster, with very limited data reported. See Table 3
Risk of bias	

Lebwohl 1998 *(Continued)*

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote (page S237): "..randomized.." Comment: Insufficient detail was reported about the method used to generate the allocation sequence to allow a clear assessment of whether it would produce comparable groups.
Allocation concealment (selection bias)	Unclear risk	The method used to conceal the allocation sequence, that is to determine whether intervention allocations could have been foreseen in advance of, or during, enrolment, was not reported. Comment: There was insufficient information to permit a clear judgement.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote (page S237): "..double-blind..". Comment: The report did not provide sufficient detail about the measures used to blind study participants and personnel from knowledge of which intervention a participant received, to permit a clear judgement.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote (page 237): "..double-blind..". Comment: Uncertainty with the effectiveness of blinding of outcomes assessors (participants/healthcare providers) during the study. Insufficient information to permit a clear judgement.
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Abstract/poster; nothing reported. Comment: Insufficient information to permit a clear judgement.
Selective reporting (reporting bias)	Unclear risk	Very limited data reported. Comment: Insufficient information to permit a clear judgement.
Other bias	High risk	Investigators (2) employed by Novartis, the manufacturer of terbinafine. Comment: A potential risk of bias cannot be excluded.

Lebwohl 2001

Methods	Randomised, double-blind, vehicle-controlled study. Report includes 2 separate studies. See 'Notes'. Setting Multi-centre (3) in US Date of study Not reported. Duration of the intervention 1 week with follow-up to 4 weeks
Participants	N = 66 (35 male/17 female; 14 gender unreported). Mean age = 42 years (range 6-82) **Inclusion criteria of the trial** • > 5 years, clinical diagnosis tinea corporis/cruris, confirmed by positive KOH **Exclusion criteria of the trial** • pregnant and breastfeeding women

Lebwohl 2001 *(Continued)*

- antibacterial, antiviral 'and' or 'or' antihelmintic treatment 2 weeks prior to study
- unwillingness, inability to comply to requirements of the study
- concomitant non-dermatophyte infection
- radiation therapy or systemic therapy with cytostatics or immunosuppressive drugs

Randomised

N = 66

Delayed exclusions

- terbinafine group (0), vehicle group (2) due to negative baseline culture

Withdrawals/losses to follow-up

- 13/66 (20%) discontinued: terbinafine group (3), vehicle group (10)
- exacerbation: terbinafine group (0), vehicle group (1)
- treatment failures: terbinafine group (3), vehicle group (9)
- 26 presented at week 4 visit in terbinafine group, 16 in vehicle group

Baseline data

Nothing reported

Interventions	**Intervention** • terbinafine (1%) lotion once a day for 7 days (32) **Comparator** • vehicle lotion once day for 7 days (34)
Outcomes	Assessments (4): baseline, weeks 1, 2 and 4 **Outcomes of the trial** (as reported) 1. Clinical assessments 2. Mycological evaluation 3. Adverse events# Denotes outcomes prespecified for this review
Notes	The report includes 2 studies one of which evaluated participants with tinea pedis. We only include the study which comprised of participants with tinea corporis/cruris.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote (page 262): "..were randomized at a 1:1 ratio..". Comment: Insufficient detail was reported about the method used to generate the allocation sequence to allow a clear assessment of whether it would produce comparable groups.
Allocation concealment (selection bias)	Unclear risk	The method used to conceal the allocation sequence, that is to determine whether intervention allocations could have been foreseen in advance of, or during, enrolment, was not reported. Comment: There was insufficient information to permit a clear judgement.

Lebwohl 2001 *(Continued)*

Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote (page 261-2): "..double-blind.." and "..in identical 20 mL bottles.." Comment: The report provided sufficient detail about the measures used to blind study participants and personnel from knowledge of which intervention a participant received, to permit a clear judgement.
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote (page 261): "..double-blind..". Outcomes were investigator-assessed. Blinding of participants and key study personnel was ensured, and it is unlikely that the blinding could have been broken. Comment: We judged this as at a low risk of bias.
Incomplete outcome data (attrition bias) All outcomes	High risk	Delayed exclusion due to negative baseline culture (2) vehicle group; discontinued vehicle group due to treatment failure or exacerbation (13). Data analysis 52/66 (26 per group). Per-protocol analysis. Comment: We judged this as at a high risk of bias.
Selective reporting (reporting bias)	Low risk	The protocol for the study was not available, but the prespecified outcomes and those mentioned in the methods section appeared to have been reported. Comment: We judged this as at a low risk of bias.
Other bias	High risk	Quote (page 261 and 266): "Supported by Novartis Pharmaceutical Corporation, East Hanover, New Jersey". Investigators include employees of Novartis Pharmaceuticals Corporation. Comment: A potential risk of bias cannot be excluded.

Ledezma 1999

Methods	Randomised, active-controlled study Setting Not reported. Venezuela Date of study Not reported. Duration of intervention 1 week with follow-up to 60 days
Participants	N = 60 (60 male) Mean age = 20 years (18-24) **Inclusion criteria of the trial** • clinical diagnosis of tinea corporis, confirmed by mycology (KOH and culture) **Exclusion criteria of the trial** • no prior antifungal oral or systemic therapy Randomised N = 60 Withdrawals/losses to follow-up

Ledezma 1999 *(Continued)*

- 18/60 (30%) due to relocation (13), non-attendance at follow-up (5)
- ajoene group (6/31), terbinafine group (12/29)

Baseline data

Duration of infection in both groups ± 11 weeks

Interventions	**Intervention** • ajoene (0.6%) gel b.i.d. for 1 week (31) **Comparator** • terbinafine (1%) cream b.i.d. for 1 week (29)
Outcomes	Assessments (4): baseline, week 1, days 30 and 60 **Outcomes of the trial** (as reported) 1. Clinical evaluation of signs and symptoms (itching, burning, redness, weeping, scaling, pustulation): 4-point Likert scale# 2. Mycological evaluation (KOH and culture) Denotes outcomes prespecified for this review
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote (page 545): "The patients were distributed in two groups at random.." Comment: Insufficient detail was reported about the method used to generate the allocation sequence to allow a clear assessment of whether it would produce comparable groups.
Allocation concealment (selection bias)	Unclear risk	The method used to conceal the allocation sequence, that is to determine whether intervention allocations could have been foreseen in advance of, or during, enrolment, was not reported. Comment: There was insufficient information to permit a clear judgement.
Blinding of participants and personnel (performance bias) All outcomes	High risk	Quote (page 545): "ajoene..was distributed in 8 g portions in hinged lid polyethylene containers"....terbinafine was obtained from the local pharmacy in its commercial presentation and similarly distributed in 8 g portions. Its final presentation, as well as the quantity was the same as for the ajoene." Comment: Dissimilar nature of the interventions would not ensure adequate blinding of either participants or assessors.
Blinding of outcome assessment (detection bias) All outcomes	High risk	Outcomes were investigator assessed and the outcome measurement is likely to be influenced by the inadequate blinding of key study personnel. Comment: We judged this as at a high risk of bias.
Incomplete outcome data (attrition bias) All outcomes	High risk	Ajoene group (6/31), terbinafine group (12/29) due to reallocation to other distant army head quarters (13), non attendance at follow-up (5) Comment: Twice as many drop-outs in the terbinafine group. Per-protocol analysis

Ledezma 1999 *(Continued)*

		Comment: We judged this as at a high risk of bias.
Selective reporting (reporting bias)	Low risk	The protocol for the study was not available, but the prespecified outcomes and those mentioned in the methods section appeared to have been reported. Comment: We judged this as at a low risk of bias.
Other bias	Low risk	Quote (page 547): "This work was partially supported by a Research Grant from the Fundación de Desarollo de la Ciencia Tecnologia". Comment: We judged this as at low risk of bias.

Leiste 1989

Methods	Randomised, double-blind, active-controlled trial Setting Multi-centre (5) in Germany Date of study Not reported. Duration of the intervention 2-4 weeks with follow-up at 2-3 weeks after end of treatment
Participants	N = 100 (58 male/42 female) Mean age = 40, range 7-81 years **Inclusion criteria of the trial** • cutaneous mycoses produced by dermatophytes or other pathogenic fungi confirmed by KOH and culture **Exclusion criteria of the trial** • previous antimycotic treatment < 2 weeks prior to study entry • pregnant or breastfeeding women • participants with serious systemic and metabolic diseases • known hypersensitivity to imidazole derivatives or to topical treatments in general • non-compliancy Randomised N = 100 Withdrawals/losses to follow-up 4/100: • fenticonazole (2); adverse event (1), non-compliance (1) • naftifine (2); protocol violation (1), lost to follow-up (1) Baseline data Location: Hands: fenticonazole (7), naftifine (3) Feet: fenticonazole (23), naftifine (26) Hands and feet: fenticonazole (2), naftifine (0) Groin: fenticonazole (8), naftifine (5)

Leiste 1989 *(Continued)*

	Body: fenticonazole (10), naftifine (14) Armpit: fenticonazole (0), naftifine (2)
Interventions	**Intervention** • fenticonazole (2%) spray once daily for 2-4 weeks (50) **Comparator** • naftifine (1%) spray once daily for 2-4 weeks (50)
Outcomes	Assessments (5): baseline, weeks 1-4, and 2-3 weeks after end of therapy **Outcomes of the trial** (as reported) 1. Mycological evaluation (KOH and culture) 2. Clinical evaluation of sign and symptoms (itching, burning, pain, erythema, exudation, weeping, pustules, scaling, rhagades, keratosis): 5-point Likert scale# 3. Global evaluation: 5-point Likert scale# 4. Adverse events# Denotes outcomes prespecified for this review
Notes	We only considered data from participants with tinea corporis or cruris. Unclear how many of the infections of the groin and body were caused by dermatophytes or other pathogens. See Table 3

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote (page 569): "Patients were allocated at random into two equal groups" Comment: Insufficient detail was reported about the method used to generate the allocation sequence to allow a clear assessment of whether it would produce comparable groups.
Allocation concealment (selection bias)	Unclear risk	The method used to conceal the allocation sequence, that is to determine whether intervention allocations could have been foreseen in advance of, or during, enrolment, was not reported. Comment: There was insufficient information to permit a clear judgement.
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote (page 569): "Both drugs were supplied in identical containers" Comment: The report provided sufficient detail about the measures used to blind study participants and personnel from knowledge of which intervention a participant received, to permit a clear judgement.
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Outcomes were investigator-assessed as well as participant assessed. Blinding of participants and key study personnel was ensured, and it is unlikely that the blinding could have been broken. Comment: We judged this as at a low risk of bias.
Incomplete outcome data (attrition bias) All outcomes	Low risk	4/100: fenticonazole (2) due to adverse event (1) and non compliance (1), naftifine (2) due to protocol violation (1), and lost to follow-up (1). Per-protocol analysis. Comment: Low and balanced number of drop-outs at follow-up, and although per-protocol analysis considered to be at low risk of bias.

Leiste 1989 *(Continued)*

Selective reporting (reporting bias)	Low risk	The protocol for the study was not available, but the prespecified outcomes and those mentioned in the methods section appeared to have been reported. Comment: We judged this as at a low risk of bias.
Other bias	Low risk	The study appeared to be free of other forms of bias.

Lesher 1997

Methods	Randomised, double-blind, vehicle-controlled trial Setting Multi-centre (6), USA Date of study Not reported. Duration of intervention 2 weeks with follow-up to 4 weeks
Participants	N = 93 (75 male/1 female; 17 gender not reported) Mean age = 37, range 16-70 years **Inclusion criteria of the trial** • men and women > 18 years with at least two of three principal signs and symptoms of tinea cruris:erythema, scaling, and pruritus; Scored 0 to 3, (0 = absent/none; 1 = mild/barely perceptible; 3 = severe/marked/intense). Participants with a combined score ≥ 5 were included • mycological confirmation (KOH and culture) **Exclusion criteria of the trial** • not reported Randomised N = 93 Delayed exclusions • butenafine (9), vehicle (6) were excluded of negative baseline cultures (14) or protocol violation (1) Withdrawals/losses to follow-up • 2/93 did not return for at least one post baseline visit Baseline data Median baseline sign/symptom score: butenafine (7), vehicle (8)
Interventions	**Intervention** • butenafine hydrochloride cream once daily for 2 weeks (46) **Comparator** • vehicle once daily for 2 weeks (45)
Outcomes	Assessments (4): baseline, days 7, 14 and 42 **Outcomes of the trial** (as reported)

Lesher 1997 *(Continued)*

1. Clinical evaluation of signs (erythema, scaling, maceration, papules, vesiculation), symptoms (pruritus): 4-point Likert scale#
2. Investigator's global assessment: 7-point Likert Scale#
3. Mycological evaluation (KOH and culture)
4. Participant's perception: 5-point Likert scale#
5. Adverse events (tolerability)

Denotes outcomes prespecified for this review

Notes

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote (page S20): "... randomized, vehicle-controlled,.. trial." Comment: Insufficient detail was reported about the method used to generate the allocation sequence to allow a clear assessment of whether it would produce comparable groups.
Allocation concealment (selection bias)	Unclear risk	The method used to conceal the allocation sequence, that is to determine whether intervention allocations could have been foreseen in advance of, or during, enrolment, was not reported. Comment: There was insufficient information to permit a clear judgement.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote (page S20): "..double-blind..". Comment: The report did not provide sufficient detail about the measures used to blind study participants and personnel from knowledge of which intervention a participant received, to permit a clear judgement.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote (page S20): "..double-blind..". Comment: Uncertainty with the effectiveness of blinding of outcomes assessors (participants/healthcare providers) during the study. Insufficient information to permit a clear judgement.
Incomplete outcome data (attrition bias) All outcomes	Low risk	Losses after randomisation due to negative baseline culture (14) or protocol violation (1): butenafine (9/46), vehicle (6/45). Losses at follow-up: 2 did not return for at least one post baseline visit (unclear which groups) Per-protocol analysis. Comment: Entry criterion (culture specimen) measured prior to randomisation. The delayed exclusions are well-balanced between groups, no attrition bias between the groups. See ICH Expert Working Group 1998. Low and balanced number of drop-outs at follow-up, and although per-protocol analysis considered to be at a low risk of bias.
Selective reporting (reporting bias)	Low risk	The protocol for the study was not available, but the prespecified outcomes and those mentioned in the methods section appeared to have been reported. Comment: We judged this as at a low risk of bias.
Other bias	Low risk	The study appeared to be free of other forms of bias.

Li 2003

Methods	Randomised, investigator-blinded, active-controlled study Setting Multi-centre (2) sites, China Date of study Not reported. Duration of intervention 4 weeks
Participants	N = 155 (gender unreported) Age range = 18-65 years **Inclusion criteria of the trial** • tinea corporis /cruris confirmed by direct microscopic evaluation **Exclusion criteria of the trial** • not reported Randomised N = 155 Withdrawals/losses to follow-up • 2/155, one in each group discontinued due to adverse events, limited information Baseline data Nothing reported
Interventions	**Intervention** • amorolfine cream (0.25%) applied for unknown length of time, frequency unreported **Comparator** • bifonazole cream (1%) applied for unknown length of time, frequency unreported
Outcomes	Assessments (at least 2): baseline and week 4 **Outcomes of the trial** (as reported) 1. Clinical evaluation (sum of erythema, scaling /desquamation, pruritus, vesicles, fissures /maceration): 4-point Likert scale# 2. Mycological evaluation (KOH and culture) 3. Clinical improvement 4. Adverse events# 5. Routine laboratory tests Denotes outcomes prespecified for this review
Notes	Abstract, limited data are reported. See Table 3

Risk of bias

Bias	Authors' judgement	Support for judgement

Li 2003 *(Continued)*

Random sequence generation (selection bias)	Unclear risk	Quote (page 319): "..randomized.." Comment: Insufficient detail was reported about the method used to generate the allocation sequence to allow a clear assessment of whether it would produce comparable groups.
Allocation concealment (selection bias)	Unclear risk	The method used to conceal the allocation sequence, that is to determine whether intervention allocations could have been foreseen in advance of, or during, enrolment, was not reported. Comment: There was insufficient information to permit a clear judgement.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote (page 319): "..investigator-blind..". Comment: The report did not provide sufficient detail about the measures used to blind personnel from knowledge of which intervention a participant received, to permit a clear judgement.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote (page 237): "..investigator-blind..". Comment: Uncertainty with the effectiveness of blinding of outcomes assessors (healthcare providers) during the study. Insufficient information to permit a clear judgement.
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Unclear, abstract and limited data are reported. Investigators report that analysis was per-protocol. Comment: Insufficient information to permit a clear judgement.
Selective reporting (reporting bias)	Unclear risk	Very limited data reported. Comment: Insufficient information to permit a clear judgement.
Other bias	Unclear risk	Comment: Insufficient information to permit a clear judgement.

Li 2004

Methods	Randomised, double-blind, active-controlled trial Setting Multi-centre in China Date of study Not reported. Duration of intervention 3 weeks with 2 weeks follow-up
Participants	N = 135 (gender unreported) Mean age = 33 years **Inclusion criteria of the trial** • tinea cruris, tinea corporis, tinea manuum 'and' or 'or' tinea pedis confirmed by KOH • 18-65 years **Exclusion criteria of the trial** • additional severe bacterial infection • other severe dermatitis which could interfere with the therapy

Li 2004 *(Continued)*

- allergy to medicine
- severe heart, liver, kidney disease, diabetes or mental illness
- long-term use of glucocorticoid or immunosuppressant
- systemic use of anti-fungal medicines in previous 4 weeks or anti-fungal cream during previous week
- pregnant or lactating women

Randomised

N = 135

Withdrawals/losses to follow-up

- no drop-outs

Baseline data

Tinea cruris/corporis: econazole nitrate (1%) + triamcinolone acetonide (0.1%) (43), econazole nitrate (1%) (42)

Mycological confirmation of infection in tinea cruris/corporis: econazole + triamcinolone (41), econazole (41)

Tinea pedis and manuum: econazole nitrate (1%) + triamcinolone acetonide (0.1%) (26), econazole nitrate (1%) (24)

Interventions	**Intervention** • econazole nitrate (1%) + triamcinolone acetonide (0.1%) cream b.i.d. for 2-3 weeks (69) **Comparator** • econazole nitrate 1% ointment b.i.d. for 2-3 weeks (66)
Outcomes	Assessments (3), baseline, weeks 3 and 5 **Outcomes of the trial** (as reported) 1. Clinical evaluation of signs and symptoms (erythema, papules, vesicles, maceration, erosion, scales and pruritus): 4-point Likert scale# 2. Clinical efficacy: 4-point Likert scale# 3. Mycological evaluation (KOH, culture and fungal identification) 4. Adverse events# Denotes outcomes prespecified for this review
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote (page 52): "randomized" Comment: Insufficient detail was reported about the method used to generate the allocation sequence to allow a clear assessment of whether it would produce comparable groups.
Allocation concealment (selection bias)	Unclear risk	The method used to conceal the allocation sequence, that is to determine whether intervention allocations could have been foreseen in advance of, or during, enrolment, was not reported. Comment: There was insufficient information to permit a clear judgement.

Li 2004 *(Continued)*

Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote (page 52): "double-blind". Comment: The report did not provide sufficient detail about the measures used to blind study participants and personnel from knowledge of which intervention a participant received, to permit a clear judgement.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote (page 52): "..double-blind..". Comment: Uncertainty with the effectiveness of blinding of outcomes assessors (participants/healthcare providers) during the study. Insufficient information to permit a clear judgement.
Incomplete outcome data (attrition bias) All outcomes	Low risk	No drop-outs reported. Intention-to-treat analysis. Comment: We judged this as at a low risk of bias
Selective reporting (reporting bias)	Low risk	The protocol for the study was not available, but the prespecified outcomes and those mentioned in the methods section appeared to have been reported. Comment: We judged this as at a low risk of bias.
Other bias	Unclear risk	The medication was provided by a pharmaceutical company. Comment: A potential risk of bias cannot be excluded.

Li 2006

Methods	Randomised, double-blind, active-controlled trial Setting Multi-centre in China Date of study Not reported. Duration of intervention 2-4 weeks with 2 weeks follow-up
Participants	N = 234 (gender unreported) Mean age = 34 years for tinea corporis/cruris and 22 years for tinea pedis **Inclusion criteria of the trial** • tinea corporis/cruris or tinea pedis confirmed by KOH **Exclusion criteria of the trial** • no moccasin type tinea pedis • severe bacterial infection or other dermatitis which could interfere with the therapy • allergy to allylamine • long-term use of glucocorticoid or immunosuppressant • systemic use of anti-fungal medicines in previous 3 months or anti-fungal cream in previous weeks • pregnant or lactating women Randomised N = 234 Withdrawals/losses to follow-up

Li 2006 *(Continued)*

	• no drop-outs Baseline data Tinea corporis/cruris: butenafine (58), bifonazole (59) Tinea pedis: butenafine (58), bifonazole (59)
Interventions	**Intervention** • butenafine hydrochloride (1%) cream once daily, 2 weeks for tinea cruris and corporis and 4 weeks for tinea pedis (116) **Comparator** • bifonazole (1%) cream once daily, 2 weeks for tinea cruris and corporis and 4 weeks for tinea pedis (118)
Outcomes	Assessments (4): baseline, during treatment, end of treatment and 2 weeks after treatment **Outcomes of the trial** (as reported) 1. Clinical evaluation of signs and symptoms (erythema, papules, vesicles, maceration, erosion, scales and pruritus): 4-point Likert scale# 2. Clinical efficacy: 4-point Likert scale# 3. Laboratory tests 4. Mycological evaluation (KOH, culture, and fungal identification) 5. Adverse events# Denotes outcomes prespecified for this review
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote (page 471): "randomized" "SAS- Program". Comment: Probably done.
Allocation concealment (selection bias)	Unclear risk	The method used to conceal the allocation sequence, that is to determine whether intervention allocations could have been foreseen in advance of, or during, enrolment, was not reported. Comment: There was insufficient information to permit a clear judgement.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote (page 571): "double-blind". Comment: The report did not provide sufficient detail about the measures used to blind study participants and personnel from knowledge of which intervention a participant received, to permit a clear judgement.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote (page 571): "..double-blind..". Comment: Uncertainty with the effectiveness of blinding of outcomes assessors (participants/healthcare providers) during the study. Insufficient information to permit a clear judgement.
Incomplete outcome data (attrition bias) All outcomes	Low risk	There were no drop-outs. Intention-to-treat analysis. Comment: We judged this as at a low risk of bias.

Li 2006 *(Continued)*

Selective reporting (reporting bias)	Low risk	The protocol for the study was not available, but the prespecified outcomes and those mentioned in the methods section appeared to have been reported. Comment: We judged this as at a low risk of bias.
Other bias	Low risk	The study appears to be free of other forms of bias.

Luciani 1988

Methods	Randomised, double-blind, active-controlled trial Setting Dermatology Clinic University of Verona, Italy Date of study Not reported. Duration of intervention up to 4 weeks with follow-up at 8 weeks
Participants	N = 49 (34 male/15 female) Mean age = 43, range 11-73 years **Inclusion criteria of the trial** • participants with dermatomycosis **Exclusion criteria of the trial** • not reported Randomised N = 49 Withdrawals/losses to follow-up • econazole (3/24), bifonazole (4/25) reasons unreported Baseline data Tinea cruris: econazole (7), bifonazole (4) Tinea corporis: econazole (3), bifonazole (3) Tinea pedis: econazole (15), bifonazole (18)
Interventions	**Intervention** • econazole (1%) cream b.i.d. for up to 4 weeks (24) **Comparator** • bifonazole (1%) cream b.i.d. for up to 4 weeks (25)
Outcomes	Assessments (3): baseline, weeks 4 and 8 **Outcomes of the trial** (as reported) 1. Mycological evaluation (KOH and culture) 2. Clinical evaluation of signs and symptoms: 5-point Likert scale# 3. Overal clinical efficacy: 4-point Likert scale#

Luciani 1988 *(Continued)*

4. Tolerability: 3-point Likert scale

Denotes outcomes prespecified for this review

Notes	We only included data for participants with tinea corporis and cruris. See Table 3

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote (page LIII): "..assegnati per randomizzazione.." Comment: Insufficient detail was reported about the method used to generate the allocation sequence to allow a clear assessment of whether it would produce comparable groups.
Allocation concealment (selection bias)	Unclear risk	The method used to conceal the allocation sequence, that is to determine whether intervention allocations could have been foreseen in advance of, or during, enrolment, was not reported. Comment: There was insufficient information to permit a clear judgement.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote (page LIII): "..doppia cecita.." Comment: The report did not provide sufficient detail about the specific measures used to blind study participants and personnel from knowledge of which intervention a participant received, to permit a clear judgement.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote (page LIII): "..doppia cecita.." Comment: Uncertainty with the effectiveness of blinding of outcomes assessors (healthcare providers and participants) during the study. Insufficient information to permit a clear judgement.
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	7/49 (14%): econazole (3/24), bifonazole (4/25) not included in analysis. Per-protocol analysis. Comment: Balanced and moderate number of drop-outs poses an unclear risk of bias.
Selective reporting (reporting bias)	Low risk	The protocol for the study was not available, but the prespecified outcomes and those mentioned in the methods section appeared to have been reported. Comment: We judged this as at a low risk of bias.
Other bias	Low risk	The study appears to be free of other forms of bias.

Macasaet 1991

Methods	Randomised, double-blind, placebo- (excipient) controlled trial Setting Manila Doctors Hospital, Manila, Philippines Date of study Not reported. Duration of intervention and follow-up 14 days
Participants	N = 53 (33 male/20 female)

Macasaet 1991 *(Continued)*

Age range 1–70, mean 30 years

Inclusion criteria of the trial

- diagnosis of tinea corporis, clinically by detecting of hyphae and KOH mount (participants withdrawn if culture at the beginning of treatment subsequently negative)

Exclusion criteria of the trial

- infection/superinfection of the skin requiring additional treatment
- systemic antifungals prior 30 days
- systemic steroids 'and' or 'or' topical antifungals prior 14 days
- topical steroids during prior 7 days

Randomised

N = 53

Withdrawals/losses to follow-up

- none

Baseline data

Duration of disease: < 1 week to 156 weeks (median 10 weeks)
"The placebo and active treatment groups were homogeneous with regard to demographic factors and clinical form".

Interventions	**Intervention** • griseofulvin (1%) solution once daily for 14 days (26) **Comparator** • vehicle solution once daily for 14 days (27)
Outcomes	Assessments (3): baseline, days 7, 14 **Outcomes of the trial** (as reported) 1. Clinical assessment of symptoms 2. Mycological evaluation (culture) 3. Overall response to treatment: 4-point Likert scale# 4. Adverse events# Denotes outcomes prespecified for this review
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote (page 110): "fifty three patients.. were recruited...twenty seven were randomly chosen to receive the placebo....". Comment: Insufficient detail was reported about the method used to generate the allocation sequence to allow a clear assessment of whether it would produce comparable groups.

Macasaet 1991 *(Continued)*

Allocation concealment (selection bias)	Unclear risk	The method used to conceal the allocation sequence, that is to determine whether intervention allocations could have been foreseen in advance of, or during, enrolment, was not reported. Comment: There was insufficient information to permit a clear judgement.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote (page 110): "..double-blind.." Comment: The report did not provide sufficient detail about the measures used to blind study participants and personnel from knowledge of which intervention a participant received, to permit a clear judgement.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote (page 110): "..double-blind.." Comment: Uncertainty with the effectiveness of blinding of outcomes assessors (participants/healthcare providers) during the study. Insufficient information to permit a clear judgement.
Incomplete outcome data (attrition bias) All outcomes	Low risk	No drop-outs reported. Data limited but reported for all participants. Comment: We judged this as at a low risk of bias.
Selective reporting (reporting bias)	Low risk	The protocol for the study was not available, but the prespecified outcomes and those mentioned in the methods section appeared to have been reported. Comment: We judged this as at a low risk of bias.
Other bias	Unclear risk	Affiliations of one investigator "Tillotts Pharma Henlow Beds UK", unclear if this presents a potential risk of bias.

Machado-Pinto 1987

Methods	Randomised, active-controlled trial Setting Not reported, Brazil Date of study Not reported. Duration of intervention 40 days
Participants	N = 28 (13 male/15 female) Age range = 10-70 years **Inclusion criteria of the trial** • tinea pedis, tinea corporis, tinea cruris or tinea manuum confirmed by KOH **Exclusion criteria of the trial** • not reported Randomised N = 28 Withdrawals/losses to follow-up • no losses to follow-up reported

Machado-Pinto 1987 *(Continued)*

	Baseline data Diagnosis: Tinea corporis: oxiconazole (6), tolnaftate (4) Tinea cruris: oxiconazole (4), tolnaftate (5) Tinea manuum: oxiconazole (1), tolnaftate (1) Tinea pedis: oxiconazole (3), tolnaftate (4)
Interventions	**Intervention** • oxiconazole (1%) cream b.i.d. for 40 days (14) **Comparator** • tolnaftate (1%) cream b.i.d. for 40 days (14)
Outcomes	Assessments (3): baseline, days 20 and 40 **Outcomes of the trial** (as reported) 1. Clinical evaluation of signs and symptoms (pain, pruritus, induration, oedema, desquamation, crusts, erythema, lichenification): 4-point Likert scale# 2. Clinical efficacy 3. Mycological evaluation (KOH)# Denotes outcomes prespecified for this review
Notes	Study has 2 phases, second phase is an RCT.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote (page 381): "Os 28 pacientes foram distribuídos aleatoriamente em dois grupos". Comment: Insufficient detail was reported about the method used to generate the allocation sequence to allow a clear assessment of whether it would produce comparable groups.
Allocation concealment (selection bias)	Unclear risk	The method used to conceal the allocation sequence, that is to determine whether intervention allocations could have been foreseen in advance of, or during, enrolment, was not reported. Comment: There was insufficient information to permit a clear judgement.
Blinding of participants and personnel (performance bias) All outcomes	High risk	No blinding reported. Comment: The outcome was likely to be influenced by the lack of blinding.
Blinding of outcome assessment (detection bias) All outcomes	High risk	No blinding reported. Comment: The outcome measurement was likely to be influenced by the lack of blinding.
Incomplete outcome data (attrition bias)	Low risk	No losses to follow-up, all data are reported. Comment: We judged this as at a low risk of bias.

Machado-Pinto 1987 *(Continued)*

All outcomes

Selective reporting (reporting bias)	Low risk	The protocol for the study was not available, but the prespecified outcomes and those mentioned in the methods section appeared to have been reported. Comment: We judged this as at a low risk of bias.
Other bias	Low risk	The study appears to be free of other forms of bias.

McVie 1986

Methods	Randomised, double-blind, active-controlled study Setting Multi-centre (4), UK Date of study Not reported. Duration of intervention 4 weeks with 4 weeks follow-up
Participants	N = 83 (75 male/8 female) Mean age = unreported **Inclusion criteria of the trial** • clinical diagnosis of tinea pedis, tinea cruris or tinea corporis confirmed by KOH and culture **Exclusion criteria of the trial** • use of griseofulvin < 8 weeks prior to study entry • use of topical antifungals < 2 weeks prior to study entry Randomised N = 83 Withdrawals/losses to follow-up • 5/83 were lost to follow-up Baseline data Localisation of infection: Feet: sulconazole (17), clotrimazole (19) Groin: sulconazole (22), clotrimazole (18) Trunk: sulconazole (3), clotrimazole (4)
Interventions	**Intervention** • sulconazole nitrate (1%) cream b.i.d. for 4 weeks (37) **Comparator** • clotrimazole (1%) cream b.i.d. for 4 weeks (41)
Outcomes	Assessment (3): baseline, weeks 4 and 8

McVie 1986 *(Continued)*

Outcomes of the trial (as reported)

1. Clinical evaluation of sign and symptoms (erythema, maceration, scaling and itching): 4-point Likert scale#
2. Mycological examination (KOH and culture)
3. Adverse events#
4. Relapse

Denotes outcomes prespecified for this review

Notes	We only included data of participants with tinea cruris and corporis. See Table 3

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote (page 614): "..patients were randomly allocated.." and "A restricted randomization in blocks of ten was employed at each centre." Comment: Probably done.
Allocation concealment (selection bias)	Unclear risk	The method used to conceal the allocation sequence, that is to determine whether intervention allocations could have been foreseen in advance of, or during, enrolment, was not reported. Comment: There was insufficient information to permit a clear judgement.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote (page 614): "..double-blind..". Comment: The report did not provide sufficient detail about the measures used to blind study participants and personnel from knowledge of which intervention a participant received, to permit a clear judgement.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote (page 614): "..double-blind..". Comment: Uncertainty with the effectiveness of blinding of outcomes assessors (healthcare providers) during the study. Insufficient information to permit a clear judgement.
Incomplete outcome data (attrition bias) All outcomes	Low risk	5/83 (6%) lost to follow-up. Per-protocol analysis. Comment: Low number of drop-outs and although per-protocol analysis considered to be at a low risk of bias.
Selective reporting (reporting bias)	Low risk	The protocol for the study was not available, but the prespecified outcomes and those mentioned in the methods section appeared to have been reported. Comment: We judged this as at a low risk of bias.
Other bias	High risk	Quote (page 617): "The authors wish to thank Nigel Levinson, Syntex Pharmaceuticals Ltd, for help and support with the study." Comment: The investigators did not confirm what support was provided, but one of the interventions under investigation was sulconazole (Syntex Pharmaceuticals), thus a potential risk of bias cannot be excluded.

Meinicke 1987

Methods	Randomised, double-blind, active-controlled, within-patient comparison

Meinicke 1987 *(Continued)*

	Setting Practice and Dermatological-Venereological Laboratory Grünwald, Germany Date of study Not reported. Duration of intervention up to 8 weeks
Participants	N = 175 (125 male/48 female: 2 gender unreported) Mean age = 38 years **Inclusion criteria of the trial** • participants with dermatomycosis confirmed by KOH and culture **Exclusion criteria of the trial** • not reported Randomised N = 175 Withdrawals/losses to follow-up • 21/175 (12%) 'did not satisfy the inclusion criteria' (unclear if this was at enrolment or after randomisation), failed follow-up visits, suffering from onychomycosis Baseline data Localisation: Arms: miconazole (2), naftifine once daily (1), naftifine b.i.d. (1) Trunk: miconazole (7), naftifine once daily (5), naftifine b.i.d. (8) Legs: miconazole (4), naftifine once daily (5), naftifine b.i.d. (3) Feet: miconazole (23), naftifine once daily (30), naftifine b.i.d. (24) Hands: miconazole (3), naftifine once daily (4), naftifine b.i.d. (5) Groin: miconazole (23), naftifine once daily (21), naftifine b.i.d. (17) Buttocks: miconazole (4), naftifine once daily (4), naftifine b.i.d. (5) Other: miconazole (0), naftifine once daily (3), naftifine b.i.d. (6)
Interventions	**Intervention** • miconazole (2%) cream b.i.d. for up to 8 weeks (59) **Comparator** • naftifine (1%) cream once daily for up to 8 weeks (59) **Comparator 2** • naftifine (1%) cream b.i.d. for up to 8 weeks (57)
Outcomes	**Outcomes of the trial** (as reported) 1. Clinical evaluation of sign and symptoms (erythema, pruritus, desquamation, blisters/pustules, infiltration, exudation and maceration): 6-point Likert scale# 2. Overall assessment of efficacy 3. Mycological evaluation (KOH and culture) Denotes outcomes prespecified for this review
Notes	Unclear how many participants matched the inclusion criteria (sites reported but unclear which pathogens at each site). See Table 3
Risk of bias	

Meinicke 1987 *(Continued)*

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote (page 99): "..were allocated in randomized sequence.." Comment: Insufficient detail was reported about the method used to generate the allocation sequence to allow a clear assessment of whether it would produce comparable groups.
Allocation concealment (selection bias)	Unclear risk	The method used to conceal the allocation sequence, that is to determine whether intervention allocations could have been foreseen in advance of, or during, enrolment, was not reported. Comment: There was insufficient information to permit a clear judgement.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote (page 99): ".on a double-blind basis." Comment: The report did not provide sufficient detail about the measures used to blind study participants and personnel from knowledge of which intervention a participant received, to permit a clear judgement.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Comment: Uncertainty with the effectiveness of blinding of outcomes assessors (healthcare providers) during the study. Insufficient information to permit a clear judgement.
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	21/175 (12%) 'did not satisfy the inclusion criteria' (unclear if this was at enrolment or after randomisation), failed follow-up visits, suffering from onychomycosis. Comment: Insufficient information to assess whether an important risk of bias exists.
Selective reporting (reporting bias)	Low risk	The protocol for the study was not available, but the prespecified outcomes and those mentioned in the methods section appeared to have been reported. Comment: We judged this as at a low risk of bias.
Other bias	Low risk	The study appears to be free of other forms of bias.

Mertens 1976

Methods	Randomised, double-blind, active-controlled trial Setting Not reported. Date of study Not reported. Duration of the intervention 4 weeks
Participants	N = 63 (35 male/28 female) Age range = 12-60 years **Inclusion criteria of the trial** • participants with inflamed infections of bacterial or mycotic origin **Exclusion criteria of the trial**

Mertens 1976 *(Continued)*

- not reported

Randomised

N = 63

Withdrawals/losses to follow-up

- no drop-outs reported

Baseline data

Localisation:

Arm/hand: Daktacort (5), miconazole (4), hydrocortisone (3)

Trunk: Daktacort (0), miconazole (1), hydrocortisone (2)

Groin: Daktacort (0), miconazole (2), hydrocortisone (1)

Leg/feet: Daktacort (15), miconazole (13), hydrocortisone (13)

Interventions	**Intervention** • Daktacort b.i.d. for 4 weeks (21) **Comparator 1** • miconazole (2%) b.i.d. for 4 weeks (20) **Comparator 2** • hydrocortisone (1%) b.i.d. for 4 weeks (22) No other treatment was permitted.
Outcomes	Assessments (3): baseline, weeks 1 and 4 **Outcomes of the trial** (as reported) 1. Clinical evaluation of sign and symptoms (pruritus, burning, erythema, inflamed appearance): 3-point Likert scale# 2. Bacterial/Mycological evaluation (KOH and culture) 3. Overall treatment effect: 5-point Likert scale# Denotes outcomes prespecified for this review
Notes	We only included data from participants with tinea cruris 'and' or 'or' corporis. Unclear how many of the infections of the groin and body were caused by dermatophytes or other pathogens. See Table 3

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote (page 229): "..their content being randomly.. determined.." Comment: Insufficient detail was reported about the method used to generate the allocation sequence to allow a clear assessment of whether it would produce comparable groups.
Allocation concealment (selection bias)	Unclear risk	The method used to conceal the allocation sequence, that is to determine whether intervention allocations could have been foreseen in advance of, or during, enrolment, was not reported.

Mertens 1976 *(Continued)*

		Comment: There was insufficient information to permit a clear judgement.
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote (page 229): "..all creams were identical in appearance.." Comment: Blinding was ensured we judged this as at a low risk of bias.
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Blinding of the outcomes assessors, key personnel, was ensured, and it was unlikely that the blinding could have been broken. Comment: We judged this as at a low risk of bias.
Incomplete outcome data (attrition bias) All outcomes	Low risk	No drop-outs reported. Comment: We judged this as at low risk of bias.
Selective reporting (reporting bias)	Low risk	The protocol for the study was not available, but the prespecified outcomes and those mentioned in the methods section appeared to have been reported. Comment: We judged this as at a low risk of bias.
Other bias	Unclear risk	Quote (page 229): "The double-blind medication was kindly provided by Janssen Pharmaceutics, Beerse, Belgium". Comment: A potential risk of bias cannot be excluded.

Millikan 1988

Methods	Randomised, double-blind, active-controlled study Setting Multi-centre, USA Date of study Not reported. Duration of intervention 4 weeks with follow-up to 6 weeks
Participants	N = 126 (78 male/26 female; 22 gender unreported) Age range (15-81), mean age 42 years **Inclusion criteria of the trial** • clinical diagnosis of tinea cruris, tinea corporis, or both • confirmed by KOH and culture **Exclusion criteria of the trial** • hypersensitivity to any of the components of the test medications • any other fungal infection • any systemic condition predisposing participants to fungal infections • any skin disease affecting the evaluation of tinea cruris/tinea corporis • use of topical antifungals or corticosteroids < 7 days prior to study • use of systemic corticosteroids < 14 days prior to study • use of systemic antifungals < 30 days prior to study Randomised

Millikan 1988 *(Continued)*

N = 126

Delayed exclusions, including withdrawals/losses to follow-up

- naftifine (8/64), econazole (14/62) due to protocol violations, mainly negative cultures

Baseline data

Tinea cruris: naftifine (35), econazole (31)
Tinea corporis: naftifine (21), econazole (15)
Tinea cruris/corporis: naftifine (0), econazole (2)

Interventions	**Intervention** • naftifine cream (1%) b.i.d. for 4 weeks (64) **Comparator** • econazole nitrate cream (1%) b.i.d. for 4 weeks (62) Concomitant systemic or topical therapy with antibiotics, antifungals, or corticosteroids not permitted.
Outcomes	Assessments (6): baseline, weeks 1, 2, 3, 4 and 6 **Outcomes of the trial** (as reported) 1. Overall clinical condition: 4-point Likert scale# 2. Signs and symptoms (erythema, scaling, vesiculation, fissuring, pustulation, papulation, maceration,crusting, pruritus, pain, and burning): 4-point Likert scale# 3. Mycological evaluation (KOH and culture) 4. Adverse events# Denotes outcomes prespecified for this review
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote (page 54): "..were assigned to treatment with naftifine or econazole according to a computer-generated randomization list." Comment: Probably done.
Allocation concealment (selection bias)	Low risk	The "web based" method used to generate the sequence would appear to indicate that intervention allocations could not have been foreseen in advance of, or during, enrolment. Comment: This was probably done.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote (page 54): "..double-blind..". Comment: The report did not provide sufficient detail about the measures used to blind study participants and personnel from knowledge of which intervention a participant received, to permit a clear judgement.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote (page 54): "..double-blind..". Comment: Uncertainty with the effectiveness of blinding of outcomes assessors (healthcare providers) during the study. Insufficient information to permit a clear judgement.

Millikan 1988 *(Continued)*

Incomplete outcome data (attrition bias) All outcomes	High risk	Missing outcome data: 22/126 (17.5%): Naftifine (8/64), econazole (14/62) protocol violations, mainly due to negative cultures. Unclear how many were delayed exclusions. Per-protocol analysis. Comment: We judged this as at a high risk of bias.
Selective reporting (reporting bias)	Low risk	The protocol for the study was not available, but the prespecified outcomes and those mentioned in the methods section appeared to have been reported. Comment: We judged this as at a low risk of bias.
Other bias	Low risk	The study appeared to be free of other forms of bias.

Millikan 1990

Methods	Randomised, double-blind, vehicle-controlled trial Setting Department of Dermatology, Tulane University School of Medicine, USA Date of study Not reported. Duration of intervention 2 weeks with follow-up to 4 weeks
Participants	N = 30 (all male) Age range 18-42, mean age 29 years **Inclusion criteria of the trial** • men 18 to 65 years with clinical and microscopic evidence of tinea cruris, subsequently confirmed by culture **Exclusion criteria of the trial** • concomitant yeast or bacterial infections of the skin • systemic antifungal drugs < 4 weeks prior to study • topical antifungal therapy < 2 weeks prior to study Randomised N = 30 Delayed exclusions • terbinafine (5/15), vehicle (3/15) due to negative pretreatment cultures Withdrawals/losses to follow-up • terbinafine (1/15), vehicle (3/15) inability to comply with study visit schedule Baseline data Duration in weeks (median): terbinafine (24), vehicle (6)
Interventions	**Intervention** • terbinafine 1% cream b.i.d. for 2 weeks (15) **Comparator**

Millikan 1990 *(Continued)*

- vehicle cream b.i.d. for 2 weeks (15)

Outcomes	Assessments (4): baseline, weeks 1, 2 and 4 **Outcomes of the trial** (as reported) 1. Clinical evaluation signs and symptoms (i.e. erythema, pustules,desquamation, incrustation, vesiculation, exudation, and pruritus): 4-point Likert scale# 2. Mycological evaluation (KOH and culture) 3. Therapeutic response: 4-point Likert scale# 4. Haematologic and biochemical blood tests 5. Local irritation or redness, burning or stinging on application of medication, and dryness: 3-point Likert scale# 6. Other adverse events: 3-point Likert scale# Denotes outcomes prespecified for this review
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote (page 795): "..were randomly assigned.." Comment: Insufficient detail was reported about the method used to generate the allocation sequence to allow a clear assessment of whether it would produce comparable groups.
Allocation concealment (selection bias)	Unclear risk	The method used to conceal the allocation sequence, that is to determine whether intervention allocations could have been foreseen in advance of, or during, enrolment, was not reported. Comment: There was insufficient information to permit a clear judgement.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote (page 795): "..double-blind..". Comment: The report did not provide sufficient detail about the measures used to blind study participants and personnel from knowledge of which intervention a participant received, to permit a clear judgement.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote (page 795): "..double-blind..". Comment: Uncertainty with the effectiveness of blinding of outcomes assessors (participants/healthcare providers) during the study. Insufficient information to permit a clear judgement.
Incomplete outcome data (attrition bias) All outcomes	High risk	Losses after randomisation due to negative baseline culture: 8/30 (27%): terbinafine group (5/15), vehicle group (3/15). Failed to attend for follow-up: 4/30 (13%): terbinafine group (1/15), vehicle group (3/15; 20%). 30 randomised, 18 analysed. Comment: Entry criterion (culture specimen) measured prior to randomisation. The delayed exclusions well-balanced between groups, no attrition bias between the groups. See ICH Expert Working Group 1998. Losses to follow-up in the vehicle group 3/12 (25%) after excluding post randomisation losses, combined with the per-protocol analysis we judged this at a high risk of bias.

Millikan 1990 *(Continued)*

Selective reporting (reporting bias)	Low risk	The protocol for the study was not available, but the prespecified outcomes and those mentioned in the methods section appeared to have been reported. Comment: We judged this as at a low risk of bias.
Other bias	High risk	Baseline imbalance in disease duration substantially higher in terbinafine treated group (67%) than in placebo group (22%). Comment: The baseline imbalance is likely to have an impact on the effect estimate.

Miura 1979

Methods	Randomised, double-blind, active- and placebo-controlled trial Setting Multi-centre (16) in Japan Date of study June-Oktober 1977. Duration of intervention 2 weeks
Participants	N = 655 (389 male/266 female) Age range from < 9 to > 70 years **Inclusion criteria of the trial** • participants with tinea pedis and manus, tinea corporis, tinea cruris, tinea versicolor or intertriginous candidiasis confirmed by KOH **Exclusion criteria of the trial** • very large areas affected Randomised N = 655 Withdrawals/losses to follow-up • 57/655 (9%); 22/219 in econazole group, 19/217 in clotrimazole group and 16/219 in placebo group • 16 due to side effects unclear which groups Baseline data Diagnosis: Tinea pedis and manus: econazole (64), clotrimazole (64), placebo (64) Tinea cruris: econazole (48, 34 in available case analysis), clotrimazole (48, 34 in available case analysis), placebo (48, 37 in available case analysis) Tinea corporis: econazole (48, 41 in available case analysis), clotrimazole (48, 39 in available case analysis), placebo (48, 45 in available case analysis) Tinea versicolor: econazole (48), clotrimazole (48), placebo (48) Intertriginous candidiasis: econazole (48), clotrimazole (48), placebo (48)
Interventions	**Intervention** • econazole cream b.i.d. for 2 weeks (219)

Miura 1979 *(Continued)*

	Comparator 1 • clotrimazole cream b.i.d. for 2 weeks (217) **Comparator 2** • placebo cream b.i.d. for 2 weeks (219)
Outcomes	**Outcomes of the trial** (as reported) 1. Clinical evaluation (global improvement): 5-point Likert scale# 2. Mycological evaluation 3. Adverse events# 4. Utility Denotes outcomes prespecified for this review
Notes	We only included data from participants with tinea cruris 'and' or 'or' corporis.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote (from translation): "..randomised..". Comment: Insufficient detail was reported about the method used to generate the allocation sequence to allow a clear assessment of whether it would produce comparable groups.
Allocation concealment (selection bias)	Unclear risk	The method used to conceal the allocation sequence, that is to determine whether intervention allocations could have been foreseen in advance of, or during, enrolment, was not reported. Comment: There was insufficient information to permit a clear judgement.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote (page 83): "..double-blind..". Comment: The report did not provide sufficient detail about the measures used to blind study participants and personnel from knowledge of which intervention a participant received, to permit a clear judgement.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote (page 83): "..double-blind..". Comment: Uncertainty with the effectiveness of blinding of outcomes assessors (participants/healthcare providers) during the study. Insufficient information to permit a clear judgement.
Incomplete outcome data (attrition bias) All outcomes	Low risk	57/655 (9%); 22/219 in econazole group, 19/217 in clotrimazole group and 16/219 in placebo group. Per-protocol analysis. Comment: Low and balanced number of drop-outs at follow-up, and although per-protocol analysis considered to be at a low risk of bias.
Selective reporting (reporting bias)	Low risk	The protocol for the study was not available, but the prespecified outcomes and those mentioned in the methods section appeared to have been reported. Comment: We judged this as at a low risk of bias.
Other bias	Low risk	Quote (page 84): "Samples were supplied by Otsuka Pharmaceuticals Co., Ltd . Comment: We judged this as at a low risk of bias.

Nolting 1980

Methods	Randomised, double-blind, active-controlled trial Setting Department of Dermatomicrobiology of University Hospital, Münster, Germany Date of study Not reported. Duration of intervention 2 weeks
Participants	N = 100 (65 male/35 female) Age range = from < 11 up to > 70 years **Inclusion criteria of the trial** • inflammatory dermatomycoses confirmed by KOH and culture **Exclusion criteria of the trial** • not reported Randomised N = 100 Withdrawals/losses to follow-up • no losses to follow-up Baseline data All localisations are mentioned and all causative species, but not per treatment arm
Interventions	**Intervention** • isoconazole nitrate (1%) combined with diflucortolone valerate (0.1%) cream b.i.d. for 14 days **Comparator** • isoconazole nitrate (1%) cream b.i.d. for 14 days
Outcomes	Assessments (3): baseline, weeks 1 and 2 **Outcomes of the trial** (as reported) 1. Clinical evaluation: 4-point Likert scale# 2. Mycological evaluation (KOH and culture) Denotes outcomes prespecified for this review
Notes	Number of participants with tinea cruris 'and' or 'or' corporis in each treatment arm unclear. Old study no contact details available. See Table 3

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote (page 701):"..randomisierter Zuordnung.."

Nolting 1980 *(Continued)*

		Comment: Insufficient detail was reported about the method used to generate the allocation sequence to allow a clear assessment of whether it would produce comparable groups.
Allocation concealment (selection bias)	Unclear risk	The method used to conceal the allocation sequence, that is to determine whether intervention allocations could have been foreseen in advance of, or during, enrolment, was not reported. Comment: There was insufficient information to permit a clear judgement.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote (page 701): "..Doppelblindstudie.." Comment: The report did not provide sufficient detail about the measures used to blind study participants and personnel from knowledge of which intervention a participant received, to permit a clear judgement.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Comment: Uncertainty with the effectiveness of blinding of outcomes assessors (participants/healthcare providers) during the study. Insufficient information to permit a clear judgement.
Incomplete outcome data (attrition bias) All outcomes	Low risk	No losses to follow-up Comment: We judged this as at a low risk of bias
Selective reporting (reporting bias)	Low risk	The protocol for the study was not available, but the prespecified outcomes and those mentioned in the methods section appeared to have been reported. Comment: We judged this as at a low risk of bias.
Other bias	High risk	One investigator was employed by Schering AG. Comment: A potential risk of bias cannot be excluded.

Nolting 1985

Methods	Randomised, double-blind, active-controlled, within-participant comparison trial Setting Dermatology Clinic, Westfälischen Wilhelms-Universität, Münster, Germany Date of study Not reported. Duration of intervention up to 12 weeks, with follow-up at 16 weeks
Participants	N = 94 (age and gender unreported) **Inclusion criteria of the trial** • severe dermatomycosis confirmed by KOH and culture **Exclusion criteria of the trial** • onychomycosis Randomised N = 94 Withdrawals/losses to follow-up

Nolting 1985 *(Continued)*

- 4/94, 2 in each group

Baseline data

Location:

Head/Face: naftifine (9), econazole (3)

Trunk: naftifine (19), econazole (27)

Extremities: naftifine (30), econazole (35)

Interventions	**Intervention** • naftifine (1%) cream b.i.d. for up to 12 weeks (47) **Comparator** • econazole (1%) cream b.i.d. for up to 12 weeks (47)
Outcomes	Assessments (7): baseline, weeks 2, 4, 6, 8, 12 and 16 **Outcomes of the trial** (as reported) 1. Clinical evaluation of signs and symptoms (vesicles, pustules, papules, granuloma, erythema, scaling, pruritus, maceration, exudation and infiltration): 6-point Likert scale# 2. Mycological evaluation (KOH and culture) 3. Adverse events: 4-point Likert scale# Denotes outcomes prespecified for this review
Notes	Tinea cruris and corporis possibly included, but unreported. Old trial. See Table 3

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote (page 70): "..die Zuteiling erfolgte zufallsbedingt.." Comment: Insufficient detail was reported about the method used to generate the allocation sequence to allow a clear assessment of whether it would produce comparable groups.
Allocation concealment (selection bias)	Unclear risk	The method used to conceal the allocation sequence, that is to determine whether intervention allocations could have been foreseen in advance of, or during, enrolment, was not reported. Comment: There was insufficient information to permit a clear judgement.
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote (page 70): "..doppelblind.." and ".. beide in 20 g Tuben verpackt waren und identisches Aussehen hatten" Comment: The report provided sufficient detail about the measures used to blind study participants and personnel from knowledge of which intervention a participant received, to permit a clear judgement.
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Outcomes were investigator-assessed as well as participant-assessed. Blinding of participants and key study personnel was ensured, and it is unlikely that the blinding could have been broken. Comment: We judged this as at a low risk of bias.

Nolting 1985 *(Continued)*

Incomplete outcome data (attrition bias) All outcomes	Low risk	4/94, 2 in each group. Comment: Balanced and low number of drop-outs, we judged this as at low risk of bias
Selective reporting (reporting bias)	Low risk	The protocol for the study was not available, but the prespecified outcomes and those mentioned in the methods section appeared to have been reported. Comment: We judged this as at a low risk of bias.
Other bias	Low risk	The study appears to be free of other forms of bias

Nolting 1992

Methods	Randomised, double-blind, active-controlled trial Setting Multicentre (4) West Germany Date of study January to December 1985. Duration of intervention 2-6 weeks
Participants	N = 232 (166 male/57 female; 9 gender unreported) Mean age = 36-42 years **Inclusion criteria of the trial** • > 16 years with diagnosis of dermatomycosis confirmed by KOH and culture **Exclusion criteria of the trial** • pregnant women and participants with a bacterial infection, onychomycosis or trichomycosis • use of other antifungals < 2 weeks prior to study entry or requirement for other antimycotic agents during the trial Randomised N =232 Withdrawals/losses to follow-up Lost to follow-up: 9/232 (4%) 0.125% amorolfine (1), 0.25% amorolfine (2), 0.5% amorolfine (3), bifonazole (3) Baseline data Location of the dermatomycosis: Foot: 0.125% amorolfine (28), 0.25% amorolfine (24), 0.5% amorolfine (25), bifonazole (27) Large body area: 0.125% amorolfine (15), 0.25% amorolfine (17), 0.5% amorolfine (17), bifonazole (14) Skin fold: 0.125% amorolfine (13), 0.25% amorolfine (13), 0.5% amorolfine (12), bifonazole (11) Other: 0.125% amorolfine (1), 0.25% amorolfine (2), 0.5% amorolfine (1), bifonazole (3)
Interventions	**Intervention**

Nolting 1992 *(Continued)*

- amorolfine (0.125%) cream once a day during 2-6 weeks (57)

Comparator 1

- amorolfine (0.25%) cream once a day during 2-6 weeks (56)

Comparator 2

- amorolfine (0.5%) cream once a day during 2-6 weeks (55)

Comparator 3

- bifonazole (1%) cream once a day during 2-6 weeks (56)

Outcomes	Assessments: baseline, weekly up to 6 weeks and 1-3 weeks after end of treatment **Outcomes of the trial** (as reported) 1. Mycological evaluations (KOH and culture) 2. Clinical evaluation of signs and symptoms: 4-point Likert scale# 3. Size of target lesion: 4-point Likert scale 4. Overall assessment: 3-point Likert scale# 5. Adverse events# 6. Relapse Denotes outcomes prespecified for this review
Notes	We only included data on tinea corporis and cruris. Unclear how many of the infections of the groin and body were caused by dermatophytes or other pathogens. See Table 3

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote (page 56): "..was randomly allocated..". Comment: Insufficient detail was reported about the method used to generate the allocation sequence to allow a clear assessment of whether it would produce comparable groups.
Allocation concealment (selection bias)	Unclear risk	The method used to conceal the allocation sequence, that is to determine whether intervention allocations could have been foreseen in advance of, or during, enrolment, was not reported. Comment: There was insufficient information to permit a clear judgement.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote (page 56): "..double-blind..". Comment: The report did not provide sufficient detail about the measures used to blind study participants and personnel from knowledge of which intervention a participant received, to permit a clear judgement.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote (page 56): "..double-blind..". Comment: Uncertainty with the effectiveness of blinding of outcomes assessors (healthcare providers and participants) during the study. Insufficient information to permit a clear judgement.
Incomplete outcome data (attrition bias) All outcomes	Low risk	9/232 (4%) were lost to follow-up; 0.125% amorolfine (1), 0.25% amorolfine (2), 0.5% amorolfine (3), bifonazole (3). Per-protocol analysis.

Nolting 1992 *(Continued)*

		Comment: Low and balanced number of drop-outs at follow-up, and although per-protocol analysis considered to be at a low risk of bias.
Selective reporting (reporting bias)	Low risk	The protocol for the study was not available, but the prespecified outcomes and those mentioned in the methods section appeared to have been reported. Comment: We judged this as at a low risk of bias.
Other bias	High risk	Three of the investigators were employed by the Clinical Research Department, F.Hoffmann-La Roche Ltd, Basel, Switzerland, the manufacturer of amorolfine. Comment: A potential risk of bias cannot be excluded.

Nuñez 1985

Methods	Randomised, double-blind, active-controlled study Setting Not reported, Costa Rica Date of study Not reported. Duration of intervention 3 weeks with follow-up to 5 weeks
Participants	N = 42 (32 male/10 female) Age range = 2-64, mean age 14 years **Inclusion criteria of the trial** • clinical diagnosis of tinea pedis, tinea faciei, tinea cruris/corporis confirmed by KOH **Exclusion criteria of the trial** • griseofulvin or other antifungal use < 1 week prior to study • pityriasis versicolor, tinea capitis, onychomycosis • participants with unstable diabetes • evidence of impaired immune function • chronic moccasin type tinea pedis lasting > 6 months Randomised N = 42 Withdrawals/losses to follow-up • sulconazole (0/21), econazole (2/21) lost to follow-up Baseline data Diagnosis: Tinea cruris: sulconazole (14), econazole (14) Tinea corporis: sulconazole (5), econazole (4) Tinea faciei: sulconazole (1), econazole (2) Tinea pedis: sulconazole (1), econazole (1)

Nuñez 1985 *(Continued)*

Interventions	**Intervention** • sulconazole nitrate 1% cream b.i.d. for 3 weeks (21) **Comparator** • econazole nitrate 1% cream b.i.d. for 3 weeks (21)
Outcomes	Assessment (6): baseline, weeks 1, 2, 3, 4 and 5 **Outcomes of the trial** (as reported) 1. Clinical evaluation of signs and symptoms (erythema, scales, itchiness, maceration, vesicles, pustules, and fissures): 4-point Likert scale# 2. Mycological evaluation (KOH and culture) 3. Overall clinical improvement: 4-point Likert scale# 4. Adverse events# 5. Relapse Denotes outcomes prespecified for this review
Notes	We only included participants with tinea corporis or cruris. See Table 3

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote (page 113): "..were assigned randomly..". Comment: Insufficient detail was reported about the method used to generate the allocation sequence to allow a clear assessment of whether it would produce comparable groups.
Allocation concealment (selection bias)	Unclear risk	The method used to conceal the allocation sequence, that is to determine whether intervention allocations could have been foreseen in advance of, or during, enrolment, was not reported. Comment: There was insufficient information to permit a clear judgement.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote (page 113): "..double-blind..". Comment: The report did not provide sufficient detail about the measures used to blind study participants and personnel from knowledge of which intervention a participant received, to permit a clear judgement.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote (page 113): "..double-blind..". Comment: Uncertainty with the effectiveness of blinding of outcomes assessors (healthcare providers) during the study. Insufficient information to permit a clear judgement.
Incomplete outcome data (attrition bias) All outcomes	Low risk	Econazole group (2/42) lost to follow-up, per-protocol analysis. Comment: Low number of drop-outs, we judged this as at low risk of bias.
Selective reporting (reporting bias)	High risk	Overall clinical improvement a pre-specified outcome was not reported. Comment: We judged this as at a high risk of bias.
Other bias	Low risk	The study appears to be free from other forms of bias.

Oladele 2010

Methods	Randomised, placebo-controlled study Setting Prison clinic, Nigeria Date of study April-May 2008. Duration of intervention 4 weeks
Participants	N = 33 (all male) Age range 20-60 years **Inclusion criteria of the trial** • participants with obvious skin infections **Exclusion criteria of the trial** • not reported Randomised N = 33 Withdrawals/losses to follow-up 6/33 discharged or out for court hearing: S. Alata group (2/19), placebo group 4/14 Baseline data Tinea corporis: Senna Alata soap (5), placebo soap (1) Tinea versicolor: Senna Alata soap (12), placebo soap (9) Other infections: Senna Alata soap (2), placebo soap (4)
Interventions	**Intervention** • Senna Alata soap used for body washing b.i.d. for 4 weeks (19) **Comparator** • placebo soap used for body washing b.i.d. for 4 weeks (14) No other treatment/medication for the lesions allowed .
Outcomes	Assessments (5): baseline, weeks 1, 2, 3 and 4 **Outcomes of the trial** (as reported) 1. Clinical examination 2. KOH# Denotes outcomes prespecified for this review
Notes	We only included participants with tinea corporis or cruris. Data available only for 6 participants with tinea corporis (5 in active treatment group and 1 in placebo group).
Risk of bias	

Oladele 2010 *(Continued)*

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote (page 98): "..randomly distributed into.." Comment: Insufficient detail was reported about the method used to generate the allocation sequence to allow a clear assessment of whether it would produce comparable groups. After email communication with investigators: Block (24) randomisation was used. Comment: This was probably done.
Allocation concealment (selection bias)	Low risk	The method used to conceal the allocation sequence, that is to determine whether intervention allocations could have been foreseen in advance of, or during, enrolment, was not reported. Comment: There was insufficient information to permit a clear judgement. After email communication with investigators: " blocks of random numbers....coded" Comment: Probably done.
Blinding of participants and personnel (performance bias) All outcomes	Low risk	The report did not describe any measures used to blind study participants and personnel from knowledge of which intervention a participant received. Comment: Insufficient detail reported. After email communication with investigators: Drug packaging was the same. Comment: Probably done.
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Method of blinding unreported. After email communication with investigators: Drug packaging was the same. Comment: Probably done.
Incomplete outcome data (attrition bias) All outcomes	High risk	6/33 (18%) due to discharged or out for court hearing. Given the high attrition rate, the per-protocol analysis of these data is likely to inflate the effect estimate, and, consequently, it may raise concerns about the reliability of the data as reported. Comment: We judged this as at a high risk of bias.
Selective reporting (reporting bias)	Low risk	The protocol for the study was not available, but the prespecified outcomes and those mentioned in the methods section appeared to have been reported. Comment: We judged this as at a low risk of bias.
Other bias	Low risk	The study appears to be free from other forms of bias.

Pariser 1995

Methods	Randomised, single-blinded, active-controlled study Setting Multi-centre (10), USA

Pariser 1995 *(Continued)*

	Date of study Not reported. Duration of intervention 2 weeks with follow-up to 4 weeks
Participants	N = 260 (age and gender unreported) **Inclusion criteria of the trial** • > 18 years of age with clinical and laboratory evidence of tinea cruris **Exclusion criteria of the trial** • use of systemic and topical anthelmintic, antifungal, or corticosteroid therapy < 1 month prior to study • immunosuppressive medication or radiation therapy < 3 months prior to study • antihistamines or any investigational drug < 30 days prior to study • presence of yeast or bacterial infection • systemic fungal infection, diabetes mellitus not controlled by diet alone, allergy to the study medication • history of noncompliance to treatment regimens • pregnant 'and' or 'or' lactating women, or of child-bearing potential and not using contraception • culture taken at baseline proved to be negative for dermatophytes (after 14 days of incubation) Randomised N = 260 Withdrawals/losses to follow-up • clotrimazole (1) did not return after first visit • 61/260 excluded from efficacy analysis because of negative baseline mycology (unclear how many), entry criteria violation, concomitant medication, or lost to follow-up • total of 62/260 (24%) not included in efficacy analysis • 93 in clotrimazole/betamethasone group attended day 14 visit, 99 in ketoconazole group Baseline data All had moderate-to-severe tinea cruris
Interventions	**Intervention** • clotrimazole (1%) with betamethasone dipropionate (0.05%) cream b.i.d. for 2 weeks (95) **Comparator** • ketoconazole (2%) cream b.i.d. for 2 weeks (103) Concomitant use of other medications that might have affected the study outcome was prohibited
Outcomes	Assessments (7): baseline, days 1, 2 , 3, 8, 14 and 29 **Outcomes of the trial** (as reported) 1. Investigator rated sign and symptoms (erythema, maceration, scaling, vesicles/papules/pustules, pruritus, and burning/stinging: 4-point Likert scale# 2. Treatment response: 6-point Likert scale# 3. Mycological evaluation (KOH and culture) 4. Participant assessment of symptom severity: 4-point Likert scale# 5. Participant's satisfaction: 7-point Likert scale# 6. Adverse events# Denotes outcomes prespecified for this review

Pariser 1995 *(Continued)*

Notes

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote (page 173): "..were randomly assigned to receive". Comment: Insufficient detail was reported about the method used to generate the allocation sequence to allow a clear assessment of whether it would produce comparable groups.
Allocation concealment (selection bias)	Unclear risk	The method used to conceal the allocation sequence, that is to determine whether intervention allocations could have been foreseen in advance of, or during, enrolment, was not reported. Comment: There was insufficient information to permit a clear judgement.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote (page 174): reported as "investigator-blinded". but participants not blinded. Comment: We judged this as at unclear risk of bias.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote (page 174): "investigator-blinded". Participants were not blinded and unclear if blinding of investigator was effective. Comment: We judged this as at unclear risk of bias.
Incomplete outcome data (attrition bias) All outcomes	High risk	62/260 (24%) excluded from efficacy analysis, unclear how many from each group. Per-protocol analysis. Comment: We judged this as at a high risk of bias.
Selective reporting (reporting bias)	High risk	Minimal data presented on the participant reported outcomes and participants satisfaction a key outcome in the trial is not addressed at all. Comment: We judged this at high risk of bias.
Other bias	Unclear risk	Quote (page 176):"This work was supported by a grant from Schering Laboratories, Kenilworth, NJ 07033, USA." Comment: It was unclear what support other than a grant was provided to the study investigators. Although the investigators did not clarify precisely what support was provided, a potential risk of bias cannot be excluded.

Parish 2011

Methods	Randomised, double-blind, vehicle-controlled study Setting Multi-centre (19), USA Date of study Sept 2008-August 2009. Duration of intervention 2 weeks with follow-up to 4 weeks
Participants	N = 334 (282 male/52 female) Mean age = 47 years

Parish 2011 *(Continued)*

Inclusion criteria of the trial

- ≥12 years of age with a clinical diagnosis of tinea cruris confirmed by KOH and culture
- absence of clinically significant disease that could interfere with interpretation of the results
- ability of the participants to understand the requirements of the study plus willingness to comply with them
- received prior antifungal, corticosteroid, or antibacterial therapies within the previous 30 days of treatment were required to undergo a 30-day washout period prior to entering the trial

Exclusion criteria of the trial

- any life-threatening condition within the last six months
- clinically significant abnormal laboratory or physical findings
- known hypersensitivity to the study drug or its components
- recent history of alcohol or drug abuse
- uncontrolled diabetes
- haemodialysis or chronic ambulatory peritoneal dialysis
- atopic or contact dermatitis at the study site
- severe dermatophytoses
- mucocutaneous candidiasis
- bacterial skin infection

Randomised

N = 334

Delayed exclusions:

- naftifine group (91/166), vehicle group (97/168) due to negative baseline culture

Withdrawals/losses to follow-up

- naftifine group (22/166), vehicle group (27/168), due to early discontinuation (AE, lost to follow-up, other reasons)

Baseline data

No differences between the groups regarding age/gender, ethnic background

Interventions	**Intervention** • naftifine (2%) cream once a day for 14 days (166) **Comparator** • vehicle once a day for 14 days (168)
Outcomes	Assessments (3): baseline weeks 2 and 4 **Outcomes of the trial** (as reported) 1. Mycological evaluation (KOH and culture) 2. Clinical manifestations of severity (erythema, scaling, and pruritus): 4-point Likert scale# 3. Adverse events# 4. Changes from baseline in clinical status 5. Laboratory tests Complete cure, treatment effectiveness, mycological cure, clinical cure, and clinical success were based on 1 and 2 Denotes outcomes prespecified for this review

Parish 2011 *(Continued)*

Notes	See http://www.naftin.com/prescribing-information.pdf

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote (page 1143): "..randomly assigned.." Comment: Insufficient detail was reported to allow a clear assessment. After e-mail contact: "a blocked unstratified randomization schedule was generated using SAS version 9.1.3 by an unblinded statistician and programmer who are not otherwise involved in the study" Comment: Probably done.
Allocation concealment (selection bias)	Low risk	The method used to conceal the allocation sequence, was not reported. After e-mail contact: "only two copies of the randomization schedule with study medication assignment were generated. One copy remained with the clinical packaging records at the labelling facility and the other was maintained in a locked, fireproof cabinet by PharmaNet. Randomization occurred at visit 1/day 1 through the PharmaNet IWRS system. Sites never received the randomization schedule at any point during the trial". Comment: Probably done.
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote (page 1142): "..double-blind..". Comment: The report did not provide sufficient detail , to permit a clear judgement. After e-mail contact: "All study drug was supplied in 60 gram tubes for topical administration. Each tube and box of study medication was labelled with a double-blind 2-part label to identify study number, carton number, application instructions, and proper storage. The tubes for the active product as well as the vehicle looked identical". Comment: Probably done.
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote (page 1142): "..double-blind..". Comment: Insufficient information to permit a clear judgement. After e-mail contact: "All study drug was supplied in 60 gram tubes for topical administration. Each tube and box of study medication was labelled with a double-blind 2-part label to identify study number, carton number, application instructions, and proper storage. The tubes for the active product as well as the vehicle looked identical". Comment: Probably done.
Incomplete outcome data (attrition bias) All outcomes	Low risk	Losses after randomisation due to negative baseline culture: naftifine group (91/166), vehicle group (97/168) = 188/334 (56%). These were not included in the analysis Further losses: naftifine group (22/166), vehicle group (27/168), due to early discontinuation (AE, lost to follow-up, other reasons). These were included in the efficacy analyses based on LOCF. 334 randomised 146 analysed.

Parish 2011 *(Continued)*

		Entry criterion (culture specimen) measured prior to randomisation. The delayed exclusions are well-balanced between groups, no attrition bias between the groups. See ICH Expert Working Group 1998. The further losses to follow-up were included in an Intention-to-treat analysis. We judged this to be at a low risk of bias.
Selective reporting (reporting bias)	Low risk	The protocol for the study was not available, but the prespecified outcomes and those mentioned in the methods section appeared to have been reported. Comment: We judged this as at a low risk of bias.
Other bias	High risk	Quote (page 1146): "Joy Willard RN, BSN of Merz Pharmaceuticals, LLC provided project management of this study which was sponsored by Merz Pharmaceuticals LLC." and "E. Avakian, B. Hardas, E. Pappert, S. Plaum, A. Fleischer, and B. Olayinka are employees of Merz Pharmaceuticals, LLC. Comment: We judged this as at a high risk of bias.

Qadripur 1984

Methods	Randomised, double-blind, active-controlled study Setting Dermatology clinic in Göttingen, Germany Date of study Not reported. Duration of intervention 4 weeks with follow-up to 8 weeks
Participants	N = 32 (gender distribution unclear) Age range 24-69 years **Inclusion criteria of the trial** • adults with diagnosis of tinea pedis or cruris confirmed by KOH **Exclusion criteria of the trial** • onychomycosis, candidiasis, tinea manuum, tinea corporis, tinea capitis, tinea versicolor Randomised N = 32 Withdrawals/losses to follow-up • none Baseline data No baseline difference regarding age, gender, disease duration, location of infection, and causative fungus tinea pedis (19), tinea cruris (13)
Interventions	**Intervention** • sulconazole (1%) cream plus sulconazole powder twice daily for 4 weeks (14) **Comparator**

Qadripur 1984 *(Continued)*

	• econazole (1%) cream plus econazole powder twice daily for 4 weeks (18) No other topical or systemic antifungal treatment was allowed during the study
Outcomes	Assessments (6): baseline, weeks 1, 2, 3, 4, 8 **Outcomes of the trial** (as reported) 1. Mycological evaluation (KOH and culture) 2. Evaluation of sign and symptoms (erythema, scaling, itching, maceration, vesiculation, fissuring and pustulation): 4-point Likert scale# 3. Overall clinical improvement: 5-point Likert scale# 4. Participants comments about pleasant/unpleasant symptoms 5. Adverse events: 3-point Likert scale# 6. Relapse rate# Denotes outcomes prespecified for this review
Notes	No separate data for tinea pedis and cruris. See Table 3

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote (page 754): "..predetermined randomisation schedule.." Comment: Insufficient detail was reported about the method used to generate the allocation sequence to allow a clear assessment of whether it would produce comparable groups.
Allocation concealment (selection bias)	Unclear risk	The method used to conceal the allocation sequence, that is to determine whether intervention allocations could have been foreseen in advance of, or during, enrolment, was not reported. Comment: There was insufficient information to permit a clear judgement.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote (page 753): "..double-blind..". Comment: The report did not provide sufficient detail about the measures used to blind study participants and personnel from knowledge of which intervention a participant received, to permit a clear judgement.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote (page 753): "..double-blind..". Comment: Uncertainty with the effectiveness of blinding of outcomes assessors (participants/healthcare providers) during the study. Insufficient information to permit a clear judgement.
Incomplete outcome data (attrition bias) All outcomes	Low risk	No drop-outs. Full data-set analysis. Comment: We judged this at a low risk of bias.
Selective reporting (reporting bias)	Unclear risk	Participant's perception of drug acceptability was a pre-specified albeit ill-defined outcome which was not addressed. Comment: We judged this as at unclear risk of bias.
Other bias	Low risk	The study appears to be free from other forms of bias.

Ramam 2003

Methods	Randomised, active-controlled study Setting Dermatology department of All India Institute of Medical Sciences, New Dehli, India Date of study March-November 2000. Duration of the intervention weeks with follow-up to 8 weeks
Participants	N = 75 (20 male/22 female; 33 gender unreported) Mean age = 30 years **Inclusion criteria of the trial** • > 18 years with clinical evidence of tinea cruris 'and' or 'or' tinea corporis confirmed by KOH test • symptoms and signs of erythema, scaling and pruritus were scored on a scale of 1 (nil) to 3 (severe). Patients were eligible for the study if they had a combined score of at least 5 • positive culture was not a pre-requisite for inclusion in the study **Exclusion criteria of the trial** • pregnant and lactating women • history or clinical evidence of severe cardiac, pulmonary, gastrointestinal, renal, hepatic or neurological disease and uncontrolled diabetes mellitus • known hypersensitivity to allylamine/benzylamine agents • treatment with systemic antifungal agents <1 month prior to study • itraconazole in the previous 6 months • systemic antibiotics in the previous 2 weeks • corticosteroids or immunosuppressants in the past 6 weeks • any investigational drug in the previous 3 months • participants with contact dermatitis, atopic dermatitis, psoriasis or any other disease that would interfere with the evaluation of the study results Randomised N = 75 Withdrawals/losses to follow-up • butenafine group 14/37 (37.8%), clotrimazole group 9/38 (23.7%) were lost to follow-up • butenafine group 1/37 due to car accident, clotrimazole group 1/38 excluded due to adverse event • butenafine group 4/37, clotrimazole group 4/38 did not return for follow-up after end of study • butenafine group 15/37, clotrimazole group 10/38 not included in analysis Baseline data Diagnosis: Tinea cruris: butenafine group (4), clotrimazole group (7) Tinea corporis: butenafine group (17), clotrimazole group (17) Both: butenafine group (1), clotrimazole group (4) Remainder unreported
Interventions	**Intervention** • butenafine (1%) once daily for 2 weeks followed by 2 weeks vehicle twice a day (37)

Ramam 2003 *(Continued)*

	Comparator • clotrimazole (1%) b.i.d. for 4 weeks (38)
Outcomes	Assessments (5): baseline, weeks 1, 2, 4 and 8 **Outcomes of the trial** (as reported) 1. Signs and symptoms (erythema, scaling, pustules, vesiculation, maceration, papules, and pruritus): 4-point Likert scale# 2. Mycological evaluation (KOH and culture) 3. Laboratory tests 4. Adverse events# Denotes outcomes prespecified for this review
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote (page 155): "patients were randomly assigned to receive butenafine or clotrimazole cream in a double-blind fashion in blocks of 10 patients". Comment: Probably done.
Allocation concealment (selection bias)	Unclear risk	The method used to conceal the allocation sequence, that is to determine whether intervention allocations could have been foreseen in advance of, or during, enrolment, was not reported. Comment: There was insufficient information to permit a clear judgement.
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote (page 155): "The medication consisted of 2 identical tubes of 5 gm labelled "Morning" and "Evening" Comment: Probably done.
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Blinding of outcomes assessors, key personnel and participants was ensured, and it was unlikely that the blinding could have been broken. Comment: We judged this as at a low risk of bias.
Incomplete outcome data (attrition bias) All outcomes	High risk	25/75 (33.3%) were not included in the analysis. Per-protocol analysis. Comment: Judged as at a high risk of bias.
Selective reporting (reporting bias)	Low risk	The protocol for the study was not available, but the prespecified outcomes and those mentioned in the methods section appeared to have been reported. Comment: We judged this as at a low risk of bias.
Other bias	High risk	Quote (page 158): This study was funded by Cipla Ltd." Comment: Cipla Ltd is the manufacturer of both products and a potential risk of bias cannot be excluded.

Ramelet 1987

Methods	Randomised, double-blind, active-controlled trial Setting Dermatology practices (4), Switzerland Date of study Not reported. Duration of intervention 7-60 days (average 3 weeks)
Participants	N = 138 (95 male/43 female) Mean age = 38, range 8-80 years **Inclusion criteria of the trial** • dermatomycosis or erythrasma confirmed by KOH and culture **Exclusion criteria of the trial** • systemic mycoses • treatment with topical or systemic antifungal treatment • hypersensitivity to imidazole derivatives Randomised N = 138 with 154 mycoses Withdrawals/losses to follow-up • 4 lost to follow-up, 75 mycoses were treated once daily, 75 twice daily (in 134 participants) Baseline data Diagnosis (number of sites): Tinea pedis: oxiconazole once a day (42), oxiconazole b.i.d. (39) Tinea cruris: oxiconazole once a day (19), oxiconazole b.i.d. (23) Tinea corporis: oxiconazole once a day (13), oxiconazole b.i.d. (10) Erythrasma: oxiconazole once a day (3), oxiconazole b.i.d. (5)
Interventions	Once daily versus twice daily oxiconazole cream **Intervention** • oxiconazole (1%) cream once a day + placebo once a day for 7-60 days (75 mycoses) **Comparator** • oxiconazole (1%) cream b.i.d. for 7-60 days (75 mycoses)
Outcomes	Assessments (2): baseline and end of treatment **Outcomes of the trial** (as reported) 1. Mycological evaluation (KOH and culture) 2. Clinical evaluation: 3-point Likert scale# 3. Tolerability 4. Adverse events# Denotes outcomes prespecified for this review

Ramelet 1987 *(Continued)*

Notes	We only included participants with tinea cruris and corporis.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote (page 293): "..randomized.." Comment: Insufficient detail was reported about the method used to generate the allocation sequence to allow a clear assessment of whether it would produce comparable groups.
Allocation concealment (selection bias)	Unclear risk	The method used to conceal the allocation sequence, that is to determine whether intervention allocations could have been foreseen in advance of, or during, enrolment, was not reported. Comment: There was insufficient information to permit a clear judgement.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote (page 293): "double-blind". Comment: The report did not provide sufficient detail about the measures used to blind study participants and personnel from knowledge of which intervention a participant received, to permit a clear judgement.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote (page 293): "double-blind". Comment: Uncertainty with the effectiveness of blinding of outcomes assessors (participants/healthcare providers) during the study. Insufficient information to permit a clear judgement.
Incomplete outcome data (attrition bias) All outcomes	Low risk	4/138 (3%) lost to follow-up. Per-protocol analysis. Comment: Low number of drop-outs and although per-protocol analysis considered to be at a low risk of bias.
Selective reporting (reporting bias)	Low risk	The protocol for the study was not available, but the prespecified outcomes and those mentioned in the methods section appeared to have been reported. Comment: We judged this as at a low risk of bias.
Other bias	High risk	Both investigators were employed by Laboratoires Sauter SA, Vernier-Genève, Switzerland and a potential risk of bias cannot be excluded.

Repiso Montero 2006

Methods	Randomised, double-blind, active-controlled study Setting Multi-centre, Spain Date of study Not reported. Duration of interventions 4 weeks with follow-up to 8 weeks
Participants	N = 653 (216 male/144 female; 293 gender not reported) Mean age = 44.6 years **Inclusion criteria of the trial**

Repiso Montero 2006 *(Continued)*

- adults with dermatophytoses (tinea pedis, tinea corporis/cruris)

Exclusion criteria of the trial

- not reported

Randomised

N = 653

Delayed exclusions:

- 284 patients with negative mycologic culture and nine patients not meeting the inclusion criteria were excluded. 293/653 (45%) excluded from efficacy analysis

Withdrawals/losses to follow-up

- none reported

Baseline data

Tinea corporis: eberconazole (76), miconazole (72)
Tinea pedis: eberconazole (84), miconazole (79)
Tinea cruris: eberconazole (24) miconazole (25)

Not reported: 293/653

Interventions	**Intervention** • eberconazole (1%) cream b.i.d. for 4 weeks (328) **Comparator** • miconazole (2%) cream b.i.d. for 4 weeks (325)
Outcomes	Assessments (4): baseline, weeks 2, 4 and 8 **Outcomes of the trial** (as reported) 1. Mycological evaluation (KOH and culture) 2. Clinical evaluation (erythema, scaling, and itching): 4-point Likert scale# 3. Effective response (combination 1 and 2)# Denotes outcomes prespecified for this review
Notes	We only included participants with tinea cruris and corporis. See Table 3

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote (page 600): "by a random-permuted-blocks procedure, using a block size of four" Comment: Probably done.
Allocation concealment (selection bias)	Unclear risk	The method used to conceal the allocation sequence, that is to determine whether intervention allocations could have been foreseen in advance of, or during, enrolment, was not reported. Comment: There was insufficient information to permit a clear judgement.

Repiso Montero 2006 *(Continued)*

Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote (page 600): "double-blind". Comment: The report did not provide sufficient detail about the measures used to blind study participants and personnel from knowledge of which intervention a participant received, to permit a clear judgement.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote (page 600): "double-blind". Comment: Uncertainty with the effectiveness of blinding of outcomes assessors (participants/healthcare providers) during the study. Insufficient information to permit a clear judgement.
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Losses after randomisation/delayed exclusions: 284 negative mycologic culture and (9) not meeting the inclusion criteria. Unclear from which group Failed to attend for follow-up: Nothing reported. 653 randomised, 360 analysed. Comment: According to ICH Expert Working Group 1998 the entry criterion was measured (material taken for culture) prior to randomisation. Number of delayed exclusions per group unreported potential risk of attrition bias judged unclear. No further drop-outs reported at follow-up, and although intention-to treat analysis after the delayed exclusions, we judged this at unclear risk of bias.
Selective reporting (reporting bias)	Low risk	The protocol for the study was not available, but the prespecified outcomes and those mentioned in the methods section appeared to have been reported. Comment: We judged this as at a low risk of bias.
Other bias	Unclear risk	Quote (page 603): "The trial was undertaken with a research grant from Laboratorios SALVAT, S.A., Barcelona, Spain." Comment: Laboratoriois SALVAT is the manufacturer of eberconazole. A potential risk of bias cannot be excluded.

Schwarz 1978

Methods	Randomised, double-blind, active-controlled trial Setting Department of Dermatology and Venereology, Städtische Poliklinik Zürich, Swiss Date of study Not reported. Duration of the intervention 14 days (second phase of trial 'open' and single intervention alone)
Participants	N = 104 (57 male/44 female; 3 gender unreported) Mean age = 2 years **Inclusion criteria of the trial** • participants with inflammatory dermatomycoses or candidiasis **Exclusion criteria of the trial**

Schwarz 1978 *(Continued)*

- topical antifungal therapy < 2 weeks, griseofulvin < 6 weeks prior to study entry

Randomised

N = 104

Withdrawals/losses to follow-up

- 3/104 lost to follow-up
- 6/104 due to adverse events: econazole (2), econazole-triamcinolone acetonide (4)

Baseline data

Diagnosis:

Tinea pedis: econazole (39), econazole-triamcinolone acetonide (24)

Tinea manus: econazole (2), econazole-triamcinolone acetonide (2)

Tinea corporis: econazole (2), econazole-triamcinolone acetonide (3)

Eczema marginatum: econazole (7), econazole-triamcinolone acetonide (11)

Candidiasis: econazole (4), econazole-triamcinolone acetonide (6)

Other: econazole (1), econazole-triamcinolone acetonide (0)

Interventions	**Intervention** • econazole-triamcinolone acetonide cream b.i.d. for 2 weeks (46) **Comparator** • econazole cream b.i.d. for 2 weeks (55)
Outcomes	Assessments (3): baseline, weeks 1 and 2 **Outcomes of the trial** (as reported) 1. Mycological evaluation 2. Clinical evaluation of signs and symptoms (pustules, vesicles, papules, scaling and itching): 4-point Likert scale# 3. Adverse events# Denotes outcomes prespecified for this review
Notes	In the second phase of study all participants received econazole cream. We only included data from participants with tinea corporis or cruris. See Table 3

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote (page 1113): "mit vollständig randomisiertem Schema.." Comment: Insufficient detail was reported about the method used to generate the allocation sequence to allow a clear assessment of whether it would produce comparable groups.
Allocation concealment (selection bias)	Unclear risk	The method used to conceal the allocation sequence, that is to determine whether intervention allocations could have been foreseen in advance of, or during, enrolment, was not reported. Comment: There was insufficient information to permit a clear judgement.

Schwarz 1978 *(Continued)*

Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote (page 1113): "..Doppelblindversuch..". Comment: The report did not provide sufficient detail about the measures used to blind study participants and personnel from knowledge of which intervention a participant received, to permit a clear judgement.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote (page 1113): "..Doppelblindversuch..". Comment: Uncertainty with the effectiveness of blinding of outcomes assessors (participants/healthcare providers) during the study. Insufficient information to permit a clear judgement.
Incomplete outcome data (attrition bias) All outcomes	Low risk	9/104 (9%), reasons reported. Per-protocol analysis. Comment: Low and well balanced number of drop-outs at follow-up, and although per-protocol analysis considered to be at a low risk of bias.
Selective reporting (reporting bias)	Low risk	The protocol for the study was not available, but the prespecified outcomes and those mentioned in the methods section appeared to have been reported. Comment: We judged this as at a low risk of bias.
Other bias	Low risk	The study appears to be free from other forms of bias.

Sehgal 1976

Methods	Randomised, double-blind, placebo-controlled trial Setting Department of Dermatology and Venereology, Goa Medical College and Hospital, Panaji, Goa, India Date of study Not reported. Duration of the intervention 4 weeks
Participants	N = 105 (age and gender unreported) **Inclusion criteria of the trial** • adults with dermatomycosis in whom the area of involvement did not exceed 10% of the body surface and not received any specific anti-mycotic treatment orally **Exclusion criteria of the trial** • pregnant women • participants with secondarily infected lesions Randomised N = 105 Withdrawals/losses to follow-up • 12/105 were lost to follow-up (failed to report) unclear from which group Baseline data Tinea corporis: ciclopirox (15), placebo (8) Tinea cruris: ciclopirox (23), placebo (27)

Sehgal 1976 *(Continued)*

	Tinea corporis and cruris: ciclopirox (2), placebo (10) Tinea pedis: ciclopirox (1), placebo (1) Tinea versicolor: ciclopirox (3), placebo (3)
Interventions	**Intervention** • ciclopirox (1%) solution in polyethylene glycol 400 b.i.d. for 4 weeks (44) **Comparator** • placebo solution b.i.d. for 4 weeks (49) Treatment was discontinued if there was no improvement within 2 weeks or cure was obtained during this period.
Outcomes	Assessments (5): baseline, daily first 5 days, weeks 1, 2, 3 and 4 **Outcomes of the trial** (as reported) 1. Clinical evaluation of signs and symptoms 2. Mycological evaluation (KOH and culture) 3. Laboratory tests 4. Adverse events# Denotes outcomes prespecified for this review
Notes	We only included data from participants with tinea corporis and tinea cruris. See Table 3

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote (page 84): "Every patient admitted to the study was assigned a serial number and as per the randomization table" Comment: Probably done.
Allocation concealment (selection bias)	Unclear risk	The method used to conceal the allocation sequence, that is to determine whether intervention allocations could have been foreseen in advance of, or during, enrolment, was not reported. Comment: There was insufficient information to permit a clear judgement.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote (page 83): "..double-blind..". Comment: The report did not provide sufficient detail about the measures used to blind study participants and personnel from knowledge of which intervention a participant received, to permit a clear judgement.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote (page 83): "..double-blind..". Comment: Uncertainty with the effectiveness of blinding of outcomes assessors (participants/healthcare providers) during the study. Insufficient information to permit a clear judgement.
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	12/105 (11%) (unclear from which group) were not included in the per-protocol analysis.

Sehgal 1976 *(Continued)*

		Comment: Although the group distribution was unreported and the number excluded from the efficacy analysis is low the risk of bias remains unclear
Selective reporting (reporting bias)	Unclear risk	Clinical evaluation data for Days 1-5 unreported. Only the 28 day assessment. Other predefined outcomes i.e. mycological evaluation and adverse events were reported. Comment: We judged this at unclear risk of bias.
Other bias	Low risk	The study appears to be free from other forms of bias.

Sharma 2011

Methods	Randomised, double-blind, active-controlled trial Setting Multi-centre (5), India Date of study Not reported. Duration of the intervention 2 weeks with follow-up to 30 days
Participants	N = 260 (217 male/43 female) Age range 18-82, mean = 37 years **Inclusion criteria of the trial** • 18–70 years with a clinical diagnosis of cutaneous dermatophytosis confirmed by microscopic examination (positive KOH), tinea corporis and cruris • women who were post-menopausal, surgically sterilised or having reliable method of birth control • participants willing to be followed up during the study **Exclusion criteria of the trial** • pregnant and lactating women • oral treatment with antimycotics during 4 weeks preceding the trial • topical treatment 1 week prior to the trial • chronic severe diseases • bacterial skin infection • history of hypersensitivity to sertaconazole Randomised N = 260 Withdrawals/losses to follow-up • sertaconazole group (6), miconazole (4) Baseline data Quote (page 219): "At baseline the occurrence of pruritus, erythema and desquamation were similar in both the groups" and "Mean baseline scores of erythema/itching, burning/weeping and scaling/pustules were similar in the two groups prior to therapy"
Interventions	**Intervention** • sertaconazole nitrate (2%) cream b.i.d. for 2 weeks (128)

Sharma 2011 *(Continued)*

	Comparator • miconazole (2%) cream b.i.d. for 2 weeks (132)
Outcomes	Assessments (3): baseline, weeks 1 and 2, day 30 (safety analysis) **Outcomes of the trial** (as reported) 1. Physician global assessment of clinical response regarding complete clinical cure confirmed by negative mycology at the end of 2 weeks# 2. Clinical evaluation of the disease condition (pruritis, erythema, desquamation, maceration): 6-point Likert scale# 3. Adverse events: 3-point Likert scale# Denotes outcomes prespecified for this review
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote (page 218): "..were assigned randomly to two therapy groups.." Comment: Insufficient detail was reported about the method used to generate the allocation sequence to allow a clear assessment of whether it would produce comparable groups.
Allocation concealment (selection bias)	Unclear risk	The method used to conceal the allocation sequence, that is to determine whether intervention allocations could have been foreseen in advance of, or during, enrolment, was not reported. Comment: There was insufficient information to permit a clear judgement.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote (page 218): "..double-blind.." Comment: The report did not provide sufficient detail about the measures used to blind study participants and personnel from knowledge of which intervention a participant received, to permit a clear judgement.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote (page 218): ".. double-blind..". Comment: Uncertainty with the effectiveness of blinding of outcomes assessors (healthcare providers) during the study. Insufficient information to permit a clear judgement.
Incomplete outcome data (attrition bias) All outcomes	Low risk	10/260 were lost to follow-up, balanced between the groups. Per-protocol analysis. Comment: Low and well balanced number of drop-outs and although per protocol analysis we considered this to be at a low risk of bias.
Selective reporting (reporting bias)	Low risk	The protocol for the study was not available, but the prespecified outcomes and those mentioned in the methods section appeared to have been reported. Comment: We judged this as at a low risk of bias.
Other bias	Low risk	The study appears to be free from other forms of bias.

Shen 2002

Methods	Randomised, double-blind, active-controlled trial Setting Department of Dermatology, Renji hospital associated to Shanghai 2nd Medical University, China Date of study Not reported. Duration of intervention 3 weeks
Participants	N = 69 (51 male/12 female; 6 gender unreported) Mean age = 36 years **Inclusion criteria of the trial** • tinea corporis and tinea cruris, including patients with bacterial infection **Exclusion criteria of the trial** • allergy to medicines • severe heart, liver, kidney disease, diabetes or patients with mental illness • systemic use of glucocorticoid, anti-fungal or anti-bacterial medicines in previous 4 weeks • glucocorticoid, anti-fungal or anti-bacterial medicines cream in previous 2 weeks • endocrine and metabolic disease or pregnant women Randomised N = 69 Withdrawals/losses to follow-up • 6/69 (9%), 3 in each group due to "stopping of the trial by the participant, could not use the medicine or unable to attend to visit; using glucocorticoid, anti-bacterial or other anti-fungal medicines during the trial" [as translated] Baseline data Tinea corporis: miconazole (16), econazole plus triamcinolone acetonide (17) Tinea cruris: miconazole (11), econazole plus triamcinolone acetonide (9) Both: miconazole (5), econazole plus triamcinolone acetonide (5)
Interventions	**Intervention** • miconazole (2%) cream, b.i.d. for 3 weeks (35) **Comparator** • econazole nitrate (1%) + triamcinolone acetonide (0.1%) b.i.d. for 3 weeks (34)
Outcomes	Assessments (3): baseline, weeks 2 and 3 **Outcomes of the trial** (as reported) 1. Clinical evaluation of signs and symptoms (erythema, papules, vesicles, maceration, erosion, crust, exudation, scales, pruritus and pain): 4-point Likert scale# 2. Clinical efficacy: 4-point Likert scale# 3. Mycological evaluation (KOH, culture and fungal identification) 4. Adverse events# Denotes outcomes prespecified for this review

Shen 2002 *(Continued)*

Notes

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote (page 145): "randomly divided" Comment: Insufficient detail was reported about the method used to generate the allocation sequence to allow a clear assessment of whether it would produce comparable groups.
Allocation concealment (selection bias)	Unclear risk	The method used to conceal the allocation sequence, that is to determine whether intervention allocations could have been foreseen in advance of, or during, enrolment, was not reported. Comment: There was insufficient information to permit a clear judgement.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote (page 143): "double-blind". Comment: The report did not provide sufficient detail about the measures used to blind study participants and personnel from knowledge of which intervention a participant received, to permit a clear judgement.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote (page 143): "..double-blind..". Comment: Uncertainty with the effectiveness of blinding of outcomes assessors (participants/healthcare providers) during the study. Insufficient information to permit a clear judgement.
Incomplete outcome data (attrition bias) All outcomes	Low risk	6/69 drop-outs, 3 in each group. Per-protocol analysis. Comment: Low and well balanced number of drop-outs, and although per-protocol analysis considered to be at a low risk of bias.
Selective reporting (reporting bias)	Low risk	The protocol for the study was not available, but the prespecified outcomes and those mentioned in the methods section appeared to have been reported. Comment: We judged this as at a low risk of bias.
Other bias	Low risk	The study appears to be free of other forms of bias.

Shi 2011

Methods	Randomised, double-blind, active-controlled trial Setting 3 Departments of Dermatology of Hospitals, China Date of study October 2006-January 2008. Duration of the intervention 2-4 weeks with follow-up to 4 weeks after end of treatment
Participants	N = 120 (74 male/23 female; 23 gender unreported) Mean age = 27 years for tinea corporis and cruris group, 34 years for tinea pedis and manuum group **Inclusion criteria of the trial**

Shi 2011 *(Continued)*

- dermatophytoses (tinea corporis 'and' or 'or' tinea cruris, tinea pedis 'and' or 'or' tinea manuum)
- positive microscopic findings and fungal culture results of skin lesion smears

Exclusion criteria of the trial

- use of any topical antifungal agents or corticosteroids within 2 weeks before the study or oral antifungal agents within the previous month
- severe combined local bacterial infection or other skin diseases that might interfere with the treatment
- diabetes mellitus or severe heart, liver, or kidney disease
- unable to cooperate with the treatment
- allergy to tetrandrine (TET) or ketoconazole (KCZ)

Randomised

N = 120

Withdrawals/losses to follow-up

23/120 (19%)

- (6) during study, (13) early termination (unclear from which group)
- (4) reasons unreported

Baseline data

Diagnosis:

Tinea corporis 'and' or 'or' cruris: KCZ+TET (16), KCZ (15), TET (12)

Tinea pedis and /or tinea manuum: KCZ+TET (24), KCZ (20), TET (10)

Interventions	**Intervention** • tetrandrine (2%) cream with ketoconazole (2%) cream b.i.d. for 2-4 weeks **Comparator 1** • ketoconazole (2%) cream b.i.d. for 2-4 weeks **Comparator 2** • tetrandrine (2%) cream b.i.d. for 2-4 weeks
Outcomes	Assessments (5-7): baseline, weeks 1-4, 2 and 4 weeks after end of treatment **Outcomes of the trial** (as reported) 1. Determination of Minimum Inhibitory Concentrations 2. Mycological evaluation 3. Clinical evaluation of signs and symptoms (severities of pruritus, erythema, papules, and scales): 4-point Likert scale# 4. Clinical efficacy: 4-point Likert scale# 5. Adverse events# 6. Laboratory tests Denotes outcomes prespecified for this review
Notes	
Risk of bias	

Shi 2011 *(Continued)*

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote (page 500): "..randomly assigned to 3 groups by means of a random number table.." Comment: Probably done.
Allocation concealment (selection bias)	Unclear risk	The method used to conceal the allocation sequence, that is to determine whether intervention allocations could have been foreseen in advance of, or during, enrolment, was not reported. Comment: There was insufficient information to permit a clear judgement.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote (page 500): ".. double-blind..". Comment: The report did not provide sufficient detail about the measures used to blind study participants and personnel from knowledge of which intervention a participant received, to permit a clear judgement.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote (page 500): ".. double-blind..". Comment: Uncertainty with the effectiveness of blinding of outcomes assessors (healthcare providers) during the study. Insufficient information to permit a clear judgement.
Incomplete outcome data (attrition bias) All outcomes	High risk	23/120 (19%) were not included in the analysis. Unclear from which groups. Per-protocol analysis. Given the high attrition rate, the per-protocol analysis of these data is likely to inflate the effect estimate, and, consequently, it may raise concerns about the reliability of the data as reported. Comment: We judged this as at a high risk of bias.
Selective reporting (reporting bias)	Low risk	The protocol for the study was not available, but the prespecified outcomes and those mentioned in the methods section appeared to have been reported. Comment: We judged this as at a low risk of bias.
Other bias	Low risk	Quote (page 499): "Supported by the National Natural Science Foundation of China, Foundation of Science and Technology Planning Project of Guangdong Province, China" Comment: We judged this as at a low risk of bias.

Singal 2005

Methods	Randomised, double-blind, active-controlled trial Setting Department of Dermatology & STD, University College of Medical Sciences & Guru Teg Bahadur Hospital, Delhi, India Date of study April- August 2003. Duration of the intervention 4 weeks with follow-up to 8 weeks
Participants	N = 80 (53 male/ 27 female)

Singal 2005 *(Continued)*

Mean age = 29 years

Inclusion criteria of the trial

- >14 years with localised tinea cruris and localised tinea corporis confirmed by KOH
- a positive culture was not a prerequisite for inclusion

Exclusion criteria of the trial

- pregnant and lactating women
- extensive (> 20% of skin surface) tinea
- concurrent skin diseases which could interfere with the clinical evaluation on subsequent visits
- other severe systemic diseases
- history of treatment with other oral or topical antifungal drugs in the previous 4 weeks
- known hypersensitivity to allylamines/imidazoles

Randomised

N = 80

Withdrawals/losses to follow-up

- butenafine: 6/40, 9/40, 13/40 and 20/40 were lost to follow-up after 1, 2, 4 and 8 weeks
- clotrimazole: 6/40, 8/40, 15/40, 19/40 were lost to follow-up after 1, 2, 4 and 8 weeks

Baseline data

Diagnosis:

Tinea cruris: butenafine (10), clotrimazole (7)

Tinea corporis: butenafine (18), clotrimazole (22)

Tinea cruris and corporis: butenafine (12), clotrimazole (11)

Interventions	**Intervention** • butenafine (1%) cream once daily for 2 weeks (40) **Comparator** • clotrimazole (1%) cream b.i.d. for 4 weeks (40)
Outcomes	Assessments (5): baseline, weeks 1, 2, 4 and 8 **Outcomes of the trial** (as reported) 1. Clinical evaluation of signs and symptoms (erythema, scaling and pruritus): 4-point Likert scale# 2. Mycological evaluation (KOH and culture) 3. Adverse events# 4. Laboratory tests 5. Relapse Denotes outcomes prespecified for this review
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement

Singal 2005 *(Continued)*

Random sequence generation (selection bias)	Low risk	Quote (page 232): ".Each patient was randomized to either the butenafine or the clotrimazole group based on random tables." Comment: Probably done.
Allocation concealment (selection bias)	Low risk	The method used to conceal the allocation sequence, that is to determine whether intervention allocations could have been foreseen in advance of, or during, enrolment, was not reported. Comment: There was insufficient information to permit a clear judgement. After e-mail communication: Quote: "The computer generated random numbers after generation were directly placed in an opaque sealed envelope and given to the clinical nurse (randomisation authority). This was opened by her and kept in a locked cupboard, the key to which was only available to her. She was briefed before the trial about need for not revealing details to patients as well as investigators. Further, the coded containers were also kept in same locked cupboard with no access to investigators at anytime during the trial." Comment: Probably done.
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote (page 332): "Individual drugs were dispensed in two identical containers of 5 g capacity for morning and evening application. As butenafine was to be applied once daily for 2 weeks, a placebo (vehicle) was supplied in a similar container for evening application for the initial 2 weeks and for twice daily application for the next 2 weeks" Comment: Probably done.
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Blinding of outcomes assessors, key personnel and participants was ensured, and it was unlikely that the blinding could have been broken. Comment: We judged this as at a low risk of bias.
Incomplete outcome data (attrition bias) All outcomes	High risk	28/80 (35%) was lost to follow-up during treatment and 39/80 (49%) at end of follow-up. Per-protocol analysis. Comment: We judged this as at a high risk of bias.
Selective reporting (reporting bias)	Low risk	The protocol for the study was not available, but the prespecified outcomes and those mentioned in the methods section appeared to have been reported. Comment: We judged this as at a low risk of bias.
Other bias	Low risk	The study appears to be free from other bias.

Sivayathorn 1979

Methods	Randomised, double-blind, active-controlled trial Setting Institute of Dermatology, Bangkok, Thailand Date of study Not reported. Duration of intervention 2 weeks
Participants	N = 140 (70 male/31 female; 39 gender unreported)

Sivayathorn 1979 *(Continued)*

	Mean age = 27, range 2-72 years **Inclusion criteria of the trial** • tinea cruris 'and' or 'or' corporis confirmed by KOH and culture **Exclusion criteria of the trial** • not reported Randomised N = 140 Withdrawals/losses to follow-up • 30/140 (21%) lost to follow-up reasons not reported • 9/140 (6%) no material for culture at end of study Baseline data Not reported
Interventions	**Intervention** • Whitfield's ointment three times a day for 2 weeks **Comparator 1** • tolnaftate (2%) ointment three times a day for 2 weeks **Comparator 2** • clotrimazole (1%) cream three times a day for 2 weeks **Comparator 3** • miconazole (2%) three times a day for 2 weeks
Outcomes	Assessments (2): baseline, week 2 **Outcomes of the trial** (as reported) 1. Clinical evaluation: 5-point Likert scale# 2. Mycological evaluation (culture) 3. Adverse events# Denotes outcomes prespecified for this review
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote (page 22): "..randomized..". Comment: Insufficient detail was reported about the method used to generate the allocation sequence to allow a clear assessment of whether it would produce comparable groups.
Allocation concealment (selection bias)	Unclear risk	The method used to conceal the allocation sequence, that is to determine whether intervention allocations could have been foreseen in advance of, or during, enrolment, was not reported.

Sivayathorn 1979 *(Continued)*

		Comment: There was insufficient information to permit a clear judgement.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote (page 22): "..double-blind..". Comment: The report did not provide sufficient detail about the specific measures used to blind study participants and personnel from knowledge of which intervention a participant received, to permit a clear judgement.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote (page 64-5): ".. double-blind..". Comment: Uncertainty with the effectiveness of blinding of outcomes assessors (healthcare providers) during the study. Insufficient information to permit a clear judgement.
Incomplete outcome data (attrition bias) All outcomes	High risk	39/140 (28%) not included in the analysis. Per-protocol analysis. Comment: We judged this as at a high risk of bias.
Selective reporting (reporting bias)	Low risk	The protocol for the study was not available, but the prespecified outcomes and those mentioned in the methods section appeared to have been reported. Comment: We judged this as at a low risk of bias.
Other bias	Unclear risk	The antimycotics were provided by United Victory, Bayer and Janssen. Comment: Insufficient information to assess whether important risk of bias exists.

Smith 1974

Methods	Randomised, double-blind, vehicle-controlled trials (2 phases) Setting Prison clinic, Houston, Texas Date of study Not reported. Duration of intervention 4 weeks, second phase another 4 weeks
Participants	N = 82 (all male) Age range 18-46 years **Inclusion criteria of the trial** • clinical evidence of tinea pedis or cruris or both confirmed by KOH 'and' or 'or' culture **Exclusion criteria of the trial** • not reported Randomised N = 82 Withdrawals/losses to follow-up • unclear Baseline data

Smith 1974 *(Continued)*

	Tinea pedis and cruris (8) Unclear how many participants were in active arm in first phase, neither how many had tinea pedis or tinea cruris in the vehicle arm in the first phase 8 had tinea cruris and 14 tinea pedis. Unclear how many were in second phase, nor how many had what kind of infection!
Interventions	**First phase** **Intervention** • clotrimazole 1% in polyethylene glycol 400 twice daily for 4 weeks (number unclear) **Comparator** • vehicle alone (22) **Second phase** **Intervention** • clotrimazole 1% in cream base twice daily for 4 weeks (number unclear) **Comparator** • vehicle alone (25) No other topical or systemic treatment was given during the study period and all previous medication had to be discontinued for at least two weeks prior to the study.
Outcomes	Assessments (5): baseline, weeks 1-4 **Outcomes of the trial** (as reported) 1. Clinical evaluation 2. Mycological evaluation Denotes outcomes prespecified for this review
Notes	Unclear how many participants with tinea cruris were in each treatment arm in the two studies. See Table 3

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote (page 64): ".. were randomly assigned.." and page 65 for second phase "..were randomly assigned..". Comment: Insufficient detail was reported about the method used to generate the allocation sequence to allow a clear assessment of whether it would produce comparable groups.
Allocation concealment (selection bias)	Unclear risk	The method used to conceal the allocation sequence, that is to determine whether intervention allocations could have been foreseen in advance of, or during, enrolment, was not reported. Comment: There was insufficient information to permit a clear judgement.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote (page 64-5): "..double-blind..". Comment: The report did not provide sufficient detail about the specific measures used to blind study participants and personnel from knowledge of which intervention a participant received, to permit a clear judgement.

Smith 1974 *(Continued)*

Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote (page 64-5): ".. double-blind..". Comment: Uncertainty with the effectiveness of blinding of outcomes assessors (healthcare providers) during the study. Insufficient information to permit a clear judgement.
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	It is unclear in the 2 studies how many participants were included in the active arms. Furthermore it was unclear how many match the inclusion criteria of this review as no indication is given of what kind of infection the participants had. No drop-outs are mentioned, nor if it is per-protocol analysis or intention-to-treat analysis. Comment: Too many uncertainties/unknown factors to permit a clear judgement.
Selective reporting (reporting bias)	Low risk	Very limited data reported. However, the prespecified outcomes and those mentioned in the methods section appeared to have been reported. Comment: We judged this at a low risk of bias.
Other bias	Unclear risk	Quote (page 66): "The test preparation were supplied by P.H. Spiekerman, Delbay Pharmaceuticals Inc, Bloomfield, New Jersey" Comment: Unclear to what extent this represents a risk of bias.

Spiekermann 1976

Methods	2 randomised, double-blind, vehicle-controlled trials Setting Multi-centre, USA Date of study Not reported. Duration of intervention 4-6 weeks.
Participants	N = 1361 for 2 studies, unclear how many in each study. Study 1 (777); study 2 (134) completed study Age and gender unreported **Inclusion criteria of the trial** • mycologically confirmed dermatomycosis (KOH and culture) **Exclusion criteria of the trial** • previous treatment < 2 weeks prior start of study Randomised N = 1361 Withdrawals/losses to follow-up • 450/1361 (33%), reasons unreported Baseline data Diagnosis Study 1:

Spiekermann 1976 *(Continued)*

	Tinea cruris or corporis: clotrimazole (87), vehicle (81) Tinea pedis: clotrimazole (133), vehicle (134) Cutaneous candidiasis: clotrimazole (63), vehicle (56) Pityriasis versicolor: clotrimazole (116), vehicle (107) Diagnosis Study 2: Tinea cruris or corporis: clotrimazole (24), vehicle (21) Tinea pedis: clotrimazole (17), vehicle (24) Cutaneous candidiasis: clotrimazole (18), vehicle (12) Pityriasis versicolor: clotrimazole (10), vehicle (8)
Interventions	**Study 1.** **Intervention** • clotrimazole (1%) solution b.i.d. for 4-6 weeks (87) **Comparator** • vehicle for 4-6 weeks (81) **Study 2.Intervention** • clotrimazole (1%) cream b.i.d. for 4-6 weeks (24) **Comparator** • vehicle for 4-6 weeks (21) Duration of treatment: Tinea pedis 6 weeks, rest 4 week. Pityriasis versicolor once a day for 2 weeks. No other topical or systemic anti-effective or anti-inflammatory agents were allowed during the studies.
Outcomes	Assessments (5-7), baseline, weeks 1, 2, 3, 4 up to 6. **Outcomes of the trial** (as reported) 1. Clinical evaluation of sign and symptoms (scaling, pruritus, vesiculation, inflammation, erythema, fissures, exudation, maceration): 4-point Likert scale# 2. Overall evaluation of improvement 3. Mycological evaluation (KOH and culture) 4. Adverse events# Denotes outcomes prespecified for this review
Notes	We only include and report data on participants with tinea corporis/cruris

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote (page 350): "..assigned to patients at random..". Comment: Insufficient detail was reported about the method used to generate the allocation sequence to allow a clear assessment of whether it would produce comparable groups.

Spiekermann 1976 *(Continued)*

Allocation concealment (selection bias)	Unclear risk	The method used to conceal the allocation sequence, that is to determine whether intervention allocations could have been foreseen in advance of, or during, enrolment, was not reported. other than " appropriately coded" Comment: There was insufficient information to permit a clear judgement.
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote (page 350): ".. appropriately coded, but otherwise identical boxes to ensure the double-blind nature.." Comment: Probably done.
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Blinding of the outcomes assessors, key personnel, was ensured, and it was unlikely that the blinding could have been broken. Comment: We judged this as at a low risk of bias.
Incomplete outcome data (attrition bias) All outcomes	High risk	450/1361 (33%), unclear from which groups, reasons unreported. Per-protocol analysis. Comment: Judged as at a high risk of bias.
Selective reporting (reporting bias)	Unclear risk	Cross-reporting of limited data for pre-specified outcomes in both studies, unclear if all outcomes reported. Comment: We judged this at unclear risk of bias.
Other bias	High risk	The investigators are employed by Delbay Pharmaceuticals, Inc, Bloomfield NJ, the manufacturer of clotrimazole. Comment: A potential risk of bias cannot be excluded.

Su 2001

Methods	Randomised, double-blind, active-controlled trial Setting One centre in China Date of study Not reported. Duration of intervention 2 weeks with one week follow-up
Participants	N = 150 (all male) Age range = 16-63 years **Inclusion criteria of the trial** • tinea cruris confirmed by KOH **Exclusion criteria of the trial** • antifungal therapy < 4 weeks prior to study entry Randomised N = 150 Withdrawals/losses to follow-up • no drop-outs

Su 2001 *(Continued)*

	Baseline data Not reported
Interventions	**Intervention** • econazole nitrate (1%) + triamcinolone acetonide (0.1%) b.i.d. for 2 weeks (75) **Comparator** • miconazole (2%) + clobetasol (0.5%) b.i.d. for 2 weeks (75)
Outcomes	Assessments (2): baseline and one week after end of therapy **Outcomes of the trial** (as reported) 1. Clinical evaluation of signs and symptoms: 4-point Likert scale# 2. Clinical efficacy: 4-point Likert scale# 3. Mycological evaluation (KOH)# 4. Adverse events# Denotes outcomes prespecified for this review
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote (page 357): "randomised". Comment: Insufficient detail was reported about the method used to generate the allocation sequence to allow a clear assessment of whether it would produce comparable groups.
Allocation concealment (selection bias)	Unclear risk	The method used to conceal the allocation sequence, that is to determine whether intervention allocations could have been foreseen in advance of, or during, enrolment, was not reported. Comment: There was insufficient information to permit a clear judgement.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote (page 357): "..double-blind..". Comment: The report did not provide sufficient detail about the measures used to blind study participants and personnel from knowledge of which intervention a participant received, to permit a clear judgement.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote (page 357): "..double-blind..". Comment: Uncertainty with the effectiveness of blinding of outcomes assessors (participants/healthcare providers) during the study. Insufficient information to permit a clear judgement.
Incomplete outcome data (attrition bias) All outcomes	Low risk	No drop-outs reported. Intention-to-treat analysis. Comment: We judged this as at a low risk of bias.
Selective reporting (reporting bias)	Low risk	The protocol for the study was not available, but the prespecified outcomes and those mentioned in the methods section appeared to have been reported. Comment: We judged this as at a low risk of bias.

Su 2001 *(Continued)*

Other bias	Low risk	The study appears to be free of other forms of bias.

Susilo 2003

Methods	Randomised, double-blind, placebo-controlled trial Setting Dermatological sites (7), Germany Date of study August 1995-April 1997. Duration of intervention 3 weeks with follow-up at 4 weeks
Participants	N = 400 (233 male/167 female) Mean age = 46 years **Inclusion criteria of the trial** • >18 years with fungal infections of the glabrous skin (particularly including tinea pedis and manus, tinea inguinalis, tinea corporis and tinea faciei) confirmed by KOH **Exclusion criteria of the trial** • chronic liver diseases • pregnancy or breast feeding • HIV infection • alcohol abuse 'and' or 'or' drug dependency • topical treatment in the study area with sertaconazole • systemic or topical treatment in the study area with antibiotics 'and' or 'or' glucocorticoids; antipruritic therapy < 2 weeks 'and' or 'or' systemic antifungal treatment < 4 weeks prior to study entry • severe chronic or malignant diseases • type 1 diabetes Randomised N = 400 Withdrawals/losses to follow-up • 26/400; sertaconazole (12), vehicle (14) withdrew from the study prematurely • sertaconazole (112/200), vehicle (118/200) were excluded from ITT analysis due to lack of positive culture (219), no data available Day 3 (11) • sertaconazole (122/200), vehicle (225/200) were excluded from per-protocol analysis. In addition to the above for protocol violations; sertaconazole (10), vehicle (7) Baseline data Not reported
Interventions	**Intervention** • sertaconazole (2%) once daily for 3 weeks (200) **Comparator** • vehicle once daily for 3 weeks (200)

Susilo 2003 *(Continued)*

Outcomes	Assessments (5): baseline, weeks 1, 2, 3 and 4 **Outcomes of the trial** (as reported) 1. Clinical evaluation of signs and symptoms (itching, burning, erythema, scaling): 4-point Likert scale# 2. Mycological evaluation (KOH and culture) 3. Tolerability Denotes outcomes prespecified for this review
Notes	Tinea cruris and corporis are included, but unclear how many in each group. See Table 3

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote (page 389): "..according to a randomisation schedule with a random block size of four patients" Comment: Probably done.
Allocation concealment (selection bias)	Unclear risk	The method used to conceal the allocation sequence, that is to determine whether intervention allocations could have been foreseen in advance of, or during, enrolment, was not reported. Comment: There was insufficient information to permit a clear judgement.
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote (page 389): "..double-blind.." and "The corresponding vehicle cream was identical to sertaconazole 2% cream.." Comment: The report provided sufficient detail about the measures used to blind study participants and personnel from knowledge of which intervention a participant received, to permit a clear judgement.
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Outcomes were investigator-assessed and participant-assessed. Blinding of participants and key study personnel was ensured, and it is unlikely that the blinding could have been broken. Comment: We judged this as at a low risk of bias.
Incomplete outcome data (attrition bias) All outcomes	Low risk	Delayed exclusions: 230/400 (58%) sertaconazole (112/200), vehicle 118/200) were excluded from intention-to-treat analysis due to lack of positive culture (219), no data available Day 3 (11) Further losses during the study period: 26/400; sertaconazole (12), vehicle (14) withdrew from the study prematurely. Sertaconazole (10/200), vehicle (7/200) were excluded from per-protocol analysis. In addition to the above for protocol violations; Total not included in analysis 43/400 (11%) Comment: Entry criterion (culture specimen) measured prior to randomisation. The delayed exclusions are well-balanced between groups, no attrition bias between the groups. See ICH Expert Working Group 1998. Low and well balanced number of drop-outs at follow-up, and although per-protocol analysis considered to be at a low risk of bias.
Selective reporting (reporting bias)	Low risk	The protocol for the study was not available, but the prespecified outcomes and those mentioned in the methods section appeared to have been reported. Comment: We judged this as at a low risk of bias.

Susilo 2003 *(Continued)*

Other bias	High risk	One of the investigators was employed by Trommsdorff GmbH & Co Arzneimittel. A potential risk of bias cannot be excluded.

Tanenbaum 1982

Methods	Randomised, double-blind, active-controlled study Setting Multi-centre, USA Date of study Not reported. Duration of the study 3 weeks for tinea corporis and cruris, 4 weeks for tinea pedis with follow-up to 3-6 weeks after end of treatment
Participants	N = 96 (85 male/11 female) Mean age = 36 years **Inclusion criteria of the trial** • participants with tinea pedis, corporis 'and' or 'or' cruris confirmed by KOH and mostly also by culture **Exclusion criteria of the trial** • < 18 years • women of child-bearing potential • tinea pedis of moccasin type > 6 months Randomised N = 96, unclear how many in each group Withdrawals/losses to follow-up • 13/96 (14%) did not completed the trial unclear from which treatment arm • 18 participants with tinea pedis and 65 with tinea cruris/corporis completed the trial Baseline data Not reported
Interventions	**Intervention** • sulconazole (1%) cream b.i.d. for 3-4 weeks **Comparator** • miconazole (2%) cream b.i.d. for 3-4 weeks
Outcomes	Assessments (7): baseline weeks 2, 3, 4, and 3 and 6 weeks after end of treatment **Outcomes of the trial** (as reported) 1. Mycological evaluation (KOH and culture) 2. Clinical evaluation of signs and symptoms (erythema, scaling, maceration, vesiculation, fissuring) 3. Overall clinical improvement: 5-point Likert scale# 4. Adverse events: 4-point Likert scale# 5. Overall efficacy: 4-point Likert scale#

Tanenbaum 1982 *(Continued)*

	6. Cosmetic acceptability: 4-point Likert scale Denotes outcomes prespecified for this review
Notes	Unclear how many were in each treatment arm, unclear number with tinea pedis or tinea corporis/cruris. See Table 3

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote (page 106): ".. were randomly assigned.." Comment: Insufficient detail was reported about the method used to generate the allocation sequence to allow a clear assessment of whether it would produce comparable groups.
Allocation concealment (selection bias)	Unclear risk	The method used to conceal the allocation sequence, that is to determine whether intervention allocations could have been foreseen in advance of, or during, enrolment, was not reported. Comment: There was insufficient information to permit a clear judgement.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote (page 105): "..double-blind..". Comment: The report did not provide sufficient detail about the specific measures used to blind study participants and personnel from knowledge of which intervention a participant received, to permit a clear judgement.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote (page 105): "..double-blind..". Comment: Uncertainty with the effectiveness of blinding of outcomes assessors (participants/healthcare providers) during the study. Insufficient information to permit a clear judgement.
Incomplete outcome data (attrition bias) All outcomes	High risk	13/83 (14%) were not included in the data analysis, reasons not stated. Per-protocol analysis. Unclear how many started in each treatment arm. Comment: We judged this as at a high risk of bias.
Selective reporting (reporting bias)	Unclear risk	Very limited data reported on each of the prespecified outcomes to enable a clear judgement of the risk of bias.
Other bias	Low risk	The study appears to be free of other forms of bias.

Tanenbaum 1989

Methods	2 randomised, double-blind, active-controlled trials Setting Unreported. Colombia Date of study Not reported. Duration of intervention 3 weeks
Participants	N = 117 (60 in Study 1, 57 in Study 2) (all male) Mean age = 20 years

Tanenbaum 1989 *(Continued)*

Inclusion criteria of the trial

- clinical diagnosis of tinea corporis/cruris confirmed by KOH

Exclusion criteria of the trial

- no concomitant antifungal therapy

Randomised

N = 117

Withdrawals/losses to follow-up

- Study 1: sulconazole (10/30), clotrimazole (4/30)
- Study 2: sulconazole (2/28), vehicle (6/29)

Baseline data

Nothing reported

Interventions	**Intervention Study 1** • sulconazole (1%) cream once daily for 3 weeks (30) **Comparator** • clotrimazole (1%) b.i.d. for 3 weeks (30) **Intervention Study 2** • sulconazole (1%) cream b.i.d. for 3 weeks (28) **Comparator** • vehicle b.i.d. for 3 weeks (29) No concomitant treatment during the study was allowed.
Outcomes	Assessments (4): baseline weeks 1, 2 and 3 **Outcomes of the trial** (as reported) 1. Mycological evaluation (KOH and culture) 2. Clinical signs and symptoms (itching, erythema, scaling, pustules, fissuring, maceration, vesiculation) 3. Overall clinical status: 4-point Likert scale# 4. Adverse events: 3-point Likert scale# Denotes outcomes prespecified for this review
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote (page 344): "..randomised..". Comment: Insufficient detail was reported about the method used to generate the allocation sequence to allow a clear assessment of whether it would produce comparable groups.

Tanenbaum 1989 *(Continued)*

Allocation concealment (selection bias)	Unclear risk	The method used to conceal the allocation sequence, that is to determine whether intervention allocations could have been foreseen in advance of, or during, enrolment, was not reported. Comment: There was insufficient information to permit a clear judgement.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote (page 344): "..double-blind.." "To maintain a double-blind format one group applied sulconazole in the morning and sulconazole vehicle in the evening, while the other group applied clotrimazole cream at both times." Comment: The report (both studies) did not provide sufficient detail about the specific measures used to blind study participants and personnel from knowledge of which intervention a participant received, to permit a clear judgement.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote (page 344): "..double-blind.." Comment: Uncertainty with the effectiveness of blinding of outcomes assessors (participants/healthcare providers) during the study. Insufficient information to permit a clear judgement.
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Study 1: sulconazole (0/30), clotrimazole (3/30), Study 2: sulconazole (1/28), vehicle (3/29) were not included in the analysis. Per-protocol analysis. Comment: in both studies slightly more participants in the comparator arm were excluded from the analysis. Reasons not stated. We judged this at unclear risk of bias.
Selective reporting (reporting bias)	Unclear risk	No data reported for clinical signs and symptoms, although this may have been included in the 'overall clinical status' evaluation. Comment: Insufficient information to permit a clear judgement.
Other bias	High risk	Two investigators were employed by Syntex Research, a research orientated pharmaceutical company and developer of sulconazole. Comment: A potential risk of bias cannot be excluded

Thomas 1976

Methods	Randomised, double-blind, active-controlled trial Setting Industrial Medical Centre, Cardiff, UK Date of study Not reported. Duration of the study 4 weeks with follow-up at 8 weeks
Participants	N = 30 (all male) Mean age = 43 years **Inclusion criteria of the trial** • suspected tinea pedis or tinea cruris confirmed by KOH and culture **Exclusion criteria of the trial** • not reported

Thomas 1976 *(Continued)*

	Randomised N = 30 Withdrawals/losses to follow-up • none reported Baseline data Diagnosis: Tinea pedis: clotrimazole (14), tolnaftate (8) Tinea cruris: clotrimazole (6), tolnaftate (10) Some participants had both areas affected
Interventions	**Intervention** • clotrimazole (1%) cream b.i.d. for 4 weeks (16) **Comparator** • tolnaftate (1%) cream b.i.d. for 4 weeks (14) The participants in this trial did not receive any other antifungal therapy.
Outcomes	Assessments (4): baseline, weeks 2, 4 and 8 **Outcomes of the trial** (as reported) 1. Clinical evaluation 2. Mycological evaluation (KOH and culture) 3. Adverse events# Denotes outcomes prespecified for this review
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote (page 631): "..were allocated treatment, according to a previously randomised treatment list." Comment: Probably done.
Allocation concealment (selection bias)	Unclear risk	The method used to conceal the allocation sequence, that is to determine whether intervention allocations could have been foreseen in advance of, or during, enrolment, was not reported. Comment: There was insufficient information to permit a clear judgement.
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote (page 631): "The creams were practically indistinguishable and were dispensed in identical, plain, sealed containers labelled A or B". Comment: The report provided sufficient detail about the measures used to blind study participants and personnel from knowledge of which intervention a participant received, to permit a clear judgement.
Blinding of outcome assessment (detection bias)	Low risk	Blinding of outcomes assessors, key personnel and participants was ensured, and it was unlikely that the blinding could have been broken.

Thomas 1976 *(Continued)*

All outcomes		Comment: We judged this as at a low risk of bias.
Incomplete outcome data (attrition bias) All outcomes	Low risk	No losses to follow-up reported. Comment: We judged this as at a low risk of bias.
Selective reporting (reporting bias)	Low risk	The protocol for the study was not available, but the prespecified outcomes and those mentioned in the methods section appeared to have been reported. Comment: We judged this as at a low risk of bias.
Other bias	Unclear risk	Quote (page 633): ".. thanks to Bayer U.K. Pharmaceutical Division for providing the materials to carry out this trial". Clotrimazole is manufactured by Bayer. Comment: Insufficient information to assess whether important risk of bias exists.

Thomas 1986

Methods	Randomised, single-blind, active-controlled trial Setting Medical centre, Wales, UK Date of study Not reported. Duration of intervention 21 days with follow-up at 7 weeks
Participants	N = 106 (all male) Mean age = 43 years **Inclusion criteria of the trial** • participants with suspected tinea pedis or cruris confirmed by mycology **Exclusion criteria of the trial** • not reported Randomised N = 106 Withdrawals/losses to follow-up • bifonazole (6), sulconazole (3) defaulted completely Baseline data Mycology positive: bifonazole (18), sulconazole (20) Tinea cruris positive mycology: bifonazole (1), sulconazole (1) Mycology negative: bifonazole (32), sulconazole (38) Data inconsistent/incorrectly reported (total 108)
Interventions	**Intervention** • bifonazole (1%) gel once daily for 21 days (52)

Thomas 1986 *(Continued)*

	Comparator • sulconazole (1%) cream b.i.d. for 21 days (54)
Outcomes	Assessments (4): baseline, weeks 1, 2, 3 and 7 **Outcomes of the trial** (as reported) 1. Clinical evaluation of signs and symptoms (erythema, maceration, fissuring): 4-point Likert scale# 2. Investigators' assessment of efficacy 3. Mycological evaluation (KOH and culture) 4. Tolerability and acceptability Denotes outcomes prespecified for this review
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote (page 70): "randomised code.." Comment: Insufficient detail was reported about the method used to generate the allocation sequence to allow a clear assessment of whether it would produce comparable groups.
Allocation concealment (selection bias)	Unclear risk	The method used to conceal the allocation sequence, that is to determine whether intervention allocations could have been foreseen in advance of, or during, enrolment, was not reported. Comment: There was insufficient information to permit a clear judgement.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote (page 70): "..single-blind.. and "each patient was given an identical box" Comment: The report provided sufficient detail about the measures used to blind study the personnel from knowledge of which intervention a participant received, to permit a clear judgement. However as bifonazole was applied as a gel once daily and sulconazole as a cream b.i.d. the participants were not blinded to the interventions and might have broken the code to the physician. We judged this as at unclear risk of bias.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Both investigators and participants were outcome assessors. The participants were not blinded and therefore the blinding can be broken. We judged this as at unclear risk of bias.
Incomplete outcome data (attrition bias) All outcomes	Low risk	9/106 (8%) were excluded from the analysis. Per-protocol analysis. Comment. Low and balanced number of drop-outs and although analysed per-protocol we judged this as at a low risk of bias.
Selective reporting (reporting bias)	Low risk	The protocol for the study was not available, but the prespecified outcomes and those mentioned in the methods section appeared to have been reported. Comment: We judged this as at a low risk of bias.
Other bias	Unclear risk	Quote (page 75): "Bayer UK Limited organising the supply of clinical materials, questionnaires and trial records". Comment: Insufficient information to assess whether important risk of bias exists.

Thulin 1975

Methods	Randomised, open, active-controlled study Setting Department of Dermatology, Marselisborg Hospital, Aarhus, Denmark Date of study October 1971-October 1972. Duration of the intervention 4 weeks
Participants	N = 94 (age and gender unreported) **Inclusion criteria of the trial** • dermatophytosis or tinea versicolor **Exclusion criteria of the trial** • participants with tinea capitis • use of griseofulvin < 4 weeks prior to entry of the study • use of topical antifungal < 24 hours prior to mycological evaluation Randomised N = 94 Withdrawals/losses to follow-up • 28/94 (30%), unclear from which groups Baseline data Data only on those who completed study Dermatophytosis group: miconazole (21), tolnaftate (18) Face: miconazole (1), tolnaftate (1) Trunk and upper extremities: miconazole (2), tolnaftate (3) Crural folds: miconazole (8), tolnaftate (7) Feet: miconazole (10), tolnaftate (7) Tinea versicolor group: miconazole (14), dixanthogen (13)
Interventions	**Intervention** • miconazole (2%) cream b.i.d. for 4 weeks (35) **Comparator 1** • tolnaftate (2%) lotion b.i.d. for 4 weeks for participants with dermatophytosis (18) **Comparator 2** • dixanthogen (2%) in petrolatum b.i.d. for 4 weeks for participants with tinea versicolor (13)
Outcomes	Assessments (5): baseline, weeks, 1, 2, 3 and 4 **Outcomes of the trial** (as reported) 1. Clinical evaluation: 3-point Likert scale#

Thulin 1975 *(Continued)*

2. Mycological evaluation (KOH and culture)
3. Adverse events#

Denotes outcomes prespecified for this review

Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote (page 250): "..the patients were randomized to four different groups" Comment: Insufficient detail was reported about the method used to generate the allocation sequence to allow a clear assessment of whether it would produce comparable groups.
Allocation concealment (selection bias)	Unclear risk	The method used to conceal the allocation sequence, that is to determine whether intervention allocations could have been foreseen in advance of, or during, enrolment, was not reported. Comment: There was insufficient information to permit a clear judgement.
Blinding of participants and personnel (performance bias) All outcomes	High risk	Quote (page 250): "..open-study..". Comment: The outcome was likely to be influenced by the lack of blinding.
Blinding of outcome assessment (detection bias) All outcomes	High risk	Quote (page 250): "..open-study..". Comment: The outcome measurement was likely to be influenced by the lack of blinding.
Incomplete outcome data (attrition bias) All outcomes	High risk	28/94 (30%), unclear from which groups excluded in the analysis, reasons unreported. Per-protocol analysis. Comment: We judged this as at a high risk of bias.
Selective reporting (reporting bias)	Low risk	The protocol for the study was not available, but the prespecified outcomes and those mentioned in the methods section appeared to have been reported. Comment: We judged this as at a low risk of bias.
Other bias	Low risk	The study appears to be free from other forms of bias.

Tronnier 1987

Methods	Randomised, double-blind, active-controlled trial Setting Department of Dermatology, Dortmund Municipal Hospitals, Germany Date of study Not reported. Duration of the intervention 4 weeks with follow-up at 8 weeks
Participants	N = 62 (36 male/21 female; 5 gender unreported) Mean age = 40 years

Tronnier 1987 *(Continued)*

Inclusion criteria of the trial

- inflammatory eczematous dermatomycoses confirmed by KOH and culture

Exclusion criteria of the trial

- systemic antifungal < 4 weeks prior to study entry 'and' or 'or' topical antifungal or corticosteroid < 7 days prior to study entry
- contraindication to corticosteroid therapy

Randomised

N = 62

Withdrawals/losses to follow-up

- 5/62; naftifine (3/31), econazole/triamcinolone (2/31)

Baseline data
Location:

Arms: naftifine (2), econazole/triamcinolone (3)
Trunk: naftifine (2), econazole/triamcinolone (3)
Feet: naftifine (12), econazole/triamcinolone (10)
Hands: naftifine (4), econazole/triamcinolone (1)

Inguinal region: naftifine (8), econazole/triamcinolone (10)
Buttocks: naftifine (3), econazole/triamcinolone (1)
Other: naftifine (3), econazole/triamcinolone (5)

Interventions	**Intervention** • naftifine (1%) cream b.i.d. for 4 weeks (31) **Comparator** • econazole (1%)/triamcinolone b.i.d. for 2 weeks, followed by econazole (1%) for 2 weeks (31)
Outcomes	Assessments (7): baseline, days 4, 7, weeks 2, 3, 4 and 8 **Outcomes of the trial** (as reported) 1. Clinical evaluation of signs and symptoms (erythema, scaling, vesiculation, pustulation, papulation, exudation, infiltration, maceration, pruritus): 7-point Likert scale# 2. Mycological evaluation (KOH and culture) 3. Adverse events: 4-point Likert scale# Denotes outcomes prespecified for this review
Notes	Tinea cruris and corporis possibly included, but unreported. Old trial. See Table 3

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote (page 79): ".. were randomly allocated.." Comment: Insufficient detail was reported about the method used to generate the allocation sequence to allow a clear assessment of whether it would produce comparable groups.

Tronnier 1987 *(Continued)*

Allocation concealment (selection bias)	Unclear risk	The method used to conceal the allocation sequence, that is to determine whether intervention allocations could have been foreseen in advance of, or during, enrolment, was not reported. Comment: There was insufficient information to permit a clear judgement.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote (page 78): ".. double-blind..". Comment: The report did not provide sufficient detail about the specific measures used to blind study participants and personnel from knowledge of which intervention a participant received, to permit a clear judgement.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Comment: Uncertainty with the effectiveness of blinding of outcomes assessors (participants/healthcare providers) during the study. Insufficient information to permit a clear judgement.
Incomplete outcome data (attrition bias) All outcomes	Low risk	Lost to follow-up/drop-outs: 5/62, naftifine (3/31), econazole/triamcinolone (2/31) Comment: We judged this as at a low risk of bias.
Selective reporting (reporting bias)	Low risk	The protocol for the study was not available, but the prespecified outcomes and those mentioned in the methods section appeared to have been reported. Comment: We judged this as at a low risk of bias.
Other bias	Low risk	The study appears to be free from other forms of bias.

van Heerden 1997

Methods	Randomised, double-blind, placebo-controlled trial Setting Multicentre (6 General Practices), South Africa Date of study Not reported. Duration of the intervention 1 week with follow-up to 8 weeks
Participants	N = 83 (48 male/13 female; 22 gender unreported) Mean age = 39, range 16-79 years **Inclusion criteria of the trial** • clinically diagnosed tinea corporis/cruris confirmed by KOH and culture • women of childbearing age should use reliable contraceptive measures **Exclusion criteria of the trial** • radiation therapy • systemic therapy with cytostatic or immunosuppressive drugs < 2 weeks prior to study entry • topical antifungals < 2 weeks prior to study entry, systemic antifungals < 6 weeks prior to study entry • presence of other dermatomycosis, requiring treatment • pregnancy or breast feeding • use of another investigational drug < 8 weeks prior to study entry • history of drug or alcohol abuse • history of severe adverse reactions or hypersensitivity to any drug • immuno deficiency

van Heerden 1997 *(Continued)*

	Randomised N = 83 Delayed exclusions: terbinafine (10), placebo (10) delayed exclusion criteria, reasons unreported. Withdrawals/losses to follow-up • terbinafine group (1) failed to comply with post-baseline safety assessment • 27 in terbinafine group and 33 in vehicle group attended week-2 visit Baseline data Not reported
Interventions	**Intervention** • terbinafine (1%) gel once daily for 1 week (29) **Comparator** • vehicle gel once daily for 1 week (33)
Outcomes	Assessments (5): baseline, weeks 1, 2, 4 and 8 **Outcomes of the trial** (as reported) 1. Clinical evaluation of signs and symptoms 2. Mycological evaluation (KOH and culture) 3. Effective treatment 4. Subjective assessment of investigator of overall efficacy 5. Adverse events# 6. Tolerability assessed by investigator Denotes outcomes prespecified for this review
Notes	See Table 1

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote (page 15): ".. randomly assigned.." Comment: Insufficient detail was reported about the method used to generate the allocation sequence to allow a clear assessment of whether it would produce comparable groups.
Allocation concealment (selection bias)	Unclear risk	The method used to conceal the allocation sequence, that is to determine whether intervention allocations could have been foreseen in advance of, or during, enrolment, was not reported. Comment: There was insufficient information to permit a clear judgement.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote (page 15): ".. double-blind..". Comment: The report did not provide sufficient detail about the specific measures used to blind study participants and personnel from knowledge of which intervention a participant received, to permit a clear judgement.
Blinding of outcome assessment (detection bias)	Unclear risk	Comment: Uncertainty with the effectiveness of blinding of outcomes assessors (participants/healthcare providers) during the study.

van Heerden 1997 *(Continued)*

All outcomes		Insufficient information to permit a clear judgement.
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Quote (page 16): " ..the ITT analysis comprised 29 subjects receiving Lamisil and 33 subjects receiving placebo". 83 randomised, 62 analysed. Delayed exclusions due to delayed exclusion criteria (no further details): terbinafine (10/40), placebo (10/43): = 20/83 (24%) Lost to follow-up: terbinafine (1/40), failed to comply with post-baseline safety assessment Comment: The delayed exclusions were well-balanced between groups but reasons unreported. See ICH Expert Working Group 1998. We judged this as at a unclear risk of bias.
Selective reporting (reporting bias)	Low risk	The protocol for the study was not available, but the prespecified outcomes and those mentioned in the methods section appeared to have been reported. Comment: We judged this as at a low risk of bias.
Other bias	Low risk	The study appears to be free from other forms of bias.

Vander Ploeg 1984

Methods	Randomised, active-controlled trial Setting Division of Dermatology, University of Texas Health Science Center, San Antonio, TX, USA Date of study Not reported. Duration of intervention 4 weeks with follow-up at 8 weeks
Participants	N = 77 (48 male/29 female) Mean age = 42, range 18-72 years **Inclusion criteria of the trial** • men and non-pregnant women > 18 years with mycologically proven infection with one of the following fungi:Trichophyton sp, Microsporum sp, Epidermophyton sp, Candida sp, and Pityrosporum orbiculare **Exclusion criteria of the trial** • participants with tinea pedis • use of griseofulvin < 8 weeks prior to study entry Randomised N = 77 Withdrawals/losses to follow-up • 8/77; tioconazole (3/38), miconazole (5/39) at end of study, reasons not reported Baseline data

Vander Ploeg 1984 *(Continued)*

	Diagnosis: Tinea corporis: tioconazole (10), miconazole (6) Tinea cruris: tioconazole (7), miconazole (10) Tinea manuum: tioconazole (11), miconazole (5) Cutaneous candidiasis: tioconazole (2), miconazole (5) Tinea versicolor: tioconazole (7), miconazole (10)
Interventions	**Intervention** • tioconazole (1%) cream b.i.d. for 4 weeks (38) **Comparator** • miconazole (2%) cream b.i.d. for 4 weeks (39)
Outcomes	Assessments (6): baseline, weeks 1, 2, 3, 4 and 8 **Outcomes of the trial** (as reported) 1. Clinical evaluation: 3-point Likert scale# 2. Mycological evaluation (KOH and culture) 3. Relapse 4. Routine haematology, chemistry, and urine studies 5. Adverse events# Denotes outcomes prespecified for this review
Notes	We only included data of participants with tinea cruris and corporis.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote (page 681): "..were randomly assigned.." Comment: Insufficient detail was reported about the method used to generate the allocation sequence to allow a clear assessment of whether it would produce comparable groups.
Allocation concealment (selection bias)	Unclear risk	The method used to conceal the allocation sequence, that is to determine whether intervention allocations could have been foreseen in advance of, or during, enrolment, was not reported. Comment: There was insufficient information to permit a clear judgement.
Blinding of participants and personnel (performance bias) All outcomes	High risk	Nothing reported on the measures used to blind participants or personnel Comment: The outcome was likely to be influenced by the lack of blinding.
Blinding of outcome assessment (detection bias) All outcomes	High risk	Nothing reported on the measures used to blind participants or personnel in outcomes assessment Comment: The outcome measurement was likely to be influenced by the lack of blinding.

Vander Ploeg 1984 *(Continued)*

Incomplete outcome data (attrition bias) All outcomes	Low risk	Missing data 8/77 (10%): tioconazole (3/38), miconazole (5/39), at end of study Comment: Low number and judged as at a low risk of bias.
Selective reporting (reporting bias)	Low risk	The protocol for the study was not available, but the prespecified outcomes and those mentioned in the methods section appeared to have been reported. Comment: We judged this as at a low risk of bias.
Other bias	Low risk	The study appears to be free from other forms of bias.

VanDersarl 1977

Methods	Randomised, double-blind, active-controlled study Setting Department of Medicine, USAF Medical Center, Keesler AFB, USA Date of study Not reported. Duration of intervention 2 weeks with follow-up to 6 weeks
Participants	N = 80 (all male) Mean age = not reported **Inclusion criteria of the trial** • clinical evidence of tinea cruris confirmed by KOH and culture **Exclusion criteria of the trial** • topical or systemic anti-infective or anti-inflammatory treatment < 2 weeks prior to study entry Randomised N = 80 Withdrawals/losses to follow-up • 14/80 (18%): clotrimazole (6/40) and haloprogin (8/40) due to protocol violations (non-compliance) Baseline data Not reported
Interventions	**Intervention** • clotrimazole (1%) lotion b.i.d. for 2 weeks (40) **Comparator** • haloprogin (1%) lotion b.i.d. for 2 weeks (40) No other topical or systemic anti-infective or anti-inflammatory drugs were allowed during the study
Outcomes	Assessments (4): baseline, weeks 1, 2 and 6 **Outcomes of the trial** (as reported) 1. Mycological evaluation (KOH and culture)

VanDersarl 1977 *(Continued)*

2. Clinical evaluation (objective signs of the disease, and participant's subjective evaluation): 4-point Likert scale#
3. Adverse events#

Denotes outcomes prespecified for this review

Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote (page 1233): "..were assigned to the patients...at random.." Comment: Insufficient detail was reported about the method used to generate the allocation sequence to allow a clear assessment of whether it would produce comparable groups.
Allocation concealment (selection bias)	Unclear risk	The method used to conceal the allocation sequence, that is to determine whether intervention allocations could have been foreseen in advance of, or during, enrolment, was not reported. Comment: There was insufficient information to permit a clear judgement.
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote (page 1233): "The medications were packed in identical containers that were numbered consecutively, but labelled identically otherwise". Comment: Blinding was ensured we judged this as at a low risk of bias.
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Blinding of the outcomes assessors, key personnel, was ensured, and it was unlikely that the blinding could have been broken. Comment: We judged this as at a low risk of bias.
Incomplete outcome data (attrition bias) All outcomes	High risk	14/80 (18%) due to protocol violations (non-compliance). Per-protocol analysis. Comment: We judged this as at a high risk of bias.
Selective reporting (reporting bias)	Low risk	The protocol for the study was not available, but the prespecified outcomes and those mentioned in the methods section appeared to have been reported. Comment: We judged this as at a low risk of bias.
Other bias	Low risk	The study appears to be free from other forms of bias.

Vannini 1988

Methods	Randomised, double-blind, active-controlled trial Setting Mycological department of the University Dermatology clinic, Florence, Italy Date of study Not reported. Duration of intervention 3 weeks
Participants	N = 60 (gender not reported)

Vannini 1988 *(Continued)*

	Mean age = 35-41 years **Inclusion criteria of the trial** • >18 years, suffering from superficial mycoses, Candida infections and tinea versicolor **Exclusion criteria of the trial** • not reported Randomised N = 60 Withdrawals/losses to follow-up • no losses reported Baseline data Diagnosis: Tinea corporis: fenticonazole b.i.d. (4), fenticonazole once daily (4), miconazole b.i.d. (3) Tinea cruris: fenticonazole b.i.d. (2), fenticonazole once daily (4), miconazole b.i.d. (2) Tinea pedis: fenticonazole b.i.d. (1), fenticonazole once daily (4), miconazole b.i.d. (0) Candidosis: fenticonazole b.i.d. (6), fenticonazole once daily (7), miconazole b.i.d. (7) Pityriasis versicolor: fenticonazole b.i.d. (7), fenticonazole once daily (5), miconazole b.i.d. (8)
Interventions	**Intervention** • fenticonazole (2%) cream b.i.d. for 3 weeks (20) **Comparator 1** • fenticonazole (2%) cream once daily for 3 weeks (20) **Comparator 2** • miconazole (2%) cream b.i.d. for 3 weeks (20) No other concomitant topical treatments or systemic antifungal treatments were allowed
Outcomes	Assessments (4): baseline, weeks 1, 2 and 3 **Outcomes of the trial** (as reported) 1. Clinical evaluation of signs and symptoms (itching, burning, erythema, oedema, desquamation, dis-colouration): 4-point Likert scale# 2. Clinical status: 5-point Likert scale# 3. Mycological evaluation (KOH and culture) 4. Final overall judgement on efficacy: 5-point Likert scale# 5. Adverse events# Denotes outcomes prespecified for this review
Notes	We only include and report on data from participants with tinea corporis or cruris. The results are not provided separately per diagnosis, but per causative micro-organism. See Table 3
Risk of bias	

Vannini 1988 *(Continued)*

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote (page 281): "..were randomly assigned..". Comment: Insufficient detail was reported about the method used to generate the allocation sequence to allow a clear assessment of whether it would produce comparable groups.
Allocation concealment (selection bias)	Unclear risk	The method used to conceal the allocation sequence, that is to determine whether intervention allocations could have been foreseen in advance of, or during, enrolment, was not reported. Comment: There was insufficient information to permit a clear judgement.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote (page 281): "Treatments were fully blinded and patients on once daily applications had an identical placebo cream applied in the morning..". Comment: Although attempts were made to blind participants who were on different daily regimens it was unclear how effective the intended blinding was.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote (page 281): "Treatments were fully blinded and patients on once daily applications had an identical placebo cream applied in the morning..". Comment: Although attempts were made to blind participants who were on different daily regimens, the impact on outcome assessment remains unclear.
Incomplete outcome data (attrition bias) All outcomes	Low risk	No losses to follow-up reported. Comment: We judged this at low risk of bias.
Selective reporting (reporting bias)	Low risk	The protocol for the study was not available, but the prespecified outcomes and those mentioned in the methods section appeared to have been reported. Comment: We judged this as at a low risk of bias.
Other bias	Low risk	The study appears to be free of other forms of bias.

Vena 1983

Methods	Randomised, "simple-blind", active-controlled, within-patient comparison trial Setting Dermatology Department, University of Bari, Italy Date of study Not reported. Duration of intervention 2 weeks with follow-up to 6 weeks
Participants	N = 30 (24 male/6 female) Age range 16-78, median age = 37 years **Inclusion criteria of the trial** • bilateral, symmetric tinea cruris **Exclusion criteria of the trial**

Vena 1983 *(Continued)*

	• treatment < 3 weeks prior to study entry Randomised N = 30 Withdrawals/losses to follow-up • none reported Baseline data Not reported
Interventions	**Intervention** • bifonazole (1%) cream once a day for two weeks **Comparator** • miconazole (2%) cream b.i.d. for 2 weeks No other antimycotics were allowed during the study
Outcomes	Assessments (4): baseline, weeks 1,2, 4 and 6 **Outcomes of the trial** (as reported) 1. Clinical evaluation of signs and symptoms (itching, burning, erythema, exudation, vesicle formation, desquamation) 2. Mycological evaluation (KOH and culture) 3. Adverse events# Denotes outcomes prespecified for this review
Notes	The report also includes a study in participants with pityriasis versicolor.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote (page 417): "..upon proper randomization.." Comment: Insufficient detail was reported about the method used to generate the allocation sequence to allow a clear assessment of whether it would produce comparable groups.
Allocation concealment (selection bias)	Unclear risk	Not applicable, as it is a within-participant design.
Blinding of participants and personnel (performance bias) All outcomes	High risk	Quote (page 417): ".. simple-blind..". Comment: As the participants were not blinded, it is very likely that the blinding have been broken for the investigators.
Blinding of outcome assessment (detection bias) All outcomes	High risk	Comment: Likely that the blinding may have been broken for the outcomes assessors (participants/healthcare providers) during the study. We judged this as at high risk of bias.
Incomplete outcome data (attrition bias)	Unclear risk	Limited data reported, but there was no indication of missing outcome data. Comment: There was insufficient information to permit a clear judgement.

Vena 1983 *(Continued)*
All outcomes

Selective reporting (reporting bias)	Low risk	The protocol for the study was not available, but the prespecified outcomes and those mentioned in the methods section appeared to have been reported. Comment: We judged this as at a low risk of bias.
Other bias	High risk	One investigator was employed by Bayer, the manufacturer of bifonazole and miconazole. Comment: A potential risk of bias cannot be excluded.

Viayna 2003

Methods	Randomised, double-blind, active-controlled trial Setting Multi-centre, Spain Date of study Not reported. Duration of the intervention 4 weeks with follow-up to 8 weeks
Participants	N = 653 (age and gender unreported) **Inclusion criteria of the trial** • adult patients with tinea pedis, tinea corporis 'and' or 'or' tinea cruris **Exclusion criteria of the trial** • not reported Randomised N = 653 Delayed exclusions: • 284/653 (43%): negative culture for dermatophytes; eberconazole (140); miconazole (144) Withdrawals/losses to follow-up • 9/653: reported as "major deviations"; eberconazole (4); miconazole (5) Baseline data Not reported
Interventions	**Intervention** • eberconazole (1%) cream b.i.d. for 4 weeks (184) **Comparator** • miconazole (2%) cream b.i.d. for 4 weeks (176)
Outcomes	Assessments (4): baseline, weeks 2, 4 and 8 **Outcomes of the trial** (as reported)

Viayna 2003 *(Continued)*

1. Mycological evaluation (culture)
2. Clinical evaluation
3. Adverse events#

Denotes outcomes prespecified for this review

Notes	Abstract, limited data reporting. See Table 3

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote (page 104): "..were randomized.." Comment: Insufficient detail was reported about the method used to generate the allocation sequence to allow a clear assessment of whether it would produce comparable groups. After e-mail contact: "According to the protocol patients were distributed and randomly assigned to two treatment groups by computerized randomization of blocks of 4." Comment: Probably done.
Allocation concealment (selection bias)	Low risk	The method used to conceal the allocation sequence, that is to determine whether intervention allocations could have been foreseen in advance of, or during, enrolment, was not reported. Comment: There was insufficient information to permit a clear judgement. After e-mail contact: "Sequentially numbered drug containers of identical appearance" Comment: Probably done.
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote (page 104): ".. double-blind..". Comment: The report did not provide sufficient detail about the specific measures used to blind study participants and personnel from knowledge of which intervention a participant received, to permit a clear judgement. After e-mail contact: "The experimental treatment, 1% eberconazole cream, was provided in properly labelled 60-g tubes. The control treatment, 2% miconazole cream, was provided by Laboratorios Esteve and repackaged and properly labelled for the clinical trial by Laboratorios SALVAT, S.A. Both treatments were labelled with the same information in order to maintain the double blind." Comment: The report provided sufficient detail about the measures used to blind study participants and personnel from knowledge of which intervention a participant received, to permit a clear judgement.
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Comment: Uncertainty with the effectiveness of blinding of outcomes assessors (participants/healthcare providers) during the study. Insufficient information to permit a clear judgement. After e-mail contact: Outcomes were investigator-assessed as well as participant assessed. Blinding of participants and key study personnel was ensured, and it is unlikely that the blinding could have been broken. Comment: We judged this as at a low risk of bias.

Viayna 2003 *(Continued)*

Incomplete outcome data (attrition bias) All outcomes	Low risk	653 randomised, 360 analysed. Losses after randomisation due to negative baseline culture: 284/653 (43%), unclear how many from each group. Failed to attend for follow-up: 9/653 due to major deviations, unclear how many from each group. Comment: Unclear how many from each group were excluded from the analysis, therefore unclear if there is any attrition bias between the groups. After e-mail contact: Losses after randomisation due to negative baseline culture: 140 eberconazole (1%), 144 miconazole (2%), and 4 in eberconazole group and 5 in miconazole group failed to attend for follow-up. Comment: Entry criterion (culture specimen) measured prior to randomisation. The delayed exclusions are well-balanced between groups, no attrition bias between the groups. See ICH Expert Working Group 1998. Low and balanced number of drop-outs at follow-up, and although per- protocol analysis considered to be at low risk of bias.
Selective reporting (reporting bias)	Low risk	The protocol for the study was not available, but the prespecified outcomes and those mentioned in the methods section appeared to have been reported. Comment: We judged this as at a low risk of bias.
Other bias	High risk	One or more authors were employed by Laboratorios SALVAT, S.A. Barcelona, Spain, the manufacturer of eberconazole. Comment: A potential risk of bias cannot be excluded.

Voravutinon 1993

Methods	Randomised, double-blinded, active-controlled trial Setting Department of Medicine, Faculty of Medicine Prince of Songkhla University, Hatyai, Songkhla, Thailand Date of study Not reported. Duration of intervention 4 weeks with follow-up at 8 weeks
Participants	N = 96 (45 male/41 female;10 gender unknown) Mean age = 34 years **Inclusion criteria of the trial** • tinea cruris and corporis confirmed by KOH and culture • > 16 years • size of lesions less than 100 cm^2 **Exclusion criteria of the trial** • lesions on the scalp, feet and nails Randomised N = 96 Withdrawals/losses to follow-up

Voravutinon 1993 *(Continued)*

- 10/96 (10%); Whitfield group (4), miconazole group (6)

Baseline data

Localisation:

Trunk: Whitfield group (29), miconazole group (24)
Groin: Whitfield group (12), miconazole group (15)
Trunk and groin: Whitfield group (3), miconazole group (3)

Interventions	**Intervention** • Whitfield's ointment four times a day for 4 weeks (48) **Comparator** • miconazole (2%) cream four times a day for 4 weeks (48)
Outcomes	Assessments (4): baseline, weeks 2, 4 and 8 **Outcomes of the trial** (as reported) 1. Clinical improvement: 4-point Likert scale# 2. Mycological evaluation (KOH and culture) 3. Adverse events# Denotes outcomes prespecified for this review
Notes	Translated from the Thai by Chinmanat Tangjaturonrusamee with additional details obtained from trial investigator.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote (page 1): "randomised". Comment: Insufficient detail was reported about the method used to generate the allocation sequence to allow a clear assessment of whether it would produce comparable groups.
Allocation concealment (selection bias)	Low risk	After contact with the investigator the allocation appeared to be pharmacy controlled and therefore the method used to conceal the allocation sequence, that is to determine whether intervention allocations could have been foreseen in advance of, or during, enrolment, seems adequate.
Blinding of participants and personnel (performance bias) All outcomes	Low risk	A pharmacist at the Prince of Songkla University prepared both medications, in the same package and arranged by code prior to patients' visits. They were distributed to patients by the pharmacist. Comment: The report provided sufficient detail about the measures used to blind study participants and personnel from knowledge of which intervention a participant received, to permit a clear judgement.
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Outcomes were investigator-assessed as well as participant assessed. Blinding of participants and key study personnel was ensured, and it is unlikely that the blinding could have been broken. Comment: We judged this as at a low risk of bias.

Voravutinon 1993 *(Continued)*

Incomplete outcome data (attrition bias) All outcomes	Low risk	10/96(10%). Per-protocol analysis. Comment: Low and balanced number of drop-out across groups and although per-protocol analysis judged as at low risk of bias
Selective reporting (reporting bias)	Low risk	The protocol for the study was not available, but the prespecified outcomes and those mentioned in the methods section appeared to have been reported. Comment: We judged this as at a low risk of bias.
Other bias	Low risk	The study appears to be free of other forms of bias.

Wagner 1987

Methods	Randomised, double-blind, active-controlled trial Setting Multi-centre (12), Germany Date of study Not reported. Duration of the intervention 25 days with follow-up at 8 weeks
Participants	N = 204 (153 male/51 female) Mean age = 40 years **Inclusion criteria of the trial** • participants with dermatomycoses or erythrasma **Exclusion criteria of the trial** • pregnancy • negative at culture • hypersensitivity to imidazoles • if bacterial superinfection predominates • onychomycosis or tinea capitis • other antimycotic < prior 2 weeks Randomised N = 204 Withdrawals/losses to follow-up 31/204 (15%) • treatment failure: oxiconazole (3), bifonazole (2) • adverse events: oxiconazole (1), bifonazole (3) • cured: oxiconazole (4), bifonazole (2) • no compliance: oxiconazole (7), bifonazole (4) • other reasons: oxiconazole (3), bifonazole (2) Baseline data Diagnosis: Erythrasma: oxiconazole (43), bifonazole (43)

Wagner 1987 *(Continued)*

	Dermatomycosis: oxiconazole (61), bifonazole (55) Pityriasis versicolor: oxiconazole (1), bifonazole (1)
Interventions	**Intervention** • oxiconazole (1%) once a day for 25 days (105) **Comparator** • bifonazole (1%) once a day for 25 days (99)
Outcomes	Assessments (9): baseline, weeks 1-8 **Outcomes of the trial** (as reported) 1. Clinical evaluation of signs and symptoms: 4-point Likert scale# 2. Mycological evaluation (KOH, culture, Woods lamp)# 3. Adverse events# Denotes outcomes prespecified for this review
Notes	Number of participants with tinea corporis or cruris unclear. In table 5 it states tinea corporis: oxiconazole (9), bifonazole (9), and tinea cruris: oxiconazole (15), bifonazole (14), but numbers do not add-up with diagnoses made under baseline data. See Table 3

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote (page (485): "..randomisierten.." Comment: Insufficient detail was reported about the method used to generate the allocation sequence to allow a clear assessment of whether it would produce comparable groups.
Allocation concealment (selection bias)	Unclear risk	The method used to conceal the allocation sequence, that is to determine whether intervention allocations could have been foreseen in advance of, or during, enrolment, was not reported. Comment: There was insufficient information to permit a clear judgement.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote (page 484): "..doppelblinden.." Comment: The report did not provide sufficient detail about the specific measures used to blind study participants and personnel from knowledge of which intervention a participant received, to permit a clear judgement.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Comment: Uncertainty with the effectiveness of blinding of outcomes assessors (participants/healthcare providers) during the study. Insufficient information to permit a clear judgement.
Incomplete outcome data (attrition bias) All outcomes	Low risk	31/204 (15%), reasons reported and intention-to-treat analysis. Comment: We judged this as at low risk of bias.
Selective reporting (reporting bias)	Low risk	The protocol for the study was not available, but the prespecified outcomes and those mentioned in the methods section appeared to have been reported. Comment: We judged this as at a low risk of bias.

Wagner 1987 *(Continued)*

Other bias	High risk	Second author was employed by Hoffman la Roche, the manufacturer of oxiconazole. Comment: A potential risk of bias cannot be excluded.

Wang 1995

Methods	Randomised, double-blind, active-controlled trial Setting Department of Dermatology, Beijing Medical University in China Date of study Not reported. Duration of intervention 1-2 weeks with 2 weeks follow-up
Participants	N = 75 (57 male/18 female) Mean age = 38 years **Inclusion criteria of the trial** • tinea corporis and tinea cruris confirmed by KOH • > 15 years **Exclusion criteria of the trial** • allergy to allylamine • pregnant or lactating women • anti-fungal medicines during the last 4 weeks (orally) or during the last 2 weeks (cream) Randomised N = 75 Withdrawals/losses to follow-up • 1/75 (1%) in terbinafine group, due to stinging Baseline data Tinea cruris: terbinafine (27), miconazole (20) Tinea corporis: terbinafine (18), miconazole (10)
Interventions	**Intervention** • terbinafine (1%) cream b.i.d. for 1 week (35) **Comparator** • terbinafine (1%) cream b.i.d. for 2 weeks (10) **Comparator** • miconazole (2%) cream b.i.d. for 2 weeks (30)
Outcomes	Assessments (3): baseline, end of therapy and 2-3 weeks after treatment **Outcomes of the trial** (as reported)

Wang 1995 *(Continued)*

1. Clinical evaluation of signs and symptoms (erythema, papules, vesicles, crust, scales and pruritus): 2-point scale#
2. Clinical efficacy: 2-point scale#
3. Laboratory tests
4. Mycological evaluation (KOH, culture, and fungal identification)
5. Adverse events#

Denotes outcomes prespecified for this review

Notes

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote (page 100): "randomised" Comment: Insufficient detail was reported about the method used to generate the allocation sequence to allow a clear assessment of whether it would produce comparable groups.
Allocation concealment (selection bias)	Unclear risk	The method used to conceal the allocation sequence, that is to determine whether intervention allocations could have been foreseen in advance of, or during, enrolment, was not reported. Comment: There was insufficient information to permit a clear judgement.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote (page 100): "double-blind". Comment: The report did not provide sufficient detail about the measures used to blind study participants and personnel from knowledge of which intervention a participant received, to permit a clear judgement.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote (page 100): "..double-blind..". Comment: Uncertainty with the effectiveness of blinding of outcomes assessors (participants/healthcare providers) during the study. Insufficient information to permit a clear judgement.
Incomplete outcome data (attrition bias) All outcomes	Low risk	1/75 dropped out. Intention-to-treat analysis Comment: We judged this as at a low risk of bias.
Selective reporting (reporting bias)	Low risk	The protocol for the study was not available, but the prespecified outcomes and those mentioned in the methods section appeared to have been reported. Comment: We judged this as at a low risk of bias.
Other bias	Low risk	The study appears to be free of other forms of bias.

Wang 2000

Methods	Randomised, double-blind, active-controlled trial Setting 2 departments of Dermatology, Jinan, China Date of study

Wang 2000 *(Continued)*

	Not reported. Duration of intervention 2-5 weeks
Participants	N = 210 (121 male/89 female) Mean age = 35 years **Inclusion criteria of the trial** • 15-70 years • clinical diagnosis of fungal infection with maceration and erosion **Exclusion criteria of the trial** • additional eczema, contact dermatitis, allergic dermatitis or bacterial infection • severe heart, liver, kidney disease, diabetes or mental patients • allergy to medicine • long-term use of glucocorticoid or immunosuppressant • oral anti-fungal medicines during the last 1 month or using anti-fungal cream during the last 2 weeks • pregnant or lactating women Randomised N = 210 Withdrawals/losses to follow-up • no drop-outs Baseline data Tinea manuum: terbinafine (6), miconazole (6) Tinea pedis: terbinafine (68), miconazole (71) Tinea corporis: terbinafine (4), miconazole (5) Tinea cruris: terbinafine (26), miconazole (24)
Interventions	**Intervention** • terbinafine (1%) powder b.i.d. for 2-3 weeks (104) **Comparator** • miconazole (2%) powder b.i.d. for 2-5 weeks (106)
Outcomes	**Outcomes of the trial** (as reported) 1. Clinical evaluation of signs and symptoms (erythema, papules, vesicles, maceration, erosion, scales and pruritus): 4-point Likert scale# 2. Clinical efficacy: 4-point Likert scale# 3. Mycological evaluation (KOH, culture and fungal identification) 4. Adverse events# 5. Determination of minimum inhibitory concentration Denotes outcomes prespecified for this review
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement

Wang 2000 *(Continued)*

Random sequence generation (selection bias)	Unclear risk	Quote (page 265): "randomised". Comment: Insufficient detail was reported about the method used to generate the allocation sequence to allow a clear assessment of whether it would produce comparable groups.
Allocation concealment (selection bias)	Unclear risk	The method used to conceal the allocation sequence, that is to determine whether intervention allocations could have been foreseen in advance of, or during, enrolment, was not reported. Comment: There was insufficient information to permit a clear judgement.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote (page 346): "double-blind". Comment: The report did not provide sufficient detail about the measures used to blind study participants and personnel from knowledge of which intervention a participant received, to permit a clear judgement.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote (page 346): "..double-blind..". Comment: Uncertainty with the effectiveness of blinding of outcomes assessors (participants/healthcare providers) during the study. Insufficient information to permit a clear judgement.
Incomplete outcome data (attrition bias) All outcomes	Low risk	No drop-outs reported. Intention-to-treat analysis. Comment: We judged this as at a low risk of bias
Selective reporting (reporting bias)	Low risk	The protocol for the study was not available, but the prespecified outcomes and those mentioned in the methods section appeared to have been reported. Comment: We judged this as at a low risk of bias.
Other bias	Low risk	The study appears to be free from other forms of bias.

Wang 2000a

Methods	Randomised, double-blind, active-controlled trial Setting Multi-centre in China Date of study Not reported. Duration of intervention 2 weeks with 2 weeks follow-up for tinea corporis/cruris
Participants	N = 162 (120 male/19 female; 23 gender unreported) Mean age = 40 years for tinea corporis/cruris group and 26 years for tinea pedis group **Inclusion criteria of the trial** • participants with tinea pedis 'and' or 'or' tinea corporis/cruris confirmed by KOH **Exclusion criteria of the trial** • pregnant or lactating women • allergy to medicine • severe systemic disease

Wang 2000a *(Continued)*

- oral glucocorticoid or anti-fungal medicines one month prior to study entry
- anti-fungal or glucocorticoid cream two weeks prior to study entry

Randomised

N = 162

Withdrawals/losses to follow-up

- 23/162 (14%); 9/80 in econazole + triamcinolone acetonide group, 14/82 in econazole group
- due to adverse events, unable to use medication or attend at follow-up, use of other medication during the trial
- Tinea corporis/cruris withdrawals: econazole + triamcinolone acetonide (3); econazole (3)

Baseline data

Tinea pedis: econazole + triamcinolone acetonide group (44); econazole group (44)

Tinea corporis/cruris: econazole + triamcinolone acetonide group (36); econazole group (38)

Interventions	**Intervention** • econazole (1%) + triamcinolone acetonide (0.1%) cream b.i.d. for 2 weeks for tinea corporis/cruris, for 4 weeks for tinea pedis **Comparator** • econazole (1%) cream b.i.d. for 2 weeks for tinea corporis/cruris, for 4 weeks for tinea pedis
Outcomes	Assessments (4): baseline weeks 1, 2 and 4 **Outcomes of the trial** (as reported) 1. Clinical evaluation of signs and symptoms (erythema, papules, vesicles, pustules, cornification, scales, maceration and pruritus): 4-point Likert scale# 2. Clinical efficacy: 4-point Likert scale# 3. Mycological evaluation (KOH, culture and fungal identification) 4. Adverse events# 5. Determination of minimum inhibitory concentration Denotes outcomes prespecified for this review
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote (page 170): "randomised" Comment: Insufficient detail was reported about the method used to generate the allocation sequence to allow a clear assessment of whether it would produce comparable groups.
Allocation concealment (selection bias)	Unclear risk	The method used to conceal the allocation sequence, that is to determine whether intervention allocations could have been foreseen in advance of, or during, enrolment, was not reported. Comment: There was insufficient information to permit a clear judgement.

Wang 2000a *(Continued)*

Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote (page 170): "double-blind" and "Intervention and comparator medicine were packaged by Xian Janssen Pharmaceutical Ltd. , labelled with random numbers, which was showed after the experiment" Comment: The report provided sufficient detail about the measures used to blind study participants and personnel from knowledge of which intervention a participant received, to permit a clear judgement.
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote (page 170): "double-blind" and "Intervention and comparator medicine were packaged by Xian Janssen Pharmaceutical Ltd. , labelled with random numbers, which was showed after the experiment". Blinding of participants and key study personnel was ensured, and it is unlikely that the blinding could have been broken. Comment: We judged this as at a low risk of bias.
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	23/162 (14%); 9/80 in econazole + triamcinolone acetonide group, 14/82 in econazole group. Per protocol analysis. Comment: We judged this as at unclear risk of bias.
Selective reporting (reporting bias)	Low risk	The protocol for the study was not available, but the prespecified outcomes and those mentioned in the methods section appeared to have been reported. Comment: We judged this as at a low risk of bias.
Other bias	Unclear risk	Intervention medication was provided by Xian Janssen Pharmaceutical Ltd, and comparator medicine by another company but it was re-packaged and provided by Xian Janssen Pharmaceutical Ltd. No statement on who sponsored the study. Comment: We judged this as at unclear risk of bias.

Weitgasser 1977

Methods	2 randomised, double-blind, active-controlled trials Setting Dermatology Department of Steiermärkischen Gebietskrankenkasse, Graz Austria Date of study Not reported. Duration of intervention 4 weeks
Participants	N = 153 (84 male/69 female)(Study I); 124 (70 male/54 female)(Study II) Majority 30-39 years, remainder 16-29 years (Study I); Majority 16-39 years in haloprogin ointment group,16-59 years clotrimazole group **Inclusion criteria of the trial** • participants with dermatomycoses, Candida infections, pityriasis versicolor and erythrasma **Exclusion criteria of the trial** • treatment with griseofulvin Randomised

Weitgasser 1977 *(Continued)*

	N = 153 (Study I); 124 (Study II) Withdrawals/losses to follow-up • 0 (Study I) • 19/124 (15%) (Study II), lost to follow-up Baseline data Diagnosis Study I: Tinea pedis: haloprogin solution (25), clotrimazole solution (17) Tinea manuum: haloprogin solution (12), clotrimazole solution (11) Tinea pedis and manuum: haloprogin solution (0), clotrimazole solution (3) Tinea corporis and cruris: haloprogin solution (15), clotrimazole solution (13) Candida: haloprogin solution (8), clotrimazole solution (10) Pityriasis versicolor: haloprogin solution (14), clotrimazole solution (15) Erythrasma: haloprogin solution (2), clotrimazole solution (1) Diagnosis Study II: Tinea pedis: haloprogin ointment (17), clotrimazole cream (19) Tinea manuum: haloprogin ointment (8), clotrimazole cream (7) Tinea corporis and cruris: haloprogin ointment (7), clotrimazole cream (7) Candida: haloprogin ointment (7), clotrimazole cream (4) Pityriasis versicolor: haloprogin ointment (12), clotrimazole cream (12) Erythrasma: haloprogin ointment (3), clotrimazole cream (1)
Interventions	**Study I** **Intervention** • haloprogin (1%) solution b.i.d. for 4 weeks (76) **Comparator** • clotrimazole (1%) solution b.i.d. for 4 weeks (77) **Study 2** **Intervention** • haloprogin ointment b.i.d. for 4 weeks (64) **Comparator** • clotrimazole cream b.i.d. for 4 weeks (60)
Outcomes	Assessments (2): baseline and week 4 **Outcomes of the trial** (as reported) 1. Mycological evaluation (KOH and culture) 2. Clinical evaluation

Weitgasser 1977 *(Continued)*

Denotes outcomes prespecified for this review

Notes	The trial also includes an open-label CCT, which was ineligible for this review.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote (page 17): "..der randomisiert vorliegenden Prüfmuster.." Comment: Insufficient detail was reported about the method used to generate the allocation sequence to allow a clear assessment of whether it would produce comparable groups.
Allocation concealment (selection bias)	Unclear risk	The method used to conceal the allocation sequence, that is to determine whether intervention allocations could have been foreseen in advance of, or during, enrolment, was not reported. Comment: There was insufficient information to permit a clear judgement.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote (page 17): "..Doppelblindprüfung..". Comment: The report did not provide sufficient detail about the specific measures used to blind study participants and personnel from knowledge of which intervention a participant received, to permit a clear judgement.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Comment: Uncertainty with the effectiveness of blinding of outcomes assessors (participants/healthcare providers) during the study. Insufficient information to permit a clear judgement.
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Study I No losses to follow-up Study II Losses 19/124 (15%) balanced between the groups, per-protocol analysis. Comment: We judged this at unclear risk of bias.
Selective reporting (reporting bias)	Low risk	The protocol for the study was not available, but the prespecified outcomes and those mentioned in the methods section appeared to have been reported. Comment: We judged this as at a low risk of bias.
Other bias	Low risk	The study appears to be free from other forms of bias.

Wortzel 1982

Methods	Randomised, double-blind, active-controlled trial Setting Multi-centre, US Date of study Not reported. Duration of intervention 2 weeks with follow-up at 4 weeks
Participants	N = 270 (age and gender unreported) **Inclusion criteria of the trial**

Wortzel 1982 *(Continued)*

- Age > 12 years with clinical diagnosis of tinea cruris confirmed by KOH and culture

Exclusion criteria of the trial

- use of topical corticosteroid < 1 week prior to study entry
- use of systemic corticosteroid < 2 weeks prior to study entry
- use of other investigational drugs
- pregnant women, or wanting to become pregnant

Randomised

N = 270 were enrolled, total randomised unclear, report only includes data for 47

Withdrawals/losses to follow-up

- betamethasone dipropionate (2/17)

Baseline data

Not reported

Interventions	**Intervention** • clotrimazole cream b.i.d. for 2 weeks (15) **Comparator** • betamethasone dipropionate cream b.i.d. for 2 weeks (17) **Comparator 2** • combination of clotrimazole cream and betamethasone dipropionate cream b.i.d. for 2 weeks (15) No concomitant therapy allowed.
Outcomes	Assessments (5): baseline, day 3, weeks 1, 2 and 4 **Outcomes of the trial** (as reported) 1. Mycological evaluation (KOH and culture) 2. Clinical evaluation of 7 signs and symptoms: 4-point Likert scale# 3. Clinical status: 4-point Likert scale# 4. Clinical response: 6-point Likert scale# 5. Adverse events: 3-point Likert scale# Denotes outcomes prespecified for this review
Notes	Multi-centre trial but the report only included data for 45/47 participants from one centre.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote (page 258): "..randomized.." Comment: Insufficient detail was reported about the method used to generate the allocation sequence to allow a clear assessment of whether it would produce comparable groups.
Allocation concealment (selection bias)	Unclear risk	The method used to conceal the allocation sequence, that is to determine whether intervention allocations could have been foreseen in advance of, or during, enrolment, was not reported.

Wortzel 1982 *(Continued)*

		Comment: There was insufficient information to permit a clear judgement.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote (page 258): ".. double-blind.." Comment: The report did not provide sufficient detail about the specific measures used to blind study participants and personnel from knowledge of which intervention a participant received, to permit a clear judgement.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Comment: Uncertainty with the effectiveness of blinding of outcomes assessors (participants/healthcare providers) during the study. Insufficient information to permit a clear judgement.
Incomplete outcome data (attrition bias) All outcomes	Low risk	2/17 (12%) of the betamethasone dipropionate group were not included in the analysis. Per-protocol-analysis Comment: Low percentage of drop-outs and although per-protocol analysis was judged as at a low risk of bias.
Selective reporting (reporting bias)	Low risk	The protocol for the study was not available, but the prespecified outcomes and those mentioned in the methods section appeared to have been reported. Comment: We judged this as at a low risk of bias.
Other bias	Unclear risk	Quote (page 261): "Lotrizone, the combination antifungal/steroid, was supplied by the Schering Corporation." Comment: Insufficient information to assess whether important risk of bias exists.

Yim 2010

Methods	Randomised, double-blind, active-controlled trial Setting Multi-centre (11) in Korea Date of study May 2005-November 2005. Duration of intervention 4 weeks with follow-up at 6 weeks
Participants	N = 275 (131 male/31 female; 113 unreported) Mean age = 39 years **Inclusion criteria of the trial** • > 10 years old having superficial mycosis confirmed by KOH and culture • > 1 clinical symptoms of tinea pedis or other dermatomycotic infections **Exclusion criteria of the trial** • onychomycosis • hypersensitivity to azole drugs • bacterial infection over dermatomycosis • severe diabetes mellitus (HbA1C > 9%) • decreased liver function (ALT, AST > 2.5 times upper limit of normal range) • decreased renal function (serum Cr > 1.5 times upper limit of normal range) • need for systemic administration, immunosuppressants

Yim 2010 *(Continued)*

- pregnancy or lactation, potential of child bearing but not using adequate contraception
- HIV
- alcoholism or drug abuse (suspected)

Randomised

N = 275

Delayed exclusion

64/275 (23%); fluconazole (0.5%); 22/92, fluconazole (1%): 17/91, flutrimazole (1%): 25/92

Withdrawals/losses to follow-up

49/275(18%)

- fluconazole (0.5%); 17/92 due to contraindication (2), poor compliance (1), visit failure (2), consent withdrawal (10), lost during study (2)
- fluconazole (1%); 17/91 due to contraindication (5), visit failure (2), consent withdrawal (5), lost during study (4), excluded by investigator 91)
- flutrimazole (1%); 15/92 due to contraindication (4), poor compliance (1), visit failure (1), consent withdrawal (6), lost during study (2), protocol violation (1)

Baseline data

Diagnosis: 162 (per-protocol analysis set):

Tinea pedis: fluconazole (0.5%) 40, fluconazole (1%) 45, flutrimazole (1%) 42
Tinea corporis: fluconazole (0.5%) 1, fluconazole (1%) 4, flutrimazole (1%) 3
Tinea cruris: fluconazole (0.5%) 8, fluconazole (1%) 5, flutrimazole (1%) 4
Pityriasis versicolor: fluconazole (0.5%) 4, fluconazole (1%) 3, flutrimazole (1%) 3

Interventions	**Intervention** • fluconazole (0.5%) cream once a day for 4 weeks (92) **Comparator 1** • fluconazole (1%) cream once a day for 4 weeks (91) **Comparator 2** • flutrimazole (1%) cream once a day for 4 weeks (92)
Outcomes	Assessments (4): baseline, weeks 2, 4 and 6 **Outcomes of the trial** (as reported) 1. Clinical evaluation of signs and symptoms (scaling, erythema, vesiculation, pruritus and burning, pain): 4-point Likert scale# 2. Mycological evaluation (KOH and culture) 3. Adverse events# Denotes outcomes prespecified for this review
Notes	We only included data of participants with tinea cruris and corporis. See Table 3

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote (page 524): "..were randomised to receive.."

Yim 2010 *(Continued)*

		Comment: Insufficient detail was reported about the method used to generate the allocation sequence to allow a clear assessment of whether it would produce comparable groups.
Allocation concealment (selection bias)	Unclear risk	The method used to conceal the allocation sequence, that is to determine whether intervention allocations could have been foreseen in advance of, or during, enrolment, was not reported. Comment: There was insufficient information to permit a clear judgement.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote (page 522): ".. double-blind.." Comment: The report did not provide sufficient detail about the specific measures used to blind study participants and personnel from knowledge of which intervention a participant received, to permit a clear judgement.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Comment: Uncertainty with the effectiveness of blinding of outcomes assessors (participants/healthcare providers) during the study. Insufficient information to permit a clear judgement.
Incomplete outcome data (attrition bias) All outcomes	High risk	Quote (page 524): "A total of 275 patients, who were included in intent to treat (ITT) analysis...." 275 randomised, 162 analysed. Losses after randomisation due to negative baseline culture: fluconazole 0.5%) group (22/92), fluconazole (1%) group (17/91) flutrimazole (1%) group (25/92) = 64/275 (23%). Failed to attend for follow-up at 4 weeks: fluconazole (0.5%) group (17), fluconazole (1%) group (17), flutrimazole (1%) group (15) = 49/275 (18%) Comment: Entry criterion (culture specimen) measured prior to randomisation. The delayed exclusions are well-balanced between groups, no attrition bias between the groups. See ICH Expert Working Group 1998. Reasonably balanced, but high number of drop-outs at follow-up, and per-protocol analysis. We judged this to be at high risk of bias.
Selective reporting (reporting bias)	Low risk	The protocol for the study was not available, but the prespecified outcomes and those mentioned in the methods section appeared to have been reported. Comment: We judged this as at a low risk of bias.
Other bias	Low risk	Quote (page 528): "This work was supported by the Second-Phase of BK (Brain Korea) 21 Project" Comment: We judged this as at a low risk of bias.

Zaias 1993

Methods	2 randomised, double-blind, placebo-controlled trials Setting Multi-centre, several countries Date of study Not reported. Duration of intervention 1 week with follow-up to 4 weeks

Zaias 1993 *(Continued)*

Participants	N = unclear, 139 analysed (age and gender unreported) **Inclusion criteria of the trial** • tinea cruris or tinea corporis confirmed by KOH and culture **Exclusion criteria of the trial** • not reported Randomised N = unclear, 139 'evaluable' and analysed, unclear how many in each study, and in each treatment arm Withdrawals/losses to follow-up • unclear, as it is unclear how many were randomised Baseline data Not reported
Interventions	**Intervention** • terbinafine (1%) cream once daily for 1 week (66) **Comparator** • placebo once daily (73)
Outcomes	Assessments (3): baseline, weeks 1 and 4 **Outcomes of the trial** (as reported) 1. Clinical evaluations of signs and symptoms (to assess erythema, desquamation, vesiculation, pustules, incrustation, and pruritus): 4-point Likert scale# 2. Mycological evaluation (KOH and culture) 3. Improvement of disease assessed by physicians and participants: 5-point Likert scale# Denotes outcomes prespecified for this review
Notes	No separate data for each of the two studies.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote (page 647): "..were randomly assigned.." Comment: Insufficient detail was reported about the method used to generate the allocation sequence to allow a clear assessment of whether it would produce comparable groups.
Allocation concealment (selection bias)	Unclear risk	The method used to conceal the allocation sequence, that is to determine whether intervention allocations could have been foreseen in advance of, or during, enrolment, was not reported. Comment: There was insufficient information to permit a clear judgement.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote (page 647): ".. double-blind.."

Zaias 1993 *(Continued)*

		Comment: The report did not provide sufficient detail about the specific measures used to blind study participants and personnel from knowledge of which intervention a participant received, to permit a clear judgement.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Comment: Uncertainty with the effectiveness of blinding of outcomes assessors (participants/healthcare providers) during the study. Insufficient information to permit a clear judgement.
Incomplete outcome data (attrition bias) All outcomes	High risk	Number of participants that were randomised is unreported, nor how many were in each group, and the separate arms. Per-protocol analysis. Comment: We judged this as at a high risk of bias.
Selective reporting (reporting bias)	Low risk	The protocol for the study was not available, but the prespecified outcomes and those mentioned in the methods section appeared to have been reported. Comment: We judged this as at a low risk of bias.
Other bias	High risk	Two authors were employees of Sandoz Research, Basles; and Sandoz Research Institute, East Hanover, the manufacturer of terbinafine. Comment: A potential risk of bias cannot be excluded.

Zarowny 1975

Methods	Randomised, double-blind, active-controlled trial Setting Department of Dermatology of Duke University Medical Center, Durham, North Carolina, USA Date of study Not reported. Duration of intervention 3 weeks with follow-up at 4 weeks
Participants	N = 57 (49 male/8 female) Age range = 20-64 years **Inclusion criteria of the trial** • participants with superficial dermatomycoses **Exclusion criteria of the trial** • tinea capitis, onychomycosis and people with bacterial superinfection • use of griseofulvin or tolnaftate < 3 months prior to study entry Randomised N = 57 Withdrawals/losses to follow-up • combined yeast infection (1), surgery (1), house moving (3): placebo (3), tolnaftate (1), griseofulvin (1) • treatment failure (3): placebo (2), tolnaftate (1) Baseline data Location:

Zarowny 1975 *(Continued)*

	Tinea pedis: griseofulvin (13), tolnaftate (10), placebo (8) Other sites: griseofulvin (5), tolnaftate (9), placebo (7)
Interventions	**Intervention** • griseofulvin (2%) ointment three times a day for 3 weeks (18) **Comparator 1** • tolnaftate (1%) cream three times a day for 3 weeks (19) **Comparator 2** • ointment base three times a day for 3 weeks (15)
Outcomes	Assessments (5): baseline, weeks 1, 2, 3 and 4 **Outcomes of the trial** (as reported) 1. Mycological evaluation (KOH and culture) 2. Clinical evaluation 3. Routine laboratory tests (serum and urine) 4. Relapse Denotes outcomes prespecified for this review
Notes	Tinea cruris and corporis possibly included, but only reported as 'all other sites'. Old trial. See Table 3.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote (page 268/9): ".. assigned at random.. predetermined randomized treatment schedule" Comment: Insufficient detail was reported about the method used to generate the allocation sequence to allow a clear assessment of whether it would produce comparable groups.
Allocation concealment (selection bias)	Unclear risk	The method used to conceal the allocation sequence, that is to determine whether intervention allocations could have been foreseen in advance of, or during, enrolment, was not reported. Comment: There was insufficient information to permit a clear judgement.
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote (page 268): ".. double-blind.....nearly identical in appearance.... all labels identifying the contents had been removed and replaced by a plain label containing the patients study number". Comment: The report provided sufficient detail about the measures used to blind study participants and personnel from knowledge of which intervention a participant received, to permit a clear judgement.
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Outcomes were investigator-assessed. Comment: Blinding of key study personnel was ensured, and it is unlikely that the blinding could have been broken.
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Lost to follow-up/drop-outs: combined yeast infection (1), surgery (1), house moving (3): placebo (3), tolnaftate (1), griseofulvin (1). Due to treatment failure (3): placebo (2), tolnaftate (1). Total 8/57 (14%)

Zarowny 1975 *(Continued)*

		Comment: We judged this as at unclear risk of bias.
Selective reporting (reporting bias)	Low risk	The protocol for the study was not available, but the prespecified outcomes and those mentioned in the methods section appeared to have been reported. Comment: We judged this as at a low risk of bias.
Other bias	High risk	One of the investigators was employed by Ayerst Laboratories and Michel Caron also employed by Ayerst laboratories is acknowledged for performing the statistical analyses. A potential risk of bias cannot be excluded.

Zaun 1984

Methods	Randomised, double-blind, active-controlled, within-patient comparison trial Setting Dermatology Clinic of the University of Saarland, Homburg/Saar, Germany Date of study Not reported. Duration of intervention 2 weeks
Participants	N = 126 (85 male/39 female; 2 unreported) Mean age = 46 years **Inclusion criteria of the trial** • clinical diagnosis of dermatomycosis, distributed symmetrically, confirmed by KOH and culture **Exclusion criteria of the trial** • not reported Randomised N = 126 Withdrawals/losses to follow-up • 14/126 are not included in the analysis, reasons unreported Baseline data Diagnosis: Tinea pedis: 81 Tinea manuum:11 Tinea corporis: 33
Interventions	**Intervention** • naftifine (1%) cream b.i.d. for 2 weeks (126) **Comparator** • clotrimazole (1%) cream b.i.d. for 2 weeks (126)
Outcomes	Assessments (6): baseline, days 2, 4, 7 ,10 and 14

Zaun 1984 *(Continued)*

Outcomes of the trial (as reported)

1. Mycological evaluation (KOH and culture)
2. Clinical evaluation of sign and symptoms (erythema, scaling, vesicles, pustules, maceration, itching, infiltration): 6-point Likert scale#
3. Adverse events#

Denotes outcomes prespecified for this review

Notes	Within-patient study. See Table 3

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote (page 1211): "..Randomisationsplan.." Comment: Insufficient detail was reported about the method used to generate the allocation sequence to allow a clear assessment of whether it would produce comparable groups.
Allocation concealment (selection bias)	Unclear risk	The method used to conceal the allocation sequence, that is to determine whether intervention allocations could have been foreseen in advance of, or during, enrolment, was not reported. Comment: There was insufficient information to permit a clear judgement.
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote (page 1211): "..zu vergleichenden identisch aussehenden Cremes in nicht unterscheidbarer neutraler Aufmachung enthielten". Comment: The report provided sufficient detail about the measures used to blind study participants and personnel from knowledge of which intervention a participant received, to permit a clear judgement.
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Outcomes were investigator-assessed as well as participant assessed. Blinding of participants and key study personnel was ensured, and it is unlikely that the blinding could have been broken. Comment: We judged this as at a low risk of bias.
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	After 14 days 14/126 (11%) not included in the mycological analysis. Within-patient comparison. Comment: We judged this as at a low risk of bias.
Selective reporting (reporting bias)	Low risk	The protocol for the study was not available, but the prespecified outcomes and those mentioned in the methods section appeared to have been reported. Comment: We judged this as at a low risk of bias.
Other bias	Low risk	The study appears to be free from other forms of bias.

AE - Accident & Emergency
ALT = alanine aminotransferase
AST = aspartate transaminase
b.i.d. = twice daily
CCT = controlled clinical trial
ITT = intenrtion-to-treat
KOH = potassium hydroxide
LOCF = last-bservation-carried forward

RCT = randomised controlled trial

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

Study	Reason for exclusion
Anderson 2012	Did not match our inclusion criteria, only healthy participants included
Arnoldi 1979	CCT
Arreaza de Arreaza 1984	CCT
Baran 1979	Case-series
Bonifaz 2000	After e-mail communication confirmed as quasi-randomised (allocation by alternation)
Comaish 1975	CCT
el Darouti 1990	CCT
Fiorini 1991	Case-series. All participants received 1% isoconazole nitrate (2 times/day for 30 days + 45 days of follow-up). Translated from the Portuguese by Regis Andriolo, Department of Public Health, Universidade do Estado do Pará, Belém, Brazil (see Acknowledgements)
Hay 1985	CCT
Kagawa 1989	CCT
Kamalam 1980	CCT
László 1991	Non RCT, no control group.
Mathur 1973	Clinical trial, no comparison, all people with superficial fungal infections were treated with Jadit ointment
Nada 1994	CCT
No authors listed 1992	CCT
Saple 2001	Although reported as a "multicentric, randomised, single blinded study", there was no comparison group. Case series
Sartani 1988	Non RCT, no control group
Scherwitz 1977	CCT
Svejgaard 1973	CCT
Szarmach 1984	No participants with tinea corporis or cruris. Included participants had Candida infections, infected eczema, contact dermatitis, nummular eczema, seborrhoic eczema, dyshidrotic eczema, intertriginous eczema or prurigo.
Tulli 1988	CCT
Tulli 1988a	Non RCT, no control group
Török 1993	CCT

Study	Reason for exclusion
Wiedey 1982	CCT

CCT = Controlled clinical trial (quasi-randomised)
RCT = Randomised controlled trial

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

Alomar 1995

Methods	Randomised, double-blind, active-controlled trial Setting Multi-centre (20) in Spain Date of study Not reported. Duration of intervention 4 weeks with follow-up at 2 months
Participants	N = 449 (214 male/235 female) Mean age = 33 years **Inclusion criteria of the trial** • clinical diagnosis of dermatomycoses confirmed by KOH and culture **Exclusion criteria of the trial** • pregnant and breastfeeding women, women at childbearing age without adequate contraception • topical antifungal < 1 week or systemic antifungal < 1 month prior to study entry • hepatic or renal failure • receiving immunosuppressive treatment Randomised N = 449 Withdrawals/losses to follow-up • None Baseline data Diagnosis: Not reported, only fungal species
Interventions	**Intervention** • bifonazole (1%) cream once a day for 4 weeks (221) **Comparator** • flutrimazole (1%) cream once a day for 4 weeks (228) Concomitant treatment with other antifungal or corticosteroid not allowed
Outcomes	Assessments (4): baseline, weeks 2, 4 and 8 **Outcomes of the trial** (as reported)

Alomar 1995 *(Continued)*

1. Clinical evaluation of sign and symptoms (erythema, desquamation, vesicles, pustules, scabs, fissures, local pain and pruritus): 4-point Likert scale#
2. Mycological evaluation (KOH and culture)
3. Adverse events#

Denotes outcomes prespecified for this review

Notes	Participants with tinea cruris and corporis are likely to be included, but separate numbers not reported. See Table 1

Binet 1994

Methods	Randomised, double-blind, active-controlled trial Setting Multi-centre, from the Dermatology Services in 36 centres (24 France, 12 Spain) Date of study Not reported. Duration of intervention 4 weeks to follow-up 4 weeks after "cure"
Participants	N = 484; Data reported only for 383 (211 male/ 171 female; 1 gender unreported) Age range 18–70, mean 38 years **Inclusion criteria of the trial** • age 18 to 70 years • clinical diagnosis of dermatomycosis confirmed by positive mycological test (direct exam with KOH 'and' or 'or' culture) **Exclusion criteria of the trial** • pregnant or breast feeding women • women of child-bearing age not using reliable method of contraception • use of topical antifungal agent in prior week • use of systemic antifungal in previous month • participants with hepatic or renal deficiency or receiving immunosuppressive therapy • concomitant therapy with other antifungals or corticosteroids Randomised N = 484 Delayed exclusions: • clotrimazole group (49/240), flutrimazole group (52/244): negative culture for dermatophytes. Excluded from ITT analysis 101/484 (21%) Withdrawals/losses to follow-up • clotrimazole group (18/191), flutrimazole group (26/192) = 44/383 (11%), failed to attend for follow-up after the treatment period Baseline data Dermatophytosis: clotrimazole group (114/191), flutrimazole group (113/192) Cutaneous candidosis: clotrimazole group (27/191), flutrimazole group (18/192)

Binet 1994 *(Continued)*

	Pityriasis versicolor: clotrimazole group (49/191), flutrimazole group (60/192) Dermatophytosis and pityriasis versicolor: clotrimazole group (1/191), flutrimazole group (1/192)
Interventions	**Intervention** • clotrimazole (1%) cream b.i.d. for 4 weeks (240) **Comparator** • flutrimazole (1%) cream b.i.d. for 4 weeks (244) Applied to the affected area twice daily for 4 weeks. Concomitant therapy with other antifungals or corticosteroids not permitted.
Outcomes	Assessments (3): baseline, days 15 and 30 **Outcomes of the trial** (as reported) 1. Clinical signs and symptoms (erythema, vesicles, desquamation, fissures, pustules, scabs, pain and pruritus): 4-point Likert scale# 2. Mycological assessment (KOH and culture) 3. Rate of relapse at day 60# 4. Laboratory tests 5. Adverse events# Denotes outcomes prespecified for this review
Notes	Tinea corporis and cruris are probably included, but not mentioned.

Choudhary 2013

Methods	Randomised, single-blind, active-controlled trial Setting Department of Dermatology, Acharya Vinoba Bhave Rural Hospital, Sawangi, Wardha, India Date of study November 2010-October 2011. Duration of the intervention 3 weeks
Participants	N = 38 (23 male/7 female; 8 unreported) Age range 16-35 years **Inclusion criteria of the trial** • untreated dermatophytosis in patients of any age • involvement of < 20% of total body surface • diagnosis confirmed by KOH microscopy **Exclusion criteria of the trial** • resolving dermatophytosis • pre-existing topical or systemic antifungal treatment • involvement of > 20% body surface area • pregnant or lactating females • immunosuppressed patients or receiving immunosuppressive medication

Choudhary 2013 *(Continued)*

	Randomised N = 38 Withdrawals/losses to follow-up • 8/38 (21%); terbinafine group (5/20), sertaconazole group (3/18). All lost to follow-up Baseline data Sites not reported, only fungal species
Interventions	**Intervention** • terbinafine (1%) cream b.i.d. for 3 weeks (20) **Comparator** • sertaconazole (2%) cream b.i.d. for 3 weeks (18)
Outcomes	Assessments (4): baseline, end of weeks 1, 2, 3 **Outcomes of the trial** (as reported) 1. Clinical signs and symptoms (itching, erythema, papules, pustules, vesicles, scaling) 2. Overall improvement: 4-point Likert scale 3. Adverse effects 4. Mycological cure (KOH and culture) Denotes outcomes prespecified for this review
Notes	Study retrieved 21 May 2014

el Darouti 1989

Methods	Randomised, double-blind, active-controlled trial Setting Department of Dermatology and Mycology, Rashid Hospital and Sief Hospital, R.A.K., United Arab Emirates Date of study Not reported. Duration of the intervention 4 weeks
Participants	N = 76 (gender and age unreported) **Inclusion criteria of the trial** • clinical signs and symptoms of dermatophytosis confirmed by KOH and culture **Exclusion criteria of the trial** • systemic antifungal treatment < 4 weeks, topical antifungal treatment < 1 week prior to study entry Randomised N = 76 Withdrawals/losses to follow-up

el Darouti 1989 *(Continued)*

	• not reported Baseline data Not reported
Interventions	**Intervention** • naftifine (1%) cream once daily for 4 weeks **Comparator** • clotrimazole (1%) cream b.i.d. for 4 weeks
Outcomes	**Outcomes of the trial** (as reported) 1. Mycological evaluation (KOH and culture) 2. Global assessment by physician 3. Regression of clinical symptoms: 4-point Likert scale# 4. Adverse events# Denotes outcomes prespecified for this review
Notes	Participants with tinea cruris and corporis are likely to be included, but separate data not reported. Unclear how many participants in each group, and drop-out rate unclear. See: Table 1

Fredriksson 1974

Methods	Randomised, double-blind, placebo-controlled trial Setting Dermatology department, Central Hospital, Västeras, Sweden Date of study Not reported. Duration of intervention 3 weeks with follow-up 3 weeks
Participants	N = 80 (29 male, 25 female; 26 gender unreported) Age range 5-84 , mean 42 years **Inclusion criteria of the trial** • participants with clinical dermatomycosis confirmed by mycology (culture) **Exclusion criteria of the trial** • not reported Randomised N = 80 Delayed exclusions/Withdrawals/losses to follow-up • 20/80 due to negative culture post randomisation unclear which groups • 6 in the vehicle group needed conventional therapy Baseline data

Fredriksson 1974 *(Continued)*

- clotrimazole group 17/31 tinea infection, 14/31 candidiasis
- placebo group 10/23 tinea infection, 13/23 candidiasis

Interventions	**Intervention** • clotrimazole (1%) solution b.i.d. for 3 weeks (31) **Comparator** • placebo b.i.d. for 3 weeks (23)
Outcomes	Assessments (3): baseline, weeks 3 and 6 **Outcomes of the trial** (as reported) 1. Mycological evaluation (culture) 2. Clinical evaluation: 3-point Likert scale# 3. Adverse events# Denotes outcomes prespecified for this review
Notes	Unclear from the report the type of tinea infections involved (tinea pedis, corporis, cruris).

Gooskens 1994

Methods	Randomised, double-blind, active-controlled trial Setting Health centres and 2 hospitals in Malawi Date of study Nov 1990-Nov 1992. Duration of the intervention 6 weeks with follow-up at 8 weeks
Participants	N = 153 (96 male/57 female) Age range 0 > 40 years **Inclusion criteria of the trial** • dermatophytoses confirmed by KOH and culture • > 15 years • agreed to testing for HIV **Exclusion criteria of the trial** • not reported Randomised N = 153 Withdrawals/losses to follow-up • no losses to follow-up Baseline data HIV positive: Whitfield's (10), clotrimazole (15)

Gooskens 1994 *(Continued)*

	HIV negative: Whitfield's (42), clotrimazole (39)
Interventions	**Intervention** • Whitfield's cream b.i.d. for 6 weeks (75) **Comparator** • clotrimazole cream b.i.d. for 6 weeks (78)
Outcomes	**Outcomes of the trial** (as reported) 1. Mycological evaluation (KOH and culture) Denotes outcomes prespecified for this review
Notes	Participants with tinea cruris and corporis are likely to be included, but separate data are not reported.

Jones 2014

Methods	Randomised, double-blind, placebo-controlled trial Setting Multi-centre (27 sites), United States of America Date of study June 2011-March 2012. Duration of the intervention 7 days with follow-up at day 28
Participants	N = 483 (212 male/44 female; 227 gender unreported) Mean age = 40 years. **Inclusion criteria of the trial** • participants >12 years with clinical evidence of tinea cruris • mycological confirmation of tinea cruris (KOH) • good general health and free of disease that may have interfered with study evaluations in the investigators' opinion **Exclusion criteria of the trial** • active atopic or contact dermatitis in the treated area • severe dermatophytoses • mucocutaneous candidiasis • bacterial skin infection • pregnant or breastfeeding females • women planning a pregnancy during the course of the study • immunocompromised participants due to illness or medication • use of topical antifungal agent within 14 days of baseline visit (30 days for terbinafine, butenafine and naftifine) • use of systemic antifungals within 8 weeks of baseline visit (8 months for terbinafine) • use of topical antibiotics within 30 days of baseline visit • use of systemic antibiotics within 30 days of baseline visit • use of antibacterial soaps on affected area within 7 days of baseline visit • Use of topical corticosteroid within 14 days of baseline visit

Jones 2014 *(Continued)*

	• use of systemic or intralesional corticosteroid within 30 days of baseline visit • recent history of known abuse of drugs or alcohol • history of intolerance or hypersensitivity to imidazoles or inactive components of the cream Randomised N = 483 Delayed exclusions/withdrawals/losses to follow-up • 227 delayed exclusions (153 luliconazole group, 74 in vehicle group) due to negative culture results • 18/256 (7%); luliconazole group 7/165, vehicle group 11/91 withdrew/lost to follow-up Baseline data Species of fungus reported. All participants had tinea cruris
Interventions	**Intervention** • luliconazole cream (1%) once daily for 7 days (318) **Comparator** • vehicle cream once daily for 7 days (165)
Outcomes	Assessments (5): baseline, days 7, 14, 21, 28 **Outcomes of the trial** (as reported) 1. Clinical severity scores: 4-point Likert scale# 2. Mycology (KOH and culture) 3. Dermatophyte susceptibility testing 4. Adverse events# Denotes outcomes prespecified for this review
Notes	Study retrieved 21 May 2014

Kuokkanen 1982

Methods	Randomised, double-blind, vehicle-controlled study Setting Department of Dermatology, University Central Hospital, Tampere, Finland Date of study Not reported. Duration of intervention 4 weeks with follow-up at 6 weeks
Participants	N = 40 (29 male/11 female) Mean age = 43, range 26-56 years **Inclusion criteria of the trial** • clinical diagnosis of fungal infection confirmed by KOH and culture **Exclusion criteria of the trial**

Kuokkanen 1982 *(Continued)*

	• not reported Randomised N = 40 Withdrawals/losses to follow-up • 6/40 (15%), • tioconazole (3): contact allergy (1), lost to follow-up (1), unclear (1) • vehicle (3): application of antifungal therapy until study entry, lost to follow-up (1), negative culture (1) Baseline data Diagnosis: Not reported, only fungal species.
Interventions	**Intervention** • tioconazole (2%) cream b.i.d. for 4 weeks **Comparator** • vehicle cream b.i.d. for 4 weeks
Outcomes	Assessments (5): baseline, weeks 1, 2 ,4 and 6 **Outcomes of the trial** (as reported) 1. Clinical evaluation 2. Mycological evaluation 3. Adverse events# 4. Relapse Denotes outcomes prespecified for this review
Notes	Participants with tinea cruris and corporis are likely to be included, but separate data are not reported. Old study no contact details available.

Male 1981

Methods	Randomised, double-blind, active-controlled trial Setting Eight centres in Germany and Austria Date of study January 1979-December 1980. Duration of intervention 4 weeks with follow-up at 8 weeks
Participants	N = 231 (111 male/80 female; 40 gender unreported) Mean age = 69 years **Inclusion criteria of the trial** • superficial dermatomycoses confirmed by KOH and culture

Male 1981 *(Continued)*

	Exclusion criteria of the trial • not reported Randomised N = 231 Withdrawals/losses to follow-up • 47/231 (20%) dropped out Baseline data Species reported but not infection sites.
Interventions	**Intervention** • naftifine (1%) cream b.i.d. for 4 weeks (72) **Comparator 1** • tolnaftate (1%) cream b.i.d. for 4 weeks (79) **Comparator 2** • clotrimazole (1%) cream b.i.d. for 4 weeks (80)
Outcomes	Assessments (6): baseline, weeks 1, 2, 3, 4 and 8 **Outcomes of the trial** (as reported) 1. Clinical evaluation 2. Mycological evaluation (KOH and culture) 3. Adverse events# 4. Relapse 5. Overall assessment Denotes outcomes prespecified for this review
Notes	Participants with tinea cruris and corporis are likely to be included, but separate data are not reported. Old study no contact details available.

Nolting 1995

Methods	Randomised, double-blind, active-controlled trial Setting Multi-centre (7) in Germany Date of study Unreported. Duration of intervention unclear >2 weeks
Participants	N = 214 (140 male/74 female) Mean age = 41, age range 12-95 years **Inclusion criteria of the trial**

Nolting 1995 *(Continued)*

	• participants with inflammatory mycosis 'and' 'or' dermatitis of various origins, with "additional superinfection" **Exclusion criteria of the trial** • pregnant women or women not using adequate contraception • dermatitis of viral or specific origin • systemic treatment with corticosteroids or simultaneous treatment with other topical agents • sensitivity to any component of the test drugs • severe liver disease • systemic diseases with abnormal skin reactions Randomised N = 214 Withdrawals/losses to follow-up • 8/214: 4 in each group, 2 in each group due to inadequate efficacy Baseline data Diagnoses unreported, only causative pathogen, no significant difference between the groups
Interventions	**Intervention** • fluprednidene acetate (0.1%) combined with miconazole (2%) in a cream b.i.d. for unspecified period > 2 weeks **Comparator** • miconazole (2%) cream
Outcomes	Assessments (5): baseline, in first week, weeks 1, 2 and at end of treatment **Outcomes of the trial** (as reported) 1. Mycological evaluation (KOH and culture) 2. Physician's and participants' assessment of overall response with respect to efficacy, tolerability, cosmetic acceptability, and patient compliance 3. Adverse events# Denotes outcomes prespecified for this review
Notes	Diagnoses unreported, unclear how many sites were tinea corporis or tinea cruris.

Tamil Selvan 2013

Methods	Randomised, unblinded, active-controlled trial Setting Multi-centre in Hyderabad, India Date of study February to August 2011. Duration of intervention 1-2 weeks with follow-up at 4 weeks
Participants	N = 150 (93 male/57 female)

Tamil Selvan 2013 *(Continued)*

	Mean age = 30 years **Inclusion criteria of the trial** • participants > 18 years old with clinical evidence of a cutaneous mycosis • a combined symptom and sign score of at least 5 (4-point Likert scale for erythema, scaling, pruritus) **Exclusion criteria of the trial** • pregnant or lactating females • known history or clinical evidence of severe cardiac, pulmonary, gastrointestinal, renal, hepatic or neurologic disease • uncontrolled diabetes mellitus • known hypersensitivity to allylamine/benzylamine agents • treatment with systemic antifungals within past month • treatment with itraconazole in past 6 months • systemic antibiotics in past 2 weeks, corticosteroids or immunosuppressant drugs in past 6 weeks • any investigational drug in past 3 months Randomised N = 150 Withdrawals/losses to follow-up • none reported Baseline data Terbinafine group: tinea corporis (19), tinea cruris (11) Eberconazole group: tinea corporis (17), tinea cruris (13) Luliconazole group: tinea corporis (15), tinea cruris (15) Sertaconazole group: tinea corporis (17), tinea cruris (13) Amorolfine group: tinea corporis (18), tinea cruris (11), tinea pedis (1)
Interventions	**Intervention** • terbinafine cream applied once daily for 1 week (30) **Comparator 1** • eberconazole cream applied once daily for 1 week (30) **Comparator 2** • luliconazole cream applied once daily for 1 week (30) **Comparator 3** • sertaconazole cream applied once daily for 1 week (30) **Comparator 4** • amorolfine cream applied once daily for 1 week in tinea cruris/corporis (29) and once daily for 2 weeks in tinea pedis (1)
Outcomes	Assessments (3): baseline, weeks 1, 2 and 4 **Outcomes of the trial** (as reported)

Tamil Selvan 2013 *(Continued)*

	1. Mycological evaluation (KOH)# 2. Clinical improvement (change in symptoms and signs score): 4-point Likert scale# 3. Adverse effects Denotes outcomes prespecified for this review
Notes	Study retrieved on 21 May 2014

Thaker 2013

Methods	Randomised, unblinded, active-controlled trial Setting Single centre, skin outpatients department, Shah Medical College, Surendranagar, Gujurat, India Date of study June 2009-2010. Duration of intervention 1 month, with follow-up 4 weeks later
Participants	N = 125 (data on gender not reported) Median age in intervention group = 34 years, range 10 to 76 yrs Median age in control group = 35 years, range 8 to 76 yrs **Inclusion criteria of the trial** • participants with new diagnosis of tinea infection in skin outpatient clinic **Exclusion criteria of the trial** • participants already being treated in the skin outpatient clinic • pregnant or lactating females • known allergy to topical imidazole or allylamine Randomised N = 125 Withdrawals/losses to follow-up • 14/125 (11%), 5/65 in sertaconazole group, 9/60 in butenafine group (all lost to follow-up) Baseline data Sertaconazole group: tinea corporis (9), tinea cruris (23), tinea corporis and cruris (18), tinea faceii (3), tinea manuum (1), tinea incognito (6) Butenafine group: tinea corporis (20), tinea cruris (5), tinea corporis and cruris (13), tinea faceii (4), tinea incognito (9)
Interventions	All participants were given oral chlorpheniramine maleate (4 mg) b.i.d. for 1 month **Intervention** • sertaconazole (2%) cream applied b.i.d. for 1 month (65) **Comparator** • butenafine (1%) cream applied b.i.d. for 1 month (60)

Thaker 2013 *(Continued)*

Outcomes	Assessments (5): baseline, day 10, day 20, day 30, 4 weeks post treatment **Outcomes of the trial** (as reported) 1. Clinical cure: 4-point Likert scale# 2. Mycological cure (KOH and culture) 3. Global evaluation response 4. Adverse effects 5. Cost effectiveness 6. Relapse Denotes outcomes prespecified for this review
Notes	Study retrieved on 21 May 2014

b.i.d. = twice daily
ITT = intention-to-treat
KOH = potassium hydroxide

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

CTRI/2009/091/000679

Trial name or title	Evaluation of efficacy and safety of naftifine versus terbinafine in the treatment of dermatophytosis: a randomized, open label, parallel group, active controlled, multi-centre study.
Methods	Multi-centre, randomised, controlled trial in India.
Participants	Participants were males and females from the ages of 18-65 with a clinical diagnosis of dermatophytosis.
Interventions	Intervention: Naftifine cream 1 %: Once daily for 4 weeks Control Intervention: Terbinafine cream 1 %: Once daily for 4 weeks
Outcomes	Primary outcomes: Assessment of following symptoms using 4-point Visual Analogue Scale (VAS). 1. Percentage of patients with erythema. 2. Percentage of patients with pruritus. 3. Percentage of patients with maceration. 4. Percentage of patients with fissuring. 5. Percentage of patients with scaling. Timepoint: Baseline (Day 0), weeks 2 and 4. Secondary outcomes: 1. Average change from baseline in Clinical Global Impression on Severity (CGI-S) in patients by investigator. 2. Clinical Global Impression on Improvement (CGI-I) in patients by investigator.Timepoint: Baseline (Day 0), weeks 2 and 4.
Starting date	September 2009 (Completed)
Contact information	Name: Dr. Surendra Borgharkar Address:

CTRI/2009/091/000679 *(Continued)*

	Sun Pharmaceutical Industries Ltd. Acme Plaza, Andheri Kurla Road, Andheri East 400059 Mumbai, MAHARASHTRA India Telephone: 02266969696 Email: medical.services@sunpharma.com
Notes	Study sponsored by Sun Pharmaceutical Industries Ltd. Retrieved from www.who.int/trialsearch on 19 October 2012, website last accessed 1 June 2014

CTRI/2009/091/001025

Trial name or title	A comparative, randomized, double blind, multicentric, prospective clinical study to evaluate the efficacy, safety and tolerability of naftifine hydrochloride 1% cream vs. Terbinafine Hydrochloride 1% cream in patients with Tinea pedis and Tinea cruris.
Methods	Multi-centre, randomised, controlled, double-blind, prospective clinical study.
Participants	Men and women over the age of 18 with microscopically proven tinea infection.
Interventions	Intervention: Naftifine Hydrochloride 1% cream: Twice a day, in the morning and evening for 28 days Control Intervention: Terbinafine Hydrochloride 1% cream: Twice a day, in the morning and evening for 28 days
Outcomes	Primary outcome: Itching, erythema, scaling/crusting, vesicles and papules at time points: Days 0, 7, 14 and 28 Secondary outcomes: Overall response by mycological assessment (KOH mount) at time points: Days 0, 7, 14 and 28 Patients and physicians global assessment of treatment efficacy and tolerability at time points: Days 0, 7, 14 and 28
Starting date	January 2010 (completed)
Contact information	Name: Dr. Shailesh Singh Address: Ajanta Pharma Ltd, Ajanta House Hindustan Naka, Kandivli(w) 400 067 Mumbai, MAHARASHTRA India

CTRI/2009/091/001025 *(Continued)*

	Telephone: 022 66061000 Email: shaileshs@ajantapharma.com Affiliation: Sr. GM (Ajanta Pharma Limited)
Notes	Trial sponsored by Ajanta Pharma Limited Retrieved from www.who.int/trialsearch on 19 October 2012, website last accessed 1 June 2014

CTRI/2010/091/000178

Trial name or title	Comparative assessment of efficacy, safety and tolerability of Sertaconazole nitrate 2% plus Beclomethasone dipropionate 0.025% cream vs Miconazole nitrate 2% cream in patients with Tinea infections associated with inflammatory dermatoses
Methods	Multi-centre, randomised, double-blind, controlled, prospective clinical study.
Participants	200 participants with inflammatory dermatoses will be recruited, aged between 18 and 70 years old, with a clinical diagnosis of tinea infection, confirmed by KOH microscopy.
Interventions	Intervention: Sertaconazole nitrate 2 % plus Beclomethasone dipropionate 0.025% cream: Every 12 hours topical Control Intervention: Miconazole nitrate 2% cream: Every 12 hours topical
Outcomes	Primary outcome: Clinical evaluation of the disease assessed in accordance with the clinical scale, Mycologic assessment, physician assessment. Time points: Baseline, Days 7, 14 and 28 Secondary outcomes: Global assessment of clinical response. Time points: Baseline, Days 7, 14 and 28 Overall response at 4 weeks. Time points: Baseline, Days 7, 14 and 28
Starting date	Not yet recruiting
Contact information	Name: Chandrashekhar S Bolmall Address: Glenmark Pharmaceuticals Ltd., Glenmark House, B D Sawant Marg Chakala, Andheri(East) 400099 Mumbai, MAHARASHTRA India Telephone: 91-22-40189999

CTRI/2010/091/000178 *(Continued)*

	Email: chandrashekharb@glenmarkpharma.com
Notes	Trial sponsored by Glenmark Pharmaceuticals Ltd. Retrieved from www.who.int/trialsearch on 19 October 2012, website last accessed 1 June 2014

CTRI/2012/03/002522

Trial name or title	A single centre, double blind, placebo controlled, randomized, confirmatory efficacy study of biovite®s calmagenTM dermaceutical cream & lotion for the topical treatment of tinea
Methods	Single centre, randomised, double-blind, controlled trial.
Participants	28 participants aged 18 or older, with clinical tinea infection and positive KOH microscopy, fungal culture and presence of live spores.
Interventions	Biovites® CalmagenTM Dermaceutical cream & lotion, twice daily, topically applied for 4 weeks and a matching placebo and cream.
Outcomes	Primary outcome: Mycological cure as determined by negative KOH microscopy, negative fungal culture and reduction in live spore counts at the end of the study period (4 weeks) Secondary outcomes: Improvement in clinical appearance of lesions as assessed by photography at baseline and end of study. Reduction in size and severity of lesions from baseline to end of study.
Starting date	March 2010 (Completed)
Contact information	Name: Dr Girisha R Address: Manipal Acunova Limited EPIP, Whitefield, 560066 Bangalore, KARNATAKA India Telephone: 08066915775 Email: girisha.r@ecronacunova.com Name: Mr Rakesh Naranbhai Dadhania

CTRI/2012/03/002522 *(Continued)*

	Address: Manipal Acunova Limited EPIP, Whitefield, 560066 Bangalore, KARNATAKA India Telephone: 08066915775 Email: girisha.r@ecronacunova.com
Notes	Sponsored by Biovite Australia Pty Ltd Retrieved from www.who.int/trialsearch on 19 October 2012, website last accessed 1 June 2014

EUCTR2005-001239-32

Trial name or title	Ensayo clínico multicéntrico, aleatorizado, paralelo, doble ciego, para evaluar la eficacia y seguridad de eberconazol solución 1% frente a placebo en el tratamiento de las dermatofitosis
Methods	This is a multi-centre, double-blind, randomised controlled trial in Spain. Participants are allocated to treatment with 1% eberconazole solution or placebo.
Participants	Patients aged 18 and over with a clinical diagnosis of dermatophytosis.
Interventions	Eberconazole 1% solution and placebo
Outcomes	Primary outcome: Effectiveness of treatment based on the percentage of clinical and mycological responses at 4 weeks of treatment. Secondary outcomes: To compare the evolving signs and symptoms of infection between groups at 2 weeks and 4 weeks. To compare the difference in mycology between groups at 4 weeks. To compare clinical relapse at 4 weeks post treatment. To compare the tolerability and safety of the treatments. To compare the improvement shown between the two groups.
Starting date	02-09-2005
Contact information	Laboratorios SALVAT, S.A Sponsor Protocol Number: EBERTOIII/05ES01

EUCTR2005-001239-32 *(Continued)*

Notes	Retrieved from https://www.clinicaltrialsregister.eu/ on 19 October 2012, website last accessed 1 June 2014

NCT01342315

Trial name or title	A randomized, multi-center, double-blind, vehicle-controlled study evaluating the efficacy and safety of Product 33525 in subjects with Tinea Cruris
Methods	Multi-centre, double-blinded placebo-controlled study taking place in the USA and Central America
Participants	Males and females of age 12 and above with clinical evidence of tinea cruris
Interventions	Product 33525 and placebo
Outcomes	Primary outcome: Proportion of patients achieving complete clearance 3 weeks post-treatment - no signs and symptoms, severity score and negative KOH and culture Secondary outcome: Proportion of patients achieving effective treatment 1 week post treatment, 2 weeks post treatment, and 3 weeks post treatment
Starting date	May 2011 (Completed)
Contact information	mgsc@studyinbox.com
Notes	Sponsored by Tinea Pharmaceuticals Retrieved from clinicaltrials.gov on 19 October 2012, website last accessed 1 June 2014

NCT01885156

Trial name or title	Evaluation of efficacy and safety of Naftin 1% Cream in adolescent subjects with Tinea Cruris
Methods	Multi-centre, double-blinded placebo-controlled study taking place in Central America
Participants	Males and females aged 12-17 years with clinical and mycological confirmation of tinea cruris
Interventions	Naftifine 1% cream once daily for 4 weeks and vehicle cream. Follow-up at 6 weeks
Outcomes	Primary outcome: Safety of naftifine 1% cream Secondary outcome: Efficacy of naftifine 1% cream
Starting date	August 2013
Contact information	Stefan Plaum MD, Merz Pharmaceuticals, LLC
Notes	Secondary ID: MUS 90200_3028_1

NCT01885156 *(Continued)*

Retrieved from www.who.int/trialsearch on 23 May 2014

KOH = potassium hydroxide

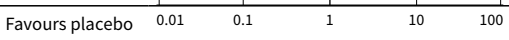
DATA AND ANALYSES

Comparison 1. Clotrimazole 1% cream versus placebo cream twice daily

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Mycological cure	2	344	Risk Ratio (M-H, Random, 95% CI)	2.87 [2.28, 3.62]

Analysis 1.1. Comparison 1 Clotrimazole 1% cream versus placebo cream twice daily, Outcome 1 Mycological cure.

Study or subgroup	Clotrimazole n/N	Placebo n/N	Risk Ratio M-H, Random, 95% CI	Weight	Risk Ratio M-H, Random, 95% CI
Miura 1979	58/65	22/66		43.36%	2.68[1.88,3.8]
Spiekermann 1976	99/111	30/102		56.64%	3.03[2.23,4.12]
Total (95% CI)	**176**	**168**		**100%**	**2.87[2.28,3.62]**
Total events: 157 (Clotrimazole), 52 (Placebo)					
Heterogeneity: Tau^2=0; Chi^2=0.28, df=1(P=0.6); I^2=0%					
Test for overall effect: Z=8.94(P<0.0001)					

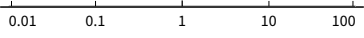


Comparison 2. Terbinafine 1% cream/gel once or twice daily versus placebo cream/gel once or twice daily

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Mycological cure	7		Risk Ratio (M-H, Random, 95% CI)	Totals not selected
2 Clinical cure	5	273	Risk Ratio (M-H, Random, 95% CI)	4.51 [3.10, 6.56]
3 Clinical cure (low risk of attrition bias)	2	77	Risk Ratio (M-H, Random, 95% CI)	4.38 [2.02, 9.52]
4 Adverse effects	7	469	Risk Ratio (M-H, Random, 95% CI)	0.43 [0.20, 0.92]
5 Participant-judged cure	2	253	Risk Ratio (M-H, Random, 95% CI)	4.46 [3.16, 6.31]

Analysis 2.1. Comparison 2 Terbinafine 1% cream/gel once or twice daily versus placebo cream/gel once or twice daily, Outcome 1 Mycological cure.

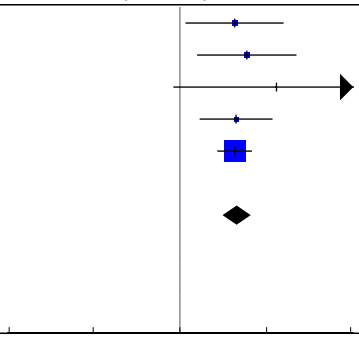
Study or subgroup	Terbinafine n/N	Placebo n/N	Risk Ratio M-H, Random, 95% CI	Risk Ratio M-H, Random, 95% CI
Budimulja 2001	53/57	11/60		5.07[2.96,8.69]
Cordero 1992	27/29	5/16		2.98[1.43,6.2]
Evans 1992	12/14	9/17		1.62[0.99,2.66]
Greer 1990	9/9	2/11		4.56[1.5,13.87]
Lebwohl 2001	21/23	10/16		1.46[0.98,2.18]
Millikan 1990	9/9	3/9		2.71[1.15,6.39]
van Heerden 1997	20/27	5/33		4.89[2.12,11.3]



Favours placebo — Favours terbinafine

Analysis 2.2. Comparison 2 Terbinafine 1% cream/gel once or twice daily versus placebo cream/gel once or twice daily, Outcome 2 Clinical cure.

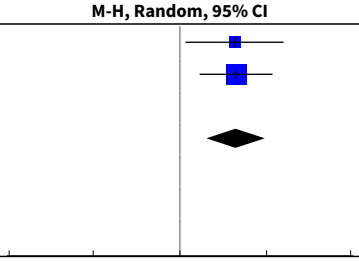
Study or subgroup	Terbinafine n/N	Placebo n/N	Risk Ratio M-H, Random, 95% CI	Weight	Risk Ratio M-H, Random, 95% CI
Greer 1990	7/9	2/11		8.31%	4.28[1.16,15.72]
Lebwohl 2001	17/23	2/16		8.09%	5.91[1.58,22.11]
Millikan 1990	6/9	0/9		1.88%	13[0.84,201.26]
van Heerden 1997	16/27	4/30		15.14%	4.44[1.69,11.66]
Zaias 1993	58/66	15/73		66.58%	4.28[2.7,6.77]
Total (95% CI)	**134**	**139**		**100%**	**4.51[3.1,6.56]**
Total events: 104 (Terbinafine), 23 (Placebo)					
Heterogeneity: Tau^2=0; Chi^2=0.83, df=4(P=0.93); I^2=0%					
Test for overall effect: Z=7.87(P<0.0001)					



Favours placebo — Favours terbinafine

Analysis 2.3. Comparison 2 Terbinafine 1% cream/gel once or twice daily versus placebo cream/gel once or twice daily, Outcome 3 Clinical cure (low risk of attrition bias).

Study or subgroup	Terbinafine n/N	Placebo n/N	Risk Ratio M-H, Random, 95% CI	Weight	Risk Ratio M-H, Random, 95% CI
Greer 1997	7/9	2/11		35.45%	4.28[1.16,15.72]
van Heerden 1997	16/27	4/30		64.55%	4.44[1.69,11.66]
Total (95% CI)	**36**	**41**		**100%**	**4.38[2.02,9.52]**
Total events: 23 (Terbinafine), 6 (Placebo)					
Heterogeneity: Tau^2=0; Chi^2=0, df=1(P=0.96); I^2=0%					
Test for overall effect: Z=3.74(P=0)					



Favours placebo — Favours terbinafine

Analysis 2.4. Comparison 2 Terbinafine 1% cream/gel once or twice daily versus placebo cream/gel once or twice daily, Outcome 4 Adverse effects.

Study or subgroup	Terbinafine n/N	Placebo n/N	Risk Ratio M-H, Random, 95% CI	Weight	Risk Ratio M-H, Random, 95% CI
Budimulja 2001	1/60	8/60		13.78%	0.13[0.02,0.97]
Cordero 1992	0/36	1/38		5.76%	0.35[0.01,8.36]
Evans 1992	0/38	0/35			Not estimable
Greer 1990	0/11	1/12		6%	0.36[0.02,8.04]
Lebwohl 2001	2/32	1/34		10.45%	2.13[0.2,22.31]
Millikan 1990	0/15	0/15			Not estimable
van Heerden 1997	5/40	12/43		64%	0.45[0.17,1.16]
Total (95% CI)	**232**	**237**		**100%**	**0.43[0.2,0.92]**
Total events: 8 (Terbinafine), 23 (Placebo)					
Heterogeneity: Tau^2=0; Chi^2=3.25, df=4(P=0.52); I^2=0%					
Test for overall effect: Z=2.17(P=0.03)					

Analysis 2.5. Comparison 2 Terbinafine 1% cream/gel once or twice daily versus placebo cream/gel once or twice daily, Outcome 5 Participant-judged cure.

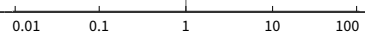
Study or subgroup	Terbinafine n/N	Placebo n/N	Risk Ratio M-H, Random, 95% CI	Weight	Risk Ratio M-H, Random, 95% CI
Budimulja 2001	48/56	9/58		32.25%	5.52[3,10.17]
Zaias 1993	62/66	17/73		67.75%	4.03[2.65,6.14]
Total (95% CI)	**122**	**131**		**100%**	**4.46[3.16,6.31]**
Total events: 110 (Terbinafine), 26 (Placebo)					
Heterogeneity: Tau^2=0; Chi^2=0.71, df=1(P=0.4); I^2=0%					
Test for overall effect: Z=8.47(P<0.0001)					

Comparison 3. Naftifine 1% cream once or twice daily versus placebo cream once or twice daily

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Mycological cure	3	187	Risk Ratio (M-H, Random, 95% CI)	2.38 [1.80, 3.14]
2 Mycological cure (low risk of attrition bias)	2	125	Risk Ratio (M-H, Random, 95% CI)	2.32 [1.69, 3.20]
3 Adverse effects	3	195	Risk Ratio (M-H, Random, 95% CI)	0.44 [0.13, 1.57]

Analysis 3.1. Comparison 3 Naftifine 1% cream once or twice daily versus placebo cream once or twice daily, Outcome 1 Mycological cure.

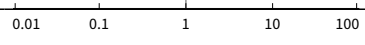
Study or subgroup	Naftifine n/N	Placebo n/N	Risk Ratio M-H, Random, 95% CI	Weight	Risk Ratio M-H, Random, 95% CI
Dobson 1991	28/34	9/28		24.59%	2.56[1.46,4.49]
Gip 1987	30/32	14/31		48.7%	2.08[1.39,3.09]
Jordon 1990	25/29	10/33		26.71%	2.84[1.66,4.87]
Total (95% CI)	**95**	**92**		**100%**	**2.38[1.8,3.14]**
Total events: 83 (Naftifine), 33 (Placebo)					
Heterogeneity: Tau^2=0; Chi^2=0.97, df=2(P=0.62); I^2=0%					
Test for overall effect: Z=6.11(P<0.0001)					



Favours placebo — Favours naftifine

Analysis 3.2. Comparison 3 Naftifine 1% cream once or twice daily versus placebo cream once or twice daily, Outcome 2 Mycological cure (low risk of attrition bias).

Study or subgroup	Naftifine n/N	Placebo n/N	Risk Ratio M-H, Random, 95% CI	Weight	Risk Ratio M-H, Random, 95% CI
Gip 1987	30/32	14/31		64.58%	2.08[1.39,3.09]
Jordon 1990	25/29	10/33		35.42%	2.84[1.66,4.87]
Total (95% CI)	**61**	**64**		**100%**	**2.32[1.69,3.2]**
Total events: 55 (Naftifine), 24 (Placebo)					
Heterogeneity: Tau^2=0; Chi^2=0.88, df=1(P=0.35); I^2=0%					
Test for overall effect: Z=5.16(P<0.0001)					



Favours placebo — Favours naftifine

Analysis 3.3. Comparison 3 Naftifine 1% cream once or twice daily versus placebo cream once or twice daily, Outcome 3 Adverse effects.

Study or subgroup	Naftifine n/N	Placebo n/N	Risk Ratio M-H, Random, 95% CI	Weight	Risk Ratio M-H, Random, 95% CI
Dobson 1991	2/34	4/28		60.76%	0.41[0.08,2.08]
Gip 1987	1/32	1/31		21.49%	0.97[0.06,14.82]
Jordon 1990	0/33	2/37		17.75%	0.22[0.01,4.49]
Total (95% CI)	**99**	**96**		**100%**	**0.44[0.13,1.57]**
Total events: 3 (Naftifine), 7 (Placebo)					
Heterogeneity: Tau^2=0; Chi^2=0.53, df=2(P=0.77); I^2=0%					
Test for overall effect: Z=1.26(P=0.21)					

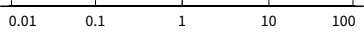
Favours naftifine — Favours placebo

Comparison 4. Azoles versus allylamines

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Mycological cure	7		Risk Ratio (M-H, Random, 95% CI)	Totals not selected
2 Clinical cure	6		Risk Ratio (M-H, Random, 95% CI)	Totals not selected
3 Mycological cure (low risk of attrition bias)	4	319	Risk Ratio (M-H, Random, 95% CI)	0.99 [0.95, 1.03]
4 Clinical cure (low risk of attrition bias)	4	319	Risk Ratio (M-H, Random, 95% CI)	0.97 [0.92, 1.02]
5 Adverse effects	5	386	Risk Ratio (M-H, Random, 95% CI)	0.70 [0.18, 2.68]

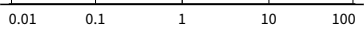
Analysis 4.1. Comparison 4 Azoles versus allylamines, Outcome 1 Mycological cure.

Study or subgroup	Favours allylamines n/N	Allylamines n/N	Risk Ratio M-H, Random, 95% CI	Risk Ratio M-H, Random, 95% CI
Budimulja 1998	84/86	87/89		1[0.95,1.05]
Hantschke 1980	3/3	7/7		1[0.66,1.51]
Haroon 1996	18/18	15/15		1[0.89,1.12]
Jerajani 2013	40/40	22/22		1[0.93,1.07]
Kagawa 1987	88/117	100/107		0.8[0.72,0.9]
Wang 1995	27/30	42/45		0.96[0.84,1.11]
Wang 2000	28/29	30/30		0.97[0.88,1.06]



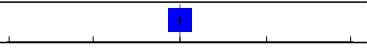
Analysis 4.2. Comparison 4 Azoles versus allylamines, Outcome 2 Clinical cure.

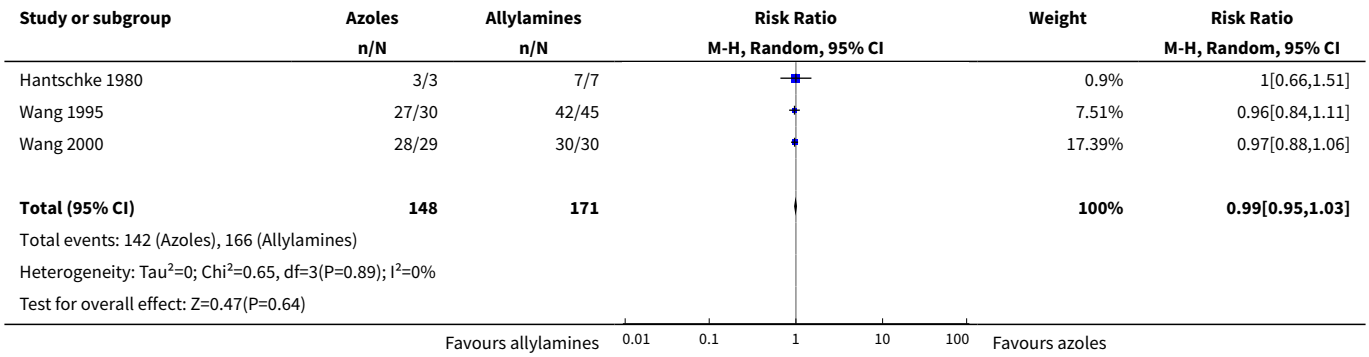
Study or subgroup	Favours allylamines n/N	Allylamines n/N	Risk Ratio M-H, Random, 95% CI	Risk Ratio M-H, Random, 95% CI
Budimulja 1998	82/86	88/89		0.96[0.92,1.02]
Hantschke 1980	3/3	7/7		1[0.66,1.51]
Jerajani 2013	39/40	19/22		1.13[0.95,1.34]
Kagawa 1987	84/117	100/107		0.77[0.68,0.87]
Wang 1995	27/30	41/45		0.99[0.85,1.15]
Wang 2000	14/29	15/30		0.97[0.57,1.62]



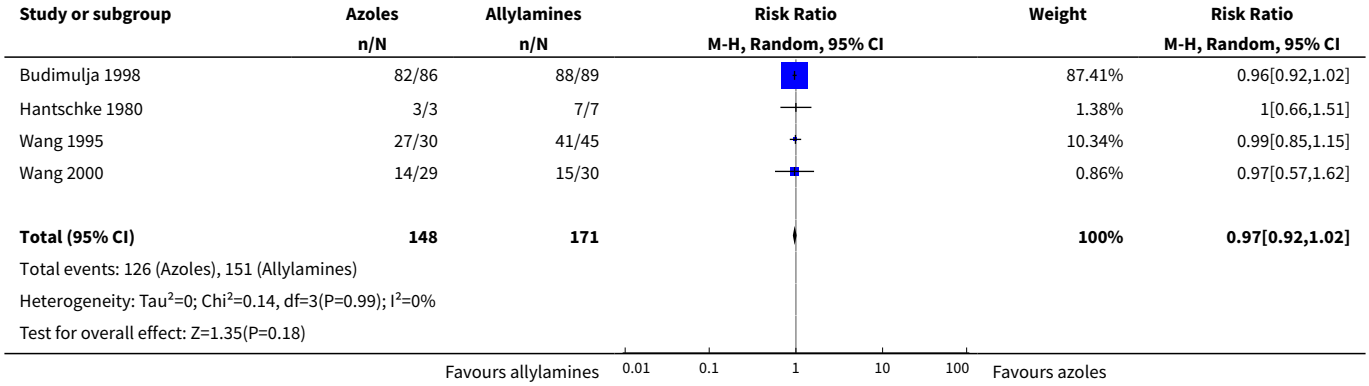
Analysis 4.3. Comparison 4 Azoles versus allylamines, Outcome 3 Mycological cure (low risk of attrition bias).

Study or subgroup	Azoles n/N	Allylamines n/N	Risk Ratio M-H, Random, 95% CI	Weight	Risk Ratio M-H, Random, 95% CI
Budimulja 1998	84/86	87/89		74.2%	1[0.95,1.05]

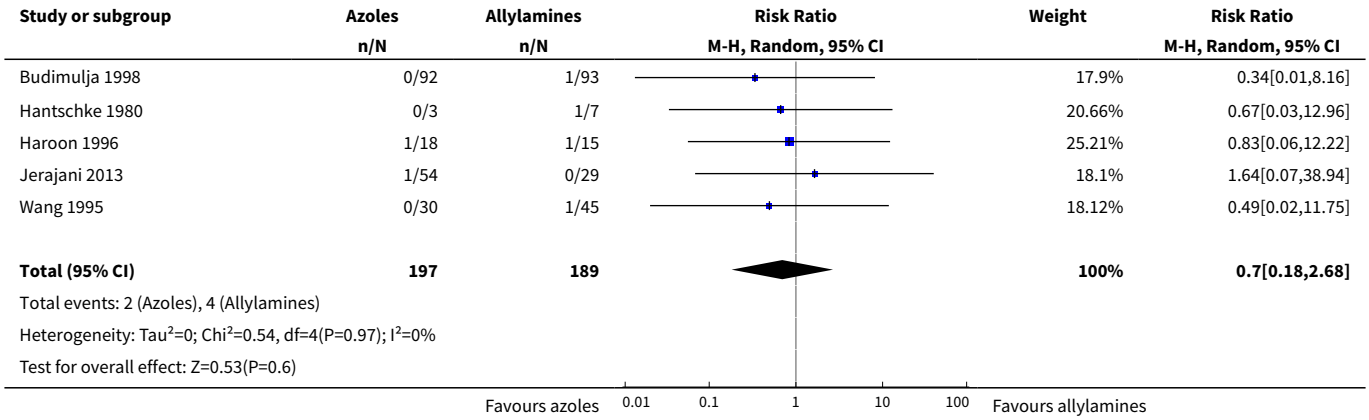




Analysis 4.4. Comparison 4 Azoles versus allylamines, Outcome 4 Clinical cure (low risk of attrition bias).



Analysis 4.5. Comparison 4 Azoles versus allylamines, Outcome 5 Adverse effects.

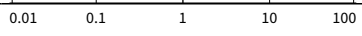


Comparison 5. Azole versus moderate-potent corticosteroid/azole combination

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Mycological cure	6	625	Risk Ratio (M-H, Random, 95% CI)	0.99 [0.93, 1.05]
2 Mycological cure (low risk of attrition bias)	5	433	Risk Ratio (M-H, Random, 95% CI)	0.99 [0.92, 1.07]
3 Clinical cure	5		Risk Ratio (M-H, Random, 95% CI)	Totals not selected
4 Clinical cure (at end of treatment)	4	353	Risk Ratio (M-H, Random, 95% CI)	0.67 [0.53, 0.84]
5 Adverse effects	5	668	Risk Ratio (M-H, Random, 95% CI)	1.36 [0.68, 2.69]

Analysis 5.1. Comparison 5 Azole versus moderate-potent corticosteroid/azole combination, Outcome 1 Mycological cure.

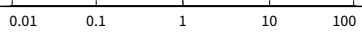
Study or subgroup	Azole n/N	Corticosteroid/azole n/N	Risk Ratio M-H, Random, 95% CI	Weight	Risk Ratio M-H, Random, 95% CI
Katz 1984	59/100	71/111		9.07%	0.92[0.74,1.14]
Li 2004	37/41	39/41		28.05%	0.95[0.84,1.07]
Pariser 1995	81/99	78/93		25.28%	0.98[0.86,1.11]
Shen 2002	22/23	17/19		13.35%	1.07[0.9,1.28]
Wang 2000a	31/35	30/33		16.23%	0.97[0.83,1.14]
Wortzel 1982	15/15	13/15		8.02%	1.15[0.91,1.44]
Total (95% CI)	**313**	**312**		**100%**	**0.99[0.93,1.05]**
Total events: 245 (Azole), 248 (Corticosteroid/azole)					
Heterogeneity: Tau^2=0; Chi^2=3.5, df=5(P=0.62); I^2=0%					
Test for overall effect: Z=0.38(P=0.7)					



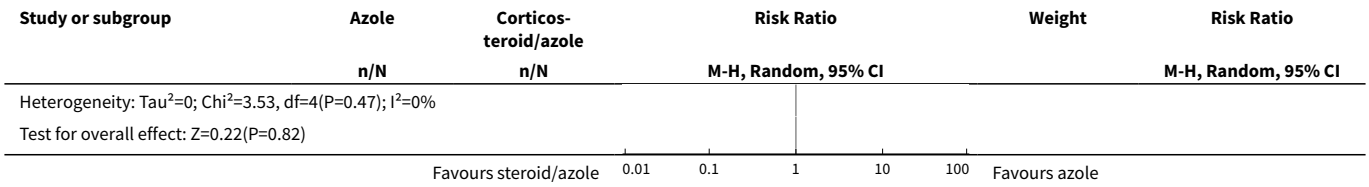
Favours steroid/azole — Favours azole

Analysis 5.2. Comparison 5 Azole versus moderate-potent corticosteroid/azole combination, Outcome 2 Mycological cure (low risk of attrition bias).

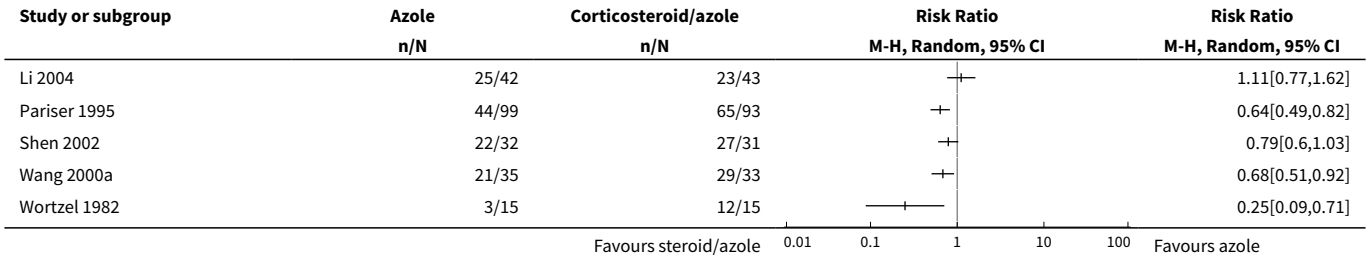
Study or subgroup	Azole n/N	Corticosteroid/azole n/N	Risk Ratio M-H, Random, 95% CI	Weight	Risk Ratio M-H, Random, 95% CI
Katz 1984	59/100	71/111		12.14%	0.92[0.74,1.14]
Li 2004	37/41	39/41		37.54%	0.95[0.84,1.07]
Shen 2002	22/23	17/19		17.87%	1.07[0.9,1.28]
Wang 2000a	31/35	30/33		21.73%	0.97[0.83,1.14]
Wortzel 1982	15/15	13/15		10.74%	1.15[0.91,1.44]
Total (95% CI)	**214**	**219**		**100%**	**0.99[0.92,1.07]**
Total events: 164 (Azole), 170 (Corticosteroid/azole)					



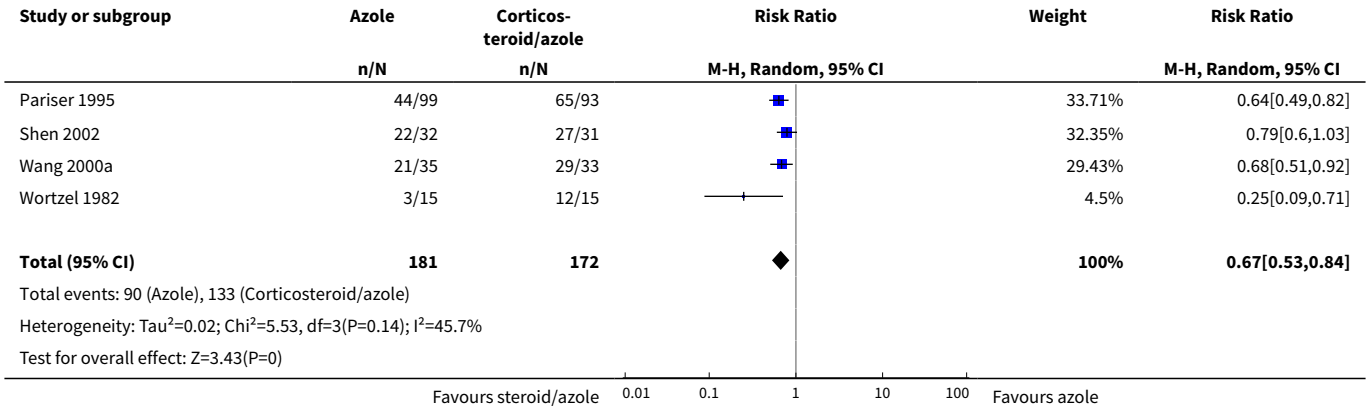
Favours steroid/azole — Favours azole



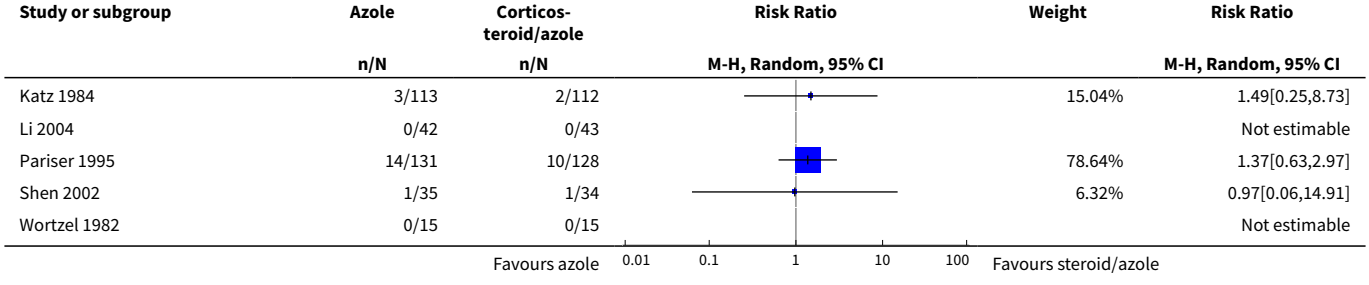
Analysis 5.3. Comparison 5 Azole versus moderate-potent corticosteroid/azole combination, Outcome 3 Clinical cure.

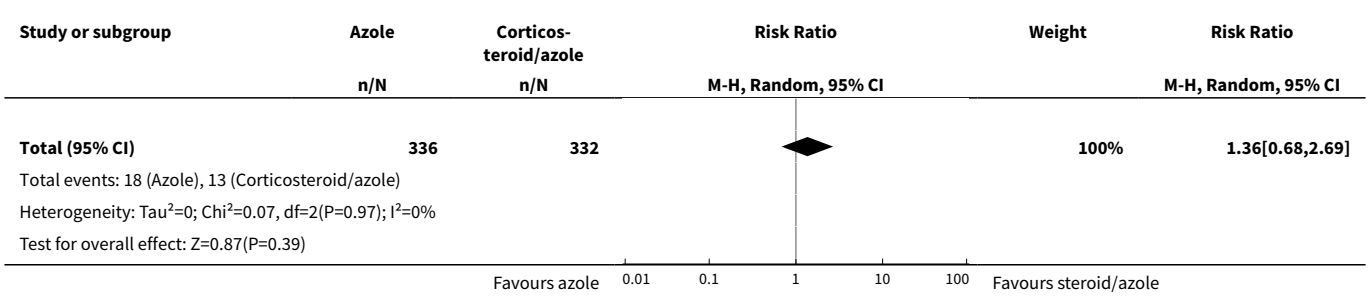


Analysis 5.4. Comparison 5 Azole versus moderate-potent corticosteroid/azole combination, Outcome 4 Clinical cure (at end of treatment).



Analysis 5.5. Comparison 5 Azole versus moderate-potent corticosteroid/azole combination, Outcome 5 Adverse effects.

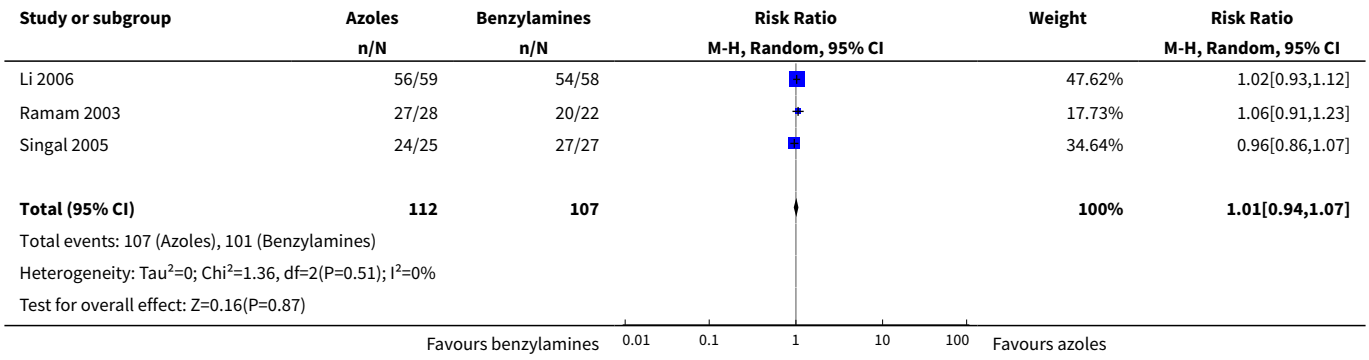




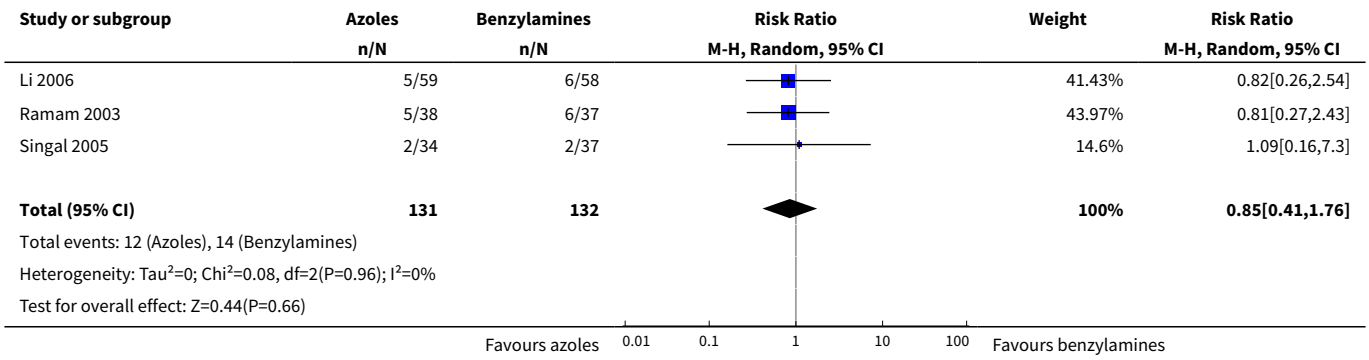
Comparison 6. Azoles versus benzylamines

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Mycological cure	3	219	Risk Ratio (M-H, Random, 95% CI)	1.01 [0.94, 1.07]
2 Adverse effects	3	263	Risk Ratio (M-H, Random, 95% CI)	0.85 [0.41, 1.76]

Analysis 6.1. Comparison 6 Azoles versus benzylamines, Outcome 1 Mycological cure.



Analysis 6.2. Comparison 6 Azoles versus benzylamines, Outcome 2 Adverse effects.



ADDITIONAL TABLES

Table 1. Contact with investigators

Study ID	Response	Additional	Comment
Alomar 1995; Alomar 1992	No	Failed to respond	agustin.alomar@usphospitales.com, emailed twice requesting subset data for TC. 12 February 2013: Investigator does not understand the question
Banerjee 2011	Yes	Yes	Dr. Manasi Banerjee, Department of Pharmacology, Medical College, Kolkata, India. E-mail manasi.bnrj123@gmail.com Response 13 February: The trial report between amorolfine and clotrimazole was published in Indian Journal of Dermatology 2011; 56(6):657-62. Recently the other part has been published as 'Comparative evaluation of efficacy and safety of topical fluconazole and clotrimazole in the treatment of tinea corporis' in Journal of Pakistan Association of Dermatologists 2012;22 (4):342-349. Randomization was achieved through Random Number Table and patients were accordingly allocated to the respective groups. Blinding could not be done in true sense of the term as we could not procure the medicines in identical containers. However, drug allotment and clinical assessment of patients were done by different set of researchers and the data were kept separately till the end of the studies.
Binet 1994	No	Unable to contact	No email address, moved to awaiting assessment Dr J Forn, Director of Research Center, J. Uriach & Cia, SA, Degà Bahi, 59-67, E-08026 Barcelona, Spain
Bogaert 1986	No	Unable to contact	No email address: Mr Peter Muller, Hoechst AG Frankfurt Germany
Bonifaz 2000	Yes	Study excluded	A. Bonifaz, A. Saúl bonyalx@servidor.unam.mx. 11 February: Reply: Allocation of the patients was by alternation
Borelli 2007	No	Failed to respond	2 emails sent to claudia.borelli@med.uni-muenchen.de
Budimulja 2001	No	Unable to contact	No email address.
Califano 1999	No	Unable to contact	No email address
Clerico 1987	No	Failed to respond	2 emails sent (2) rita.clerico@uniroma1.it
del Palacio 1989;up to del Palacio 2001	No	Failed to respond	Emails sent (3) Jan/Feb 2013 apalacioh.hdoc@salud.madrid.org; amaliadelpalacio@gmail.com
Dinkela 2007	Yes	Yes	Email sent sequence generation/concealment inconsistency in data. christoph.hatz@unibas.ch Reply: Randomisation was computer based and carried out by a statistician at Swiss Tropical and Public Health Institute, Basel, before the onset of the clinical trial. First verum and

Table 1. Contact with investigators *(Continued)*

			placebo were randomly assigned to letters A to U. Every one but the statistician and those involved in the production of the soap were blinded with regard to this allocation sequence. Randomisation of the study population was completed by attributing the letters A to U randomly to the serial numbers of 1 to 400 for 400 possible study units. During the screening examination all the study participants living in one household were identified and formed one unit. A unit could consist of one or more children. At both schools the serial numbers assigned to the randomised letters were distributed in the order of the names on the list of the study participants. The list had been created by the field investigators in the order in which the children had been included in the study. After the field investigators had collected all the data and returned to Switzerland for evaluation, they were unblinded. 3. We also have a query regarding the total numbers of participants as reported in Fig1. the title states the number of cases as 224 but the totals in the figure add up to 250? This is also inconsistent with Fig1 and numbers in the text on Pg 24 i.e. 278-34= 244 and a further loss of 20 during and after the trial =224. Reply: Some children had multiple infections. In Fig. 1 the number of cases are presented, not the number of patients. Thus, the total number of cases is higher (250) than the number of study participants (224). 4. There is missing data/participants in Table 2 for both screening and follow-up. Reply: The samples of 45 children taken during the screening examination could not be evaluated. At the follow-up examination the samples of 8 children could not be evaluated in this study. In these missing cases not enough material could be collected or samples were contaminated by dust and therefore did not allow microscopic assessment. No samples were taken in the case of tinea pedis.
el Darouti 1989	No	Failed to respond	2 emails sent mohammad_eldarouti@yahoo.com
Evans 1992	No	Unable to contact	No email address or contact number.
Fredriksson 1983		Unable to contact	No email address or contact number.
Ghaninejad 2009	No	Failed to respond	emails sent (2) Jan/Feb 2013 rasidiarmin@yahoo.com
Gooskens 1994		Unable to contact	No email address or contact number
Greer 1997; Greer 1990	No	Unable to contact	No email address
Guillano 2005	Yes	Unable retrieve data	Email sent 15 February re further outcome data, reply received 'if not printed in published paper than difficulty in retrieving raw data'
Haroon 1996	No	Unable to contact	No email address Prof T S Haroon, 35/1 Main Gulberg, Lahore Pakistan
Yim 2010	No	Failed to respond	2 emails sent kjahn@kuh.ac.kr

Table 1. Contact with investigators *(Continued)*

Leiste 1989	No	Unable to contact	No email address or contact number
Li 2003;	No	Failed to respond	Email sent Jan 2013 lrywdh@public.bta.net.cn
Lesher 1997	No	Failed to respond	Emails sent (2) Nov 2012, Feb 2013 JLESHER@georgiahealth.edu
Luciani 1988	No	Unable to contact	No email address or contact number
Macasaet 1991	No	Unable to contact	EN Macaset, Manila Doctors Hospital Ermita Manila Philippines. P Pert, Tillotts Pharma Henlow Beds UK.
Nolting 1992	No	Unable to contact	No email address or contact number
Oladele 2010	Yes	Yes	kunleladele@yahoo.com " Block (24) randomisation was used in the selection of the subjects" " Drug packaging was the same but coded by researcher to conceal the differences from the subjects such that no subject can distinguish between treatment and control drugs for intervention".
Parish 2011	Yes	Responded	lparish@parishdermatology.com and jparish@parishdermatology.com. Both mails seem to be incorrect Alan Fleischer: afleisch@wakehealth.edu 1. The method used to generate the allocation sequence A blocked, unstratified randomization schedule was generated using SAS version 9.1.3 by an unblinded statistician and programmer who are not otherwise involved in the study. Subjects were presumptively enrolled prior to the availability of culture results. Randomization occurred at visit 1/day 1 through the PharmaNet IWRS system. Drug was supplied in a target/threshold fashion to the study centers through interaction between PharmaNet IWRS and Fisher Clinical Services. Subjects who met all eligibility requirements were randomly allocated following all baseline evaluations using a 1:1 ratio to 1 of the two groups: Naftifine cream applied QD or vehicle applied QD. 2. The method used to conceal the allocation sequence to ensure that intervention allocations could not have been foreseen in advance of, or during, enrolment ie participants and investigators enrolling participants could not foresee the upcoming assignment (this is not the same as blinding!!) In order to account for bias during the study, only two copies of the randomization schedule with study medication assignment were generated. One copy remained with the clinical packaging records at the labelling facility and the other was maintained in a locked, fireproof cabinet by PharmaNet. Sites never received the randomization schedule at any point during the trial. 3. The method used to blind the investigators and the patients. It states double-blind, but without the method of blinding All study drug was supplied in 60gram tubes for topical administration. The site entered the PharmaNet IWRS system for the randomized subject to receive the carton number for the study medication to be dispensed. All results from the PharmaNet IWRS system were printed and stored in the source for each randomized patient. Each tube and box of study medication was

Table 1. Contact with investigators *(Continued)*

			labelled with a double-blind 2-part label to identify study number, carton number, application instructions, and proper storage. Each carton was subject specific. The tubes for the active product as well as the vehicle looked identical. Investigators and subjects were not provided any information as to the treatment allocation.
Ramam 2003	No	Failed to respond	Only allocation concealment, but high risk in view losses. mramam@hotmail.com
Repiso Montero 2006	No	Emails undeliverable	Email sent 17 March re separate outcome data for tinea cruris and tinea corporis. 27629trm@comb.es and 29815jrt@comb.es
Schwarz 1978	No	Unable to contact	Old study no email address available
Sharma 2011	No	Failed to respond	e-mailed twice vidyagaurib@glenmarkpharma.com
Shi 2011	No	Failed to respond	Email sent 1st March to enquire re further outcome details - clinical efficacy rates at week 2 and mycological clearance at week 2
Singal 2005	No	Yes	Correspondence: deepikapandhi@rediffmail.com Response": The computer generated random numbers after generation were directly placed in an opaque sealed envelope and given to the clinical nurse (randomisation authority). This was opened by her and kept in a locked cupboard, the key to which was only available to her. She was briefed before the trial about need for not revealing details to patients as well as investigators. Further, the coded containers were also kept in same locked cupboard with no access to investigators at anytime during the trial. Hence, pharmacy controlled concealment of randomisation was carried out and treatment assignment could not be known to both investigators and patients any time during the trial
Susilo 2003	No	Failed to respond	E-mail Jan 2013 susilo@trommsdorff.de
van Heerden 1997	No	Yes	emails sent (2) Dec 2012, Feb 2013 dermdoc@telkomsa.net Reply: I apologise for final communication. Unfortunately neither Novartis nor the previous Sandoz group can trace any records with respect to this trial so I cannot answer your question. I don't remember the fine points of my publication with regards to patient selection and randomization.
Viayna 2003	Yes	Yes	cviayna@salvatbiotech.com Reply 1. The method used to generate the allocation sequence According to the protocol patients were distributed and randomly assigned to two treatment groups by computerized randomization of blocks of 4. 2. The method used to conceal the allocation sequence to ensure that intervention allocations could not have been foreseen in advance of, or during, enrolment i.e. participants and investigators enrolling participants could not foresee the upcoming assignment (this is not the same as blinding)

Table 1. Contact with investigators *(Continued)*

	In each center, the numbers assigned to each patient followed a specific sequence and the investigator had to strictly follow the sequence indicated. 3. You state that the study was " double-blind". Can you indicate what measures were used, to blind study participants and personnel from knowledge of which intervention a participant received? The experimental treatment, 1% eberconazole cream, was provided in properly labelled 60-g tubes. One tube per patient was prepared. The control treatment, 2% miconazole cream, was provided by Laboratorios Esteve and repackaged and properly labelled for the clinical trial by Laboratorios SALVAT, S.A. One 60-g tube per patient was prepared. Both treatments were labelled with the same information in order to maintain the double blind. 4. We would also kindly request your help with incomplete data as below: 653 randomised, 360 analysed. Losses after randomisation due to negative baseline culture: 284/653 (43%), unclear how many from each group. ?? 140 Eberconazole 1%, 144 Miconazole 2% Failed to attend for follow-up: 9/653 due to major deviations, unclear how many from each group.?? 4 Eberconazole 1% 5 Miconazole 2% Further E-mail on allocation concealment the 15th: Sequentially numbered drug containers of identical appearance

Table 2. Types of interventions

Azoles	
Bifonazole (1%)	(Bagatell 1986; Budimulja 1998; del Palacio 1989; Jung 1988; Kuhlwein 1990; Li 2003; Li 2006; Luciani 1988; Nolting 1992; Thomas 1976; Vena 1983; Wagner 1987)
Clotrimazole (1%)	(Kagawa 1987; Banerjee 2011; Bogaert 1986; Clayton 1973; Clayton 1976; del Palacio 2001;Duweb 1997; Effendy 1987; Evans 1993; Fan 1991; Fan 1994; Finzi 1986; Gong 1991; Hall-Smith 1974; Katz 1984; Keczkes 1975; Lassus 1983; McVie 1986; Pariser 1995; Ramam 2003; Singal 2005; Smith 1974; Spiekermann 1976; Tanenbaum 1989; Thomas 1986; VanDersarl 1977; Weitgasser 1977; Wortzel 1982; Zaun 1984)
Croconazole (1%)	(Kuhlwein 1990)
Eberconazole (1-2%)	(del Palacio 1995; del Palacio 2001; Friederich 1985; Repiso Montero 2006; Viayna 2003)
Econazole (1%)	(Califano 1999; Gip 1984; Grigoriu 1983; Kokoschka 1986; Lassus 1984; Luciani 1988; Millikan 1988; Nolting 1985; Nuñez 1985; Qadripur 1984; Schwarz 1978; Tronnier 1987; Wang 2000a)
Econazole (1%) combined with triamcinolone acetonide (0.1%)	(Li 2004; Shen 2002; Su 2001; Wang 2000a)
Fenticonazole (2%)	(Altmeyer 1990; Athow-Frost 1986; Clerico 1987; Finzi 1986; Jung 1988; Kokoschka 1986; Leiste 1989; Vannini 1988)

Table 2. Types of interventions *(Continued)*

Fluconazole (various concentrations)	(Banerjee 2011; Califano 1999; Yim 2010)
Flutrimazole (1%)	(del Palacio 1999)
Isoconazole nitrate (1%)	(Gip 1980;Nolting 1980)
Isoconazole nitrate (1%) combined with diflucortolone valerate (0.1%)	(Gip 1980; Nolting 1980)
Ketoconazole (2%)	(Gong 1991; del Palacio 1999; Kalis 1996; Pariser 1995; Shi 2011)
Luliconazole (1%)	(Jerajani 2013)
Miconazole (2%)	(Alomar 1992; Athow-Frost 1986; Avila 1985; Björnberg 1986; Clayton 1976;Clayton 1979; Clayton 1982; Clerico 1987; Cucè 1980; Fredriksson 1983; Fulton 1975; Ghaninejad 2009; Gip 1983; Guillano 2005; Meinicke 1987; Mertens 1976; Repiso Montero 2006; Sharma 2011; Shen 2002; Tanenbaum 1982; Thulin 1975; Vander Ploeg 1984; Vannini 1988; Vena 1983; Viayna 2003; Voravutinon 1993; Wang 1995; Wang 2000)
Miconazole combined with hydrocortisone	(Björnberg 1986; Mertens 1976)
Oxiconazole (1%)	(Gip 1984; Kalis 1996; Machado-Pinto 1987; Ramelet 1987; Wagner 1987)
Sertaconazole (2%)	(Alomar 1992; Borelli 2007; Ghaninejad 2009; Jerajani 2013; Sharma 2011;Susilo 2003)
Sulconazole (1%)	(Avila 1985; Gip 1983; Lassus 1983; Lassus 1984; McVie 1986; Nuñez 1985; Qadripur 1984; Tanenbaum 1982; Tanenbaum 1989; Thomas 1976)
Tioconazole (2%)	(Clayton 1982; Fredriksson 1983; Grigoriu 1983; Haroon 1996; Kashin 1985; Vander Ploeg 1984)
Allylamines	
Naftifine (1-2%)	(Dobson 1991; Effendy 1987; Evans 1993; Friederich 1985; Gip 1987; Haroon 1996; Jordon 1990; Kagawa 1987; Leiste 1989; Meinicke 1987; Millikan 1988; Nolting 1985; Parish 2011; Tronnier 1987; Zaun 1984)
Terbinafine (1%)	(Budimulja 1998; Budimulja 2001; Cordero 1992; Duweb 1997; Evans 1992; Evans 1994; Greer 1990; Jerajani 2013; Lebwohl 1998; Lebwohl 2001; Ledezma 1999; Millikan 1990; van Heerden 1997; Wang 1995; Wang 2000; Zaias 1993)
Benzylamines	
Butenafine (1%)	(Greer 1997; Lesher 1997; Li 2006; Ramam 2003; Singal 2005)
Hydroxy pyridones	
Cyclopirox olamine (1%)	(Altmeyer 1990; Bogaert 1986; Lassus 1988; Sehgal 1976)
Thiocarbamates	
Tolciclate (1%)	(Cucè 1980)
Tolnaftate (1%)	(Hall-Smith 1974;Hantschke 1980; Katz 1972; Keczkes 1975; Machado-Pinto 1987; Sivayathorn 1979;Thomas 1986; Thulin 1975; Zarowny 1975)

Table 2. Types of interventions *(Continued)*

Other	
Ajoene	(Ledezma 1999)
Amorolfine (several concentrations)	(Banerjee 2011; del Palacio 1989; del Palacio 1991; del Palacio 1992; Li 2003; Nolting 1992)
Griseofulvine (2%)	(Macasaet 1991;Zarowny 1975)
Haloprogin (1%)	(Clayton 1979; Katz 1972; VanDersarl 1977; Weitgasser 1977)
Kakawate	(Guillano 2005)
Pecilocin	(Holti 1970)
Senna alata soap	(Oladele 2010)
Tetrandine	(Shi 2011)
Triclosan soap	(Dinkela 2007)
Whitfield's cream	(Clayton 1973; Holti 1970; Sivayathorn 1979; Voravutinon 1993)
Xianglian cream	(Fan 1991; Fan 1994)

Table 3. Included studies with no usable or irretrievable data

Study ID	Interventions & comparisons	N	Comments
Abdul Bari 2012	butenafine (1%) vs bifonazole (1%)	96	No separate data for the outcomes of the different tinea infections.
Alomar 1992	sertaconazole (2%) vs miconazole (2%)	631	No separate data for the outcomes of the different tinea infections. Except clinical cure is reported separately, and there is a discrepancy between data on clinical cure given in the text and illustrated in the figures.
Altmeyer 1990	fenticonazole (2%) vs cyclopyroxolamine (1%)	100	Locations mentioned, mainly all caused by dermatophytes, just 4-5 other pathogens. The localisation of the infection is mentioned, but some of them are not caused by dermatophytes, and it is not clear how many match the inclusion criteria of tinea corporis or tinea cruris i.e. caused by dermatophytes (and how many are e.g. candida infections or erythrasma in the folds).
Athow-Frost 1986	fenticonazole (2%) vs miconazole (2%)	60	No separate data for the outcomes of the different tinea infections and pityriasis versicolor.
Avila 1985	sulconazole (1%) vs miconazole (2%)	40	No separate data for the outcomes of the different tinea infections.
Björnberg 1986	miconazole (2%) vs miconazole (2%)-hydrocortisone (1%)	26	No separate data for the outcomes of the different tinea infections.

Table 3. Included studies with no usable or irretrievable data *(Continued)*

Borelli 2007	sertaconazole (2%) cream vs sertaconazole (2%) solution	535	No separate data for the outcomes of the different tinea infections.
Califano 1999	fluconazole (0.5%) vs econazole (1%)	61	No separate data for the outcomes of the different tinea infections.
Clayton 1973	clotrimazole (1%) vs Whitfield's cream	43	No separate data for the outcomes of the different tinea infections.
Clayton 1982	tioconazole (1%) vs miconazole (2%)	99	No separate data for the outcomes of the different tinea infections.
Cucè 1980	tolciclate (1%) vs miconazole (2%)	81	No separate data for the outcomes of the different tinea infections and pityriasis versicolor.
del Palacio 1989	amorolfine (0.5%) vs bifonazole (1%)	40	No separate data for the outcomes of the different tinea infections.
del Palacio 1991	amorolfine in 3 concentrations (0.125%), (0.25%) and (0.5%)	75	No separate data for the outcomes of the different tinea infections.
del Palacio 1992	amorolfine in 3 concentrations (0.125%), (0.25%) and (0.5%)	725	No separate data for the outcomes of the different tinea infections.
del Palacio 1999	ketoconazole (2%) vs flutrimazole (1%)	59	No separate data for the outcomes of the different tinea infections.
del Palacio 2001	clotrimazole (1%) vs eberconazole (1%)	157	No separate data for the outcomes of the different tinea infections.
Duweb 1997	terbinafine (1%) vs clotrimazole (1%)	25	Abstract, limited data
Effendy 1987	clotrimazole (1%) vs naftifine (1%)	99	Unclear how many participants matched the inclusion criteria (sites reported but unclear which pathogens at each site).
Finzi 1986	fenticonazole (2%) vs clotrimazole (1%)	29	No separate data for the outcomes of the different tinea infections.
Fredriksson 1983	tioconazole (1%) vs miconazole (2%)	60	Unclear how many participants matched the inclusion criteria (sites reported but unclear which pathogens at each site).
Friederich 1985	naftifine vs econazole-triamcinolone acetonide cream	62	Unclear how many participants matched the inclusion criteria (sites reported but unclear which pathogens at each site). No separate data for the outcomes of the different sites.
Fulton 1975	miconazole 2% vs vehicle	99	No separate data for the outcomes of the different tinea infections.
Ghaninejad 2009	miconazole 2% vs sertaconazole	100	No separate data for the outcomes of the different tinea infections.

Table 3. Included studies with no usable or irretrievable data *(Continued)*

Gip 1980	isoconazole nitrate (1%) + diflucortolone valerate (0.1%) vs isoconazole nitrate (1%)	30	7 participants with tinea cruris included, however data combined with candida infections of the groin, no separate data available for tinea cruris.
Gip 1983	sulconazole (1%) vs miconazole (2%)	40	No separate data for the outcomes of the different tinea infections.
Gip 1984	oxiconazole (1%) vs econazole (1%)	120	No separate data for the outcomes of the different tinea infections.
Gong 1991	ketoconazole (2%) vs clotrimazole (1%)	140	No separate data for the outcomes of the different tinea infections.
Grigoriu 1983	tioconazole (1%) vs econazole (1%)	61	Unclear how many participants matched the inclusion criteria (sites reported but unclear which pathogens at each site). No separate data for the outcomes of the different sites.
Hall-Smith 1974	tolnaftate (1%) vs clotrimazole (1%)	60	No separate data for the outcomes of the different tinea infections.
Jung 1988	fenticonazole (1%) vs bifonazole (1%)	41	No separate data for the outcomes of the different tinea infections.
Kashin 1985	tioconazole (1%) once daily vs tioconazole (1%) b.i.d.	100	No separate data for the tinea infections for mycology, clinical outcomes do not distinguish between cure and improvement
Katz 1972	haloprogin (1%) cream vs haloprogin (1%) solution vs tolnaftate (1%) cream vs tolnaftate (1%) solution vs haloprogin vehicle cream vs haloprogin vehicle solution	74	No separate data for the outcomes of the different tinea infections.
Keczkes 1975	clotrimazole (1%) vs tolnaftate (1%)	70	Tinea corporis and cruris are likely to be included, but no data.
Kokoschka 1986	fenticonazole (2%) vs econazole (1%)	52	Unclear how many participants matched the inclusion criteria (sites reported but unclear which pathogens at each site). No separate data for the outcomes of the different sites.
Kuhlwein 1990	bifonazole (1%) vs croconazole (1%)	60	No separate data for the outcomes of the different tinea infections.
Lassus 1983	sulconazole (1%) vs clotrimazole	40	No separate data for the outcomes of the different tinea infections.
Lassus 1984	sulconazole (1%) vs econazole (1%)	40	No separate data for the outcomes of the different tinea infections.

Table 3. Included studies with no usable or irretrievable data *(Continued)*

Lassus 1988	ciclopirox olamine (1%) vs ciclopirox olamine (1%) - hydrocortisone acetate (1%)	140	Unclear how many participants matched the inclusion criteria (sites reported but unclear which pathogens at each site). No separate data for the outcomes of the different sites.
Lebwohl 1998	terbinafine (1%) vs vehicle	?	Poster, no data reported
Leiste 1989	fenticonazole (2%) vs naftifine (1%)	100	Unclear how many participants matched the inclusion criteria (sites reported but unclear which pathogens at each site). No separate data for the outcomes of the different sites.
Li 2003	amorolfine cream (0.25%) vs bifonazole cream (1%)	155	Abstract, limited data reporting. Unclear how many participants in each arm.
Luciani 1988	econazole (1%) vs bifonazole (1%)	49	No separate data for the outcomes of the different tinea infections.
McVie 1986	sulconazole (1%) vs clotrimazole (1%)	83	No separate data for the outcomes of the different tinea infections.
Meinicke 1987	miconazole (2%) vs naftifine (1%) once daily vs naftifine (1%) b.i.d.	175	Unclear how many participants matched the inclusion criteria (sites reported but unclear which pathogens at each site). No separate data for the outcomes of the different sites.
Mertens 1976	Daktacort vs miconazole (2%) vs hydrocortisone (1%)	63	Unclear how many participants matched the inclusion criteria (sites reported but unclear which pathogens at each site). No separate data for the outcomes of the different sites.
Nolting 1980	isoconazole nitrate 1% + diflucortolone valerate 0.1% vs isoconazole nitrate 1%	100	Unclear how many participants matched the inclusion criteria (sites reported but unclear which pathogens at each site). No separate data for the outcomes of the different sites.
Nolting 1985	naftifine 1% vs econazole 1%	94	Unclear how many participants matched the inclusion criteria (sites reported but unclear which pathogens at each site). No separate data for the outcomes of the different sites.
Nolting 1992	amorolfine (0.125%), vs (0.25%) vs (0.5%) vs bifonazole (1%)	232	Unclear how many participants matched the inclusion criteria (sites reported but unclear which pathogens at each site). No separate data for the outcomes of the different sites.
Nuñez 1985	sulconazole (1%) vs econazole (1%)	42	No separate data for the outcomes of the different tinea infections.
Qadripur 1984	sulconazole (1%) vs econazole (1%)	32	No separate data for the outcomes of the different tinea infections.
Repiso Montero 2006	eberconazole (1%) vs miconazole (2%)	653	No separate data for the outcomes of the different tinea infections.

Table 3. Included studies with no usable or irretrievable data *(Continued)*

Schwarz 1978	econazole (1%)-triamcinolone acetonide vs econazole (1%)	104	No separate data for the outcomes of the different tinea infections.
Sehgal 1976	ciclopirox (1%) vs placebo	105	No separate data for the outcomes of the different tinea infections.
Smith 1974	clotrimazole 1% vs vehicle	84	Unclear how many participants with tinea cruris were in each treatment arm in the two studies.
Susilo 2003	sertaconazole (2%) vs vehicle	400	Tinea cruris and corporis are included, but unclear how many in each group.
Tanenbaum 1982	sulconazole (1%) vs miconazole (2%)	96	Unclear how many were randomised to each treatment arm, unclear number with tinea pedis or tinea corporis/cruris.
Tronnier 1987	naftifine (1%) vs econazole (1%) + triamcinolone	62	Tinea cruris and corporis possibly included, but unreported. No separate data for the outcomes of the different sites.
Vannini 1988	miconazole (2%) vs fenticonazole (1%) once daily vs fenticonazole (1%) b.i.d.	60	The results are not provided separately per diagnosis, but per causative micro-organism.
Viayna 2003	eberconazole (1%) vs miconazole (2%)	653	Abstract, limited data reporting.
Wagner 1987	oxiconazole (1%) vs bifonazole (1%)	204	No separate data for tinea corporis and cruris.
Yim 2010	fluconazole (0.5%) vs fluconazole (1%) vs flutrimazole (1%)	275	No separate data for the outcomes of the different tinea infections.
Zarowny 1975	griseofulvin (2%) vs tolnaftate (1%) vs vehicle	57	Tinea cruris and corporis possibly included, but unreported. No separate data for the outcomes of the different sites.
Zaun 1984	naftifine (1%) vs clotrimazole (1%)	126	No separate data for the outcomes of the different tinea infections.

Table 4. Research recommendations based on a gap in the evidence of the effects of topical antifungal treatments for tinea cruris and tinea corporis

Core elements	Issues to consider	Status of research for this review
Evidence (E)	What is the current state of the evidence?	This systematic review identified 129 RCTs of which 66 provided usable data. Rate of mycological and clinical cure as well as adverse events were in part addressed in most of the studies although hardly any of them directly assessed duration of treatment until clinical or participant judged cure had been achieved.

Table 4. Research recommendations based on a gap in the evidence of the effects of topical antifungal treatments for tinea cruris and tinea corporis *(Continued)*

		All of the topical antifungals demonstrated some evidence of effectiveness against placebo. There is evidence from pooled data that both terbinafine and naftifine are effective for tinea corporis and cruris.
Population (P)	Diagnosis, disease stage, comorbidity, risk factors, gender, age, ethnic group, specific inclusion or exclusion criteria, clinical setting	**Inclusion criteria** • Participants of any age with tinea corporis and cruris, confirmed by positive KOH and culture for dermatophytes **Exclusion criteria** • Infections with non-dermatophytes • Immunocompromising illness or use of immunosuppressant medication • In case of tinea corporis, exclusion of lesions on head, hands and feet
Intervention (I)	Type, frequency, dose, duration, prognostic factor	Any regimen of topical treatments for tinea corporis or tinea cruris either used alone or in combination with other treatments. As there are many treatment options, no recommendations regarding dosing and duration can be made. In particular, if naftifine 2% once a day is as effective as naftifine 1% twice a day then once a day application might improve compliance. Also comparisons between antifungals with different vehicles are warranted as gel application might be more user friendly than creams. Combination of topical steroid and antifungal versus antifungal alone.
Comparison (C)	Type, frequency, dose, duration, prognostic factor	Other topical treatment, different dosing regimen. Placebo-controlled trials are no longer necessary, unless to establish efficacy of new compounds
Outcome (O)	Which clinical or patient-related outcomes will the researcher need to measure, improve, influence, or accomplish? Which methods of measurement should be used?	1. Rate of mycological cure (negative microscopy findings, the absence of any growth of dermatophytes in culture, or both) 2. Clinical cure - defined as the resolution of clinical signs and symptoms suggestive of dermatophyte infection, as judged by study investigators with trial participants 3. Participant-judged cure 4. Relapse or recurrence 5. Duration of treatment until mycological and clinical cure is reached 6. Adverse events
Time Stamp (T)	Date of literature search or recommendation	13 August 2013
Study Type	What is the most appropriate study design to address the proposed question?	• Randomised controlled trial (adequately powered or multi-centred) • Methods: concealment of allocation sequence • Blinding: participants, trialists, outcomes assessors, data analysts • Setting: hospital, university or general practice with adequate follow-up • Analysis should also cover participants who may have received intervention but were declared ineligible post-randomisation i.e. negative mycological culture at baseline either postpone randomisation until information is available or ensure "blinded independent adjudication" See Fergusson 2002. Ideally, two analyses should be performed, one intention-to treat analysis including all randomised participants which might provide additional data on

Table 4. Research recommendations based on a gap in the evidence of the effects of topical antifungal treatments for tinea cruris and tinea corporis *(Continued)*

	potential harms, and a further analysis with only the participants which met the inclusion criteria to increase precision of the effect estimate

KOH = potassium hydroxide
RCTs = randomised controlled trials

APPENDICES

Appendix 1. CENTRAL (*The Cochrane Library*) search strategy

#1 MeSH descriptor Tinea explode all trees
#2 (tinea)
#3 (#1 OR #2)
#4 (cruris or corporis or glabrosa or circinata or body)
#5 (#3 AND #4)
#6 (ringworm) or (crotch itch) or (crotch rot) or (jock itch) or (dhobie itch)
#7 (gym itch) or (eczema marginatum)
#8 (#5 OR #6 OR #7)

Appendix 2. MEDLINE (OVID) search strategy

1. exp Tinea/
2. tinea$.mp.
3. 1 or 2
4. (cruris or corporis or glabrosa or circinata or body).mp.
5. 3 and 4
6. ringworm.mp.
7. crotch itch.mp.
8. crotch rot.mp.
9. jock itch.mp.
10. dhobie itch.mp.
11. gym itch.mp.
12. eczema marginatum.mp.
13. or/5-12
14. randomized controlled trial.pt.
15. controlled clinical trial.pt.
16. randomized.ab.
17. placebo.ab.
18. clinical trials as topic.sh.
19. randomly.ab.
20. trial.ti.
21. 14 or 15 or 16 or 17 or 18 or 19 or 20
22. (animals not (humans and animals)).sh.
23. 21 not 22
24. 13 and 23

Appendix 3. EMBASE (OVID) search strategy

1. crotch itch.mp.
2. crotch rot.mp.
3. jock itch.mp.
4. dhobie itch.mp.
5. gym itch.mp.
6. eczema marginatum.mp.
7. exp tinea cruris/
8. exp tinea corporis/
9. ringworm.mp.
10. or/1-9

11. tinea$.mp.
12. (cruris or corporis or glabrosa or circinata or body).mp.
13. 11 and 12
14. 10 or 13
15. crossover procedure.sh.
16. double-blind procedure.sh.
17. single-blind procedure.sh.
18. (crossover$ or cross over$).tw.
19. placebo$.tw.
20. (doubl$ adj blind$).tw.
21. allocat$.tw.
22. trial.ti.
23. randomized controlled trial.sh.
24. random$.tw.
25. or/15-24
26. (ANIMAL/ or NONHUMAN/ or ANIMAL EXPERIMENT/) and HUMAN/
27. ANIMAL/ or NONHUMAN/ or ANIMAL EXPERIMENT/
28. 27 not 26
29. 25 not 28
30. 14 and 29

Appendix 4. LILACS search strategy

(Tina and (crural or corporal or corporis or inguinal)) or “eczema marginado” or ringworm or “eczema marginatum” or (tinea and (cruris or corporis or glabrosa or circinata or body))

CONTRIBUTIONS OF AUTHORS

Link with editorial base and co-ordinate contributions from co-review authors (MEG)
Identify relevant titles and abstracts from searches (EvZ, ZF)
Screen ongoing trials and congress proceedings (MEG, EvZ)
Obtain copies of trials (MEG, EvZ, HB, LD)
Selection of trials (EvZ, ZF)
Contact with trialists (MEG, EvZ, ZF)
Extract data from trials (MEG, EvZ, HB, ZF, LD)
Enter data into Review Manager (MEG, EvZ)
Carry out analysis (MEG, EvZ, BS)
Interpret data (MEG, EvZ, ZF, BS)
Draft final review (MEG, EvZ, ZF)
Update review (MEG, EvZ, ZF)
The guarantor of the review (MEG)

Disclaimer

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

DECLARATIONS OF INTEREST

There are no financial conflicts of interest; the authors declare that they do not have any associations with any parties who may have vested interests in the results of this review.

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DIFFERENCES BETWEEN PROTOCOL AND REVIEW

After consultation and based on the recommendations of the Cochrane Skin Group editorial base, we performed an available case analysis with respect to the primary outcomes and the secondary outcomes of relapse and participant-judged cure. As this differs somewhat from what was originally planned in the protocol i.e. an intention-to-treat (ITT) analysis, we provide the following rationale for the amendments:

- Many authors reported using an ITT analysis, but data were analysed on an available case basis.
- Many trials had substantial losses to follow-up, with little information about reasons for drop-out. The use of ITT analyses in these circumstances would result in vast assumptions being made on trial results. In this clinical condition, non attendance at follow-up can be argued to be just as likely to represent treatment success as failure. There is a recognised treatment effect seen with placebo in this condition and so making assumptions about drop-outs in placebo groups can also be problematic.
- Discrepancies and inconsistencies were noted between data sets in the same studies, e.g. the number of participants in the same group at the same follow-up visit varied between mycology assessment and clinical assessment. We used the data as reported, i.e. available case analysis in order to avoid making further assumptions.
- In several studies it was unclear what the actual ITT population was in each group - only the overall total number of participants randomised was reported.
- The majority of studies were >10 years old, rendering contact with original study authors very difficult if not impossible, hence some of the issues noted above were not able to be resolved.

No consideration was given, in the protocol, to dealing with data in the event of identifying studies with multiple treatment groups. As several such studies were found, the methods used have been subsequently described in the 'Methods, 'Data collection and analysis' section. Due to the very limited data for the 'duration of treatment in days' outcome, these were generally described narratively where available as opposed to reporting hazard ratios as stated in the protocol. Sensitivity analyses were performed in the review to look at the impact of missing data (i.e. studies with high levels of missing data) in place of studies considered low quality as specified in the protocol, as most pooled studies were of unclear or high risk of bias. 'Summary of findings' tables were not previously specified in the protocol, but have been included in the review to present the key findings as recommended in Chapter 11.5.1 of the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011).

The authors Peter Hearn and Elizabeth Johnson who worked on the protocol are listed in the Acknowledgments section of the review. Esther J van Zuuren and Zbys Fedorowicz joined the review team and are listed in the authorship accordingly.

INDEX TERMS

Medical Subject Headings (MeSH)

Administration, Cutaneous; Adrenal Cortex Hormones [therapeutic use]; Allylamine [analogs & derivatives] [therapeutic use]; Antifungal Agents [administration & dosage] [*therapeutic use]; Azoles [therapeutic use]; Benzoates [therapeutic use]; Drug Combinations; Naphthalenes [therapeutic use]; Pruritus [*drug therapy]; Randomized Controlled Trials as Topic; Salicylates [therapeutic use]; Terbinafine; Tinea [*drug therapy]

MeSH check words

Female; Humans; Male