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Interventions for treating scabies (Review)

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Interventions for treating scabies

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A B S T R A C T

Background

Scabies is an intensely itchy parasitic infection of the skin caused by the *Sarcoptes scabiei* mite. It is a common public health problem with an estimated global prevalence of 300 million cases. Serious adverse effects have been reported for some drugs used to treat scabies.

Objectives

To evaluate topical and systemic drugs for treating scabies.

Search methods

In June 2010, we searched the Cochrane Infectious Diseases Group Specialized Register, CENTRAL (*The Cochrane Library* 2010, Issue 2), MEDLINE, EMBASE, LILACS, and INDMED. In August 2010, we also searched the grey literature and sources for registered trials. We also checked the reference lists of retrieved studies.

Selection criteria

Randomized controlled trials of drug treatments for scabies.

Data collection and analysis

Two authors independently assessed trial quality and extracted data. Results were presented as risk ratios with 95% confidence intervals and data combined where appropriate.

Main results

Twenty-two small trials involving 2676 people were included. One trial was placebo controlled, 18 compared two or more drug treatments, three compared treatment regimens, and one compared different drug vehicles.

Fewer treatment failures occurred by day seven with oral ivermectin compared with placebo in one small trial (55 participants). Topical permethrin appeared more effective than oral ivermectin (140 participants, 2 trials), topical crotamiton (194 participants, 2 trials), and topical lindane (753 participants, 5 trials). Permethrin also appeared more effective in reducing itch persistence than either crotamiton (94 participants, 1 trial) or lindane (490 participants, 2 trials). No difference was detected between permethrin (a synthetic pyrethroid) and a natural pyrethrin-based topical treatment (40 participants, 1 trial), and between permethrin and benzyl benzoate (53 participants, 1 trial), however both these trials were small.

No significant difference was detected in the number of treatment failures between crotamiton and lindane (100 participants, 1 trial), lindane and sulfur (68 participants, 1 trial), benzyl benzoate and sulfur (158 participants, 1 trial), and benzyl benzoate and natural synergized pyrethrins (240 participants, 1 trial); all were topical treatments. No trials of malathion were identified.

No serious adverse events were reported. A number of trials reported skin reactions in participants randomized to topical treatments. There were occasional reports of headache, abdominal pain, diarrhoea, vomiting, and hypotension.

Authors' conclusions

Topical permethrin appears to be the most effective treatment for scabies. Ivermectin appears to be an effective oral treatment. More research is needed on the effectiveness of malathion, particularly when compared to permethrin, and on the management of scabies in an institutional setting and at a community level.

23 April 2019

No update planned

Review superseded

This review includes an evaluation of crotamiton, lindane, sulfur, and benzyl benzoate. However, these are not active areas of research and are not widely used for treatment. A new assessment of ivermectin and permethrin alone is justified and thus this Cochrane Review has been superseded by Rosumeck 2018 https://doi.org/10.1002/14651858.CD012994

P L A I N   L A N G U A G E   S U M M A R Y

Interventions for treating scabies

Scabies is a parasitic infection of the skin. It occurs throughout the world, but is particularly problematic in areas of poor sanitation, overcrowding, and social disruption, and is endemic in many resource-poor countries. The global prevalence of scabies is estimated at 300 million cases, but the level of infection varies between countries and communities. The female mite burrows into the skin to lay eggs which then hatch out and multiply. The infection can spread from person to person via direct skin contact, including sexual contact. It causes intense itching with eruptions on the skin. Various drugs have been developed to treat scabies, and herbal and traditional medicines are also used. The review of trials attempted to cover all these. The authors identified 22 small trials involving 2676 people, with 19 of the trials taking place in resource-poor countries. Permethrin appeared to be the most effective topical treatment for scabies, and ivermectin appeared to be an effective oral treatment. However, ivermectin is unlicensed for this indication in many countries. Adverse events such as rash, vomiting, and abdominal pain were reported, but the trials were too small to properly assess serious but rare potential adverse effects. No trials of herbal or traditional medicines were identified for inclusion.

BACKGROUND

What is scabies?

Scabies is an intensely itchy parasitic infection of the skin that is caused by the *Sarcoptes scabiei* mite. It occurs throughout the world, but is particularly problematic in areas of poor sanitation, overcrowding, and social disruption. The global prevalence of scabies is estimated at 300 million cases (Alexander 1984), with large variations between countries. In the UK, no up-to-date robust prevalence data exist, but general practitioners recorded approximately 1200 new cases per year in the 1990s (Downs 1999). In resource-rich communities, scabies tends to occur in cyclical epidemics, particularly within institutional-living situations such as nursing homes (Scheinfeld 2004) or the army (Mimouni 1998; Mimouni 2003). There is some seasonal variation with incidence being greater in the winter than the summer, perhaps related to the tendency for more indoor overcrowding in colder weather (Downs 1999). In resource-poor communities, the occurrence pattern is quite different with the disease being endemic in many areas (Chosidow 2000). For example, the prevalence of scabies among the remote Aboriginal communities of Northern Australia is around 50% in children and 25% in adults (Wong 2002). The prevalence of infection in a community is potentially influenced by changes in social attitudes, population movements, wars, misdiagnosis, inadequate treatment, and changes in the immune status of the population. Scabies infestation represents a considerable burden of ill health in many communities, and although the disease is rarely life threatening, it causes widespread debilitation and misery (Green 1989).

The life cycle of *S.scabiei* begins with the pregnant female laying two to three eggs a day in burrows several millimetres to several centimetres in length in the stratum corneum (outermost layer) of the skin. After about 50 to 72 hours, larvae emerge and make new burrows. They mature, mate, and repeat this 10- to 17-day cycle. Mites usually live for 30 to 60 days (Green 1989).

Humans are the main reservoir for *S.scabiei* var. *hominis* (variety of the mite named to reflect the main host species). Scabies is usually spread person to person via direct skin contact, including sexual contact, though transfer via inanimate objects such as clothing or furnishings is also possible (Hay 2004). The mite can burrow beneath the skin within 2.5 minutes, though around 20 minutes is more usual (Alexander 1984). The level of infectiousness of an individual depends in part on the number of mites harboured, which can vary from just a single mite to millions (Chosidow 2000). Humans can also be transiently infected by the genetically distinct animal varieties of *S. scabiei* (eg var. *canis*), though cross infectivity is low (Fain 1978; Walton 2004).

Clinical infection with the scabies mite causes discomfort and often intense itching of the skin, particularly at night, with irritating papular or vesicular eruptions. While infestation with the scabies mite is not life threatening, the severe, persistent itch debilitates and depresses people (Green 1989). The classical sites of infestation are between the fingers, the wrists, axillary areas, female breasts (particularly the skin of the nipples), peri-umbilical area, penis, scrotum, and buttocks. Infants are usually affected on the face, scalp, palms, and soles. Much of the itching associated with scabies is as a result of the host immune reaction, and symptoms can take several weeks to appear after initial infection in a person exposed to scabies for the first time. Symptoms appear after a much shorter interval (one to two days) after reinfestation (Arlian 1989).

A more severe or 'crusted' presentation of infestation is associated with extreme incapacity and with disorders of the immune system, such as HIV infection. Clinically this atypical form of scabies presents with a hyperkeratotic dermatosis resembling psoriasis. Lymphadenopathy and eosinophilia can be present, but itching may be unexpectedly mild. Patients with crusted scabies may harbour millions of mites and are highly infectious (Meinking 1995a). The dermatological distribution of mites in such patients is often atypical (eg including the head), and treatment in hospital is often advised (Chosidow 2000).

Complications are few although secondary bacterial infection of the skin lesions by group A *Streptococcus pyogenes* or *Staphylococcus aureus*, or both, can occur following repeated scratching, particularly in warmer climates (Meinking 1995a). Secondary infection with group A *Streptococcus* can lead to acute glomerulonephritis, outbreaks of which have been associated with scabies (Green 1989).

Diagnosis, treatment, and prevention

Diagnosis on clinical grounds is usually made on a history of itching (particularly if contacts are also affected) and the finding of lesions in the classical sites. The diagnosis can in most cases be confirmed by microscopically identifying a mite, egg, or mite faeces in a skin scraping, or by extracting a mite from a burrow (Chosidow 2000).

Various treatments are available for scabies. These include sulfur compounds, which have been used for centuries; benzyl benzoate (first used in 1931); crotamiton (used since the late 1970s); hexachlorocyclohexane, which is also known as gamma benzene hexachloride or the commercial purified form lindane ('lindane' is used in this review) (available since 1948); malathion (used since the mid 1970s); permethrin (first licensed in 1985 by the US Food and Drug Administration); and oral ivermectin (first used in humans in the 1980s). A number of herbal remedies have also been proposed (Oladimeji 2000; Alebiosu 2003; Oladimeji 2005).

Serious adverse effects have been associated with the use of some antiscabietic treatments. Convulsions and aplastic anaemia have been reported with the use of lindane (Rauch 1990; Elgart 1996), and an increased risk of death amongst elderly patients has been reported with the use of ivermectin (Barkwell 1997).

Evidence of cure ideally requires follow up for about one month. This allows time for lesions to heal and for any eggs and mites to reach maturity if treatment fails (ie beyond the longest incubation interval). Patients should be warned that itching may persist for one to two weeks after treatment, even if the mite is successfully eradicated (Buffet 2003). Because of this delay in symptom relief it may sometimes be difficult to distinguish reinfestation from primary treatment failure.

Contacts of cases are usually advised to treat themselves at the same time as the case in order to reduce the risk of reinfestation (Orkin 1976). Prevention is based on principles common to most infectious diseases, that is, limitation of contact with the mite.

Using data from randomized controlled trials, this review examines the existing evidence of effectiveness of treatments for scabies.

O B J E C T I V E S

To evaluate topical and systemic drugs for treating scabies.

M E T H O D S

Criteria for considering studies for this review

Types of studies

Randomized controlled trials.

Types of participants

Children or adults with a clinical or parasitological diagnosis of scabies.

Types of interventions

Intervention

- Drug treatment (systemic or local).
- Herbal or traditional medicine treatment.
- Any combination of above.
- Treatment of contacts in addition to cases.

Control

- Placebo or no intervention.
- A different drug intervention, drug intervention vehicle, intervention regimen, or combination of interventions.
- Different or no treatment of contacts.

Types of outcome measures

Primary

- Treatment failure in a clinically diagnosed case.
- Treatment failure in a parasitologically confirmed case.

Treatment failure is defined in both the above cases as the persistence of original lesions, the appearance of new lesions, or confirmation of a live mite.

Secondary

- Persistence of patient-reported itch.

Adverse events

- Serious adverse event that leads to death, is life threatening, results in persistent or significant disability or incapacity, or requires hospitalization.
- Adverse event that requires discontinuation of treatment.
- Other adverse event.

Search methods for identification of studies

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

Databases

We searched the following databases using the search terms and strategy described in Appendix 1: Cochrane Infectious Diseases Group Specialized Register (June 2010); Cochrane Central Register of Controlled Trials (CENTRAL) (*The Cochrane Library* 2010, Issue 2); MEDLINE (1966 to June 2010); EMBASE (1974 to June 2010); LILACS (1982 to June 2010); and INDMED (June 2010).

Grey literature

In August 2010, we searched the following sources for published and unpublished trials using the term 'scabies': British Library Index of Conference Proceedings (catalogue.bl.uk/); British Library for Development Studies (blds.ids.ac.uk/); BRIDGE (www.bridge.ids.ac.uk/); Social Care Online (www.scie-socialcareonline.org.uk/); EconLit; ERIC; Institute for Development Studies (www.ids.ac.uk/ids/particip/information/readrm.html); IIED (www.iied.org/). We searched Science.gov (www.science.gov/) using the terms 'scabies' AND ('trial' OR 'study').

Registered trials

In August 2010, we searched the following sources for registered trials using the term 'scabies': Current Controlled Trials (www.controlled-trials.com/); Thompson CenterWatch Clinical Trials Listing Service (www.centerwatch.com/); US National Institutes of Health ClinicalTrials.gov (www.clinicaltrials.gov/); TrialsCentral (www.trialscentral.org/); and the UK Department of Health National Research Register (www.nihr.ac.uk/).

Reference lists

We checked the reference lists of all retrieved trials.

Data collection and analysis

Selection of studies

All identified trials were entered into a trials register. MS and PJ independently applied the inclusion criteria to the potentially relevant trials. If a trial's eligibility was unclear, we attempted to contact the trial authors for further information. MS reassessed all included and excluded trials cited in the previous review version (Walker 2000). Where the review authors disagreed, the Co-ordinating Editor of the Cochrane Infectious Diseases Group was consulted, and a consensus reached among the three parties; this process was also used for assessing the risk of bias in trials, and extracting data. The trial reports were scrutinized to ensure that multiple publications from the same trial were included only once. We listed the reasons for excluding studies in the 'Characteristics of excluded studies'.

Data extraction and management

We independently extracted data from the newly included trials. Where important data were missing, we attempted to contact the trial authors for further information. MS entered the data into Review Manager 5.0. We extracted the number of patients randomized and the number analysed for each group for each trial. For each dichotomous outcome, we recorded the number of participants experiencing the event in each arm of the trial.

Assessment of risk of bias in included studies

Both authors independently assessed the quality of the newly included trials. We assessed the generation of allocation sequence and allocation concealment as adequate, inadequate, or unclear (Juni 2001). We assessed the inclusion of randomized participants in the analysis to be adequate if greater than 80%. We recorded who was blinded (eg participants or investigators) rather than using

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potentially ambiguous terms such as double blind or single blind. MS reassessed the included trials from the previous review version (Walker 2000).

Data synthesis

MS analysed the data using Review Manager 5.0. Analyses were stratified by comparison. We undertook an available case analysis, that is, participants were analysed in the group to which they were randomized regardless of treatment received, but only where an outcome was recorded (Higgins 2005).

Results were presented as risk ratios (RRs) with 95% confidence intervals (CIs) around these estimates. RRs less than one were taken to demonstrate a favourable outcome of the intervention of interest, and these are presented to the left of the line of no effect.

For those comparisons in which there were data from more than one trial we assessed heterogeneity by visually inspecting forest plots, calculating an I^2 statistic, and carrying out a chi square test for heterogeneity. If heterogeneity was detected we undertook a subgroup analysis, grouping trials according to drug regimen and follow up time (1 week vs 2 weeks vs 3 weeks vs 4 weeks) in order to explore causes of heterogeneity. If heterogeneity was not detected we pooled results from trials in a fixed-effect meta-analysis.

R E S U L T S

Description of studies

Trial selection

Of the 79 trials identified and included in our trials register, 57 were excluded (see 'Characteristics of excluded studies') and 22 met the inclusion criteria (see 'Characteristics of included studies'). All trials were identified from published literature. One ongoing study, Naeyaert ongoing has also been identified.

Trial location

Nineteen of the 22 included studies were conducted in resource-poor countries, although one, Schultz 1990, was a large multicentre trial involving eight centres (four sexually transmitted disease clinics, two dermatology clinics, and two family practice clinics), with one of the family practice centres in Mexico and the others in the USA. Of the other three trials, one was carried out in the USA (Hansen 1986) and two in Italy (Amerio 2003; Biele 2006).

Participants

Three trials included only adults (Chouela 1999; Amerio 2003; Biele 2006), six included only children (Maggi 1986; Schenone 1986; Taplin 1990; Avila-Romay 1991; Brooks 2002; Singalavanija 2003); and the other 13 included both adults and children. The total number of participants randomized in the 22 trials was 2676; all had a clinical diagnosis of scabies, with a subset of 903 identified as having their diagnosis confirmed parasitologically.

Interventions

The effectiveness of the following drugs was tested: topical benzyl benzoate; crotamiton; decamethrin; lindane; permethrin; synergized natural pyrethrins; sulfur; and oral ivermectin. Eighteen trials compared one drug with at least one other drug, one trial compared ivermectin against placebo, three trials compared different drug treatment regimens, and one trial compared two different vehicles for the same drug. No randomized controlled trials investigating malathion were identified.

Clinicians and drug companies recommended treatment of family members and close contacts at the same time as cases, to improve cure rates and reduce reinfection (Taplin 1986). None of the trials tested this hypothesis. Close and family contacts in both intervention and control groups were treated, however, in all but six trials (Hansen 1986; Maggi 1986; Amer 1992; Macotela-Ruiz 1993; Amerio 2003; Biele 2006).

Five trials stipulated that a bath or shower should be taken before treatment (Gulati 1978; Schenone 1986; Taplin 1990; Avila-Romay 1991; Bachewar 2009); and ten trials stipulated that participants should change and wash their linen after treatment (Avila-Romay 1991; Glaziou 1993; Chouela 1999; Usha 2000; Madan 2001; Nnoruka 2001; Brooks 2002; Singalavanija 2003; Zargari 2006; Ly 2009).

Dosing and regimen

Benzyl benzoate

The strength of the topical benzyl benzoate solution varied with three trials using 10% (Glaziou 1993; Brooks 2002; Biele 2006), one trial using 12.5% (Ly 2009) and three trials using 25% (Gulati 1978; Nnoruka 2001; Bachewar 2009). The treatment regimen was different in each trial: it was applied once and left overnight in Brooks 2002; applied twice, 12 hours apart in Glaziou 1993; applied twice and left overnight on two consecutive nights in Bachewar 2009; applied three times, 12 hours apart in Gulati 1978; applied on five consecutive days in Biele 2006; and a single application was left for 72 hours in Nnoruka 2001. Ly 2009 included two benzyl benzoate intervention groups, one in which the drug was applied once and left for 24 hours, and another in which the drug was applied twice, 24 hours apart, left in each case for 24 hours.

Crotamiton

A 10% topical preparation was used in two trials (Taplin 1990; Amer 1992). It was applied overnight on two consecutive nights in Amer 1992, and was applied once overnight in Taplin 1990.

Decamethrin

Schenone 1986 compared 0.02% decamethrin lotion applied daily for two days repeated on two more days a week later with 0.02% decamethrin lotion applied daily for four consecutive days.

Lindane

Each lindane trial used a 1% topical preparation, except for Singalavanija 2003, which used a 0.3% preparation. The number of applications ranged from one (Hansen 1986; Maggi 1986; Taplin 1986; Schultz 1990; Chouela 1999) to two (Amer 1992; Zargari 2006) to seven (Singalavanija 2003). Maggi 1986 compared a single application of lindane left on for four days, washed off and then repeated after a week with a single one-hour application of lindane, repeated after a week.

Permethrin

A 5% topical preparation was used in each permethrin trial. The number of applications ranged from one (Schultz 1990; Taplin 1990; Usha 2000; Bachewar 2009) to two (Amer 1992; Zargari 2006) to two consecutive overnight applications repeated after 14 days (Amerio 2003).

Synergized natural pyrethrins

A 0.16% topical preparation of natural pyrethrins synergized with pyperonil butoxide was used in Amerio 2003, applied on two successive nights and repeated 14 days later. In Biele 2006, a 0.165% preparation was applied on three consecutive days.

Sulfur

Two of the three sulfur trials used a 10% topical preparation (Avila-Romay 1991; Singalavanija 2003). In the third trial, Gulati 1978, the strength of the preparation was not stated. Avila-Romay 1991 compared sulfur in cold cream with sulfur in pork fat; both medications were applied nightly for three nights and then once three nights later. Singalavanija 2003 applied the sulfur on seven consecutive nights. Gulati 1978 applied sulfur once in the morning, once in the evening, and once again the next morning; treatment was repeated after 10 days if lesions persisted.

Ivermectin

The oral dose of ivermectin varied from a 100 µg/kg bodyweight (Glaziou 1993) to 200 µg/kg bodyweight (Macotela-Ruiz 1993; Usha 2000; Madan 2001; Nnoruka 2001; Brooks 2002; Bachewar 2009). The Chouela 1999 and Ly 2009 trials used an ivermectin dose between 150 µg/kg and 200 µg/kg bodyweight. Each trial gave a single dose.

Length of follow up

Follow up ranged from seven days to one month. In 11 trials it was possible to extract outcome data at 28 to 31 days after treatment (Hansen 1986; Taplin 1986; Schultz 1990; Taplin 1990; Amer 1992; Glaziou 1993; Madan 2001; Nnoruka 2001; Amerio 2003; Singalavanija 2003; Biele 2006). Follow up was at 21 days in two trials (Schenone 1986; Brooks 2002); 14 to 15 days in six trials (Gulati 1978; Maggi 1986; Chouela 1999; Usha 2000; Zargari 2006; Ly 2009); and seven to 10 days in the remaining three trials (Avila-Romay 1991; Macotela-Ruiz 1993; Bachewar 2009).

Outcome measures

The review's primary outcome measure (treatment failure) was reported in 21 of the 22 trials. Six of these 21 trials reported treatment failure in both clinically diagnosed cases and in microscopically confirmed cases (Schultz 1990; Taplin 1990; Amer 1992; Amerio 2003; Singalavanija 2003; Biele 2006); the other 13 trials reported treatment failure in clinically diagnosed cases who may or may not have been confirmed microscopically. Seven trials reported the secondary outcome measure (itch persistence) in addition to treatment failure (Hansen 1986; Schultz 1990; Taplin 1990; Brooks 2002; Amerio 2003; Singalavanija 2003; Biele 2006). Itch persistence alone was reported by Maggi 1986. Adverse events were reported as an outcome in all trials except Gulati 1978 and Maggi 1986.

The seven trials that reported on itch varied in their methods to assess this outcome:

- Hansen 1986: did not report on the method used.
- Maggi 1986: participants reported on itch using a three-point scale ("absent", "moderate", and "intense") before and after treatment; numbers in each category were reported.
- Schultz 1990: participants reported the presence or absence of itch before and after treatment; numbers in each category were reported.
- Taplin 1990: participants were reported as either having presence or absence of itch; no further details of assessment were given.
- Brooks 2002: participants described itch severity on a visual analogue scale before and after treatment; mean scores were reported along with the number of participants with absence of night-time itch.
- Amerio 2003 and Biele 2006: participants reported on itch using a five-point scale (from 0 = "no itch" to 4 = "severe itch") before and after treatment; mean scores were reported along with the number of participants with complete relief from itching.
- Singalavanija 2003: participants were divided into those who reported a decrease or absence of itch, and those who reported no improvement.

Sources of support

Seven trials stated that funding or support had been provided by drug companies (Taplin 1986; Schultz 1990; Taplin 1990; Glaziou 1993; Usha 2000; Amerio 2003; Zargari 2006).

Background prevalence

Fifteen trial reports did not state the background prevalence of scabies. In the four trials where prevalence was stated, it ranged from 9% in India (Gulati 1978) to 14% among children in a boarding school in Chile (Schenone 1986) to 36% in French Polynesia (Glaziou 1993) to 67% in Panama (Taplin 1990).

Risk of bias in included studies

See Table 1 for a summary assessment and the 'Characteristics of included studies' for details.

Generation of allocation sequence

Eight trials described an adequate method of generating a random allocation sequence: by computer in Usha 2000, Brooks 2002, Amerio 2003, Biele 2006 and Bachewar 2009; and by random-number table in Nnoruka 2001, Singalavanija 2003 and Ly 2009. The method was unclear in the other trials.

Allocation concealment

Six trials reported adequate allocation concealment: by phone call to third party-based procedure in Amerio 2003; by use of identical coded medication containers in Taplin 1986, Schultz 1990, Taplin 1990, and Zargari 2006; and the author of Usha 2000 confirmed that the allocation was by a third party, not the investigator. The remaining trials had methods of concealment that were either unclear or not reported.

Blinding

Twelve trials reported blinding. In two of these trials both the investigators or outcome assessors and the participants were described as blinded (Macotela-Ruiz 1993; Zargari 2006), and in eight trials the investigators or outcome assessors alone were described as blinded (Taplin 1986; Schultz 1990; Taplin 1990; Glaziou 1993; Madan 2001; Brooks 2002; Amerio 2003; Biele 2006). Chouela 1999 described the participants as blinded but also

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reported the trial as "double blind". Hansen 1986 described the trial as "single blind", but it is unclear who was blinded.

Inclusion of randomized participants in the analysis

Ten trials included all randomized participants in the analysis with no mention of losses to follow up. The completeness of follow up was greater than 80% (ie adequate) in eight trials (Hansen 1986; Taplin 1986; Schultz 1990; Taplin 1990; Macotela-Ruiz 1993; Chouela 1999; Zargari 2006; Ly 2009). The remaining four trials reported completeness of follow up less than 80% (Brooks 2002 – 27% lost to follow up, Madan 2001 – 25% lost to follow up, Singalavanija 2003 – 32% lost to follow up; Bachewar 2009 - 22% lost to follow up).

Effects of interventions

1. Ivermectin

Only one trial assessed the effectiveness against placebo, while eight trials compared it with another drug.

1.1. Versus placebo (55 participants, 1 trial)

Macotela-Ruiz 1993 compared 200 µg/kg bodyweight oral ivermectin with placebo.

Treatment failure in clinically diagnosed cases

Macotela-Ruiz 1993 reported fewer treatment failures in the ivermectin group at seven days (RR 0.24, 95% CI 0.12 to 0.51; 55 participants, Analysis 1.1). Figure 1.

Figure 1. Forest plot of comparison: 1 Ivermectin versus placebo, outcome: 1.1 Treatment failure in clinically diagnosed cases.
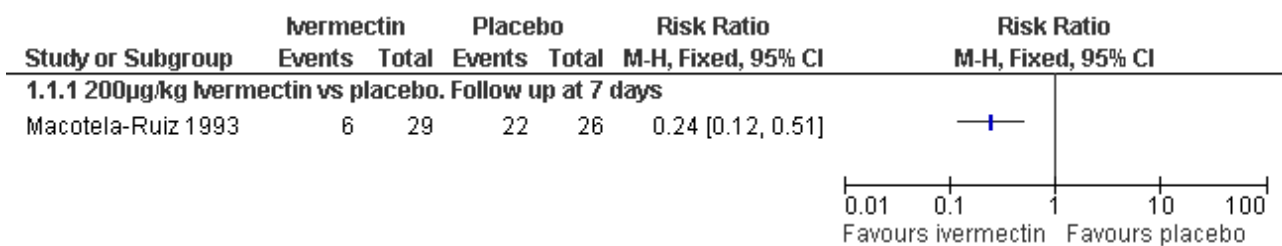
Adverse events.

None were reported.

1.2. Versus permethrin (153 participants, 2 trials)

Usha 2000 and Bachewar 2009 both compared 200 µg/kg bodyweight oral ivermectin with 5% topical permethrin cream.

Treatment failure in clinically diagnosed cases

Usha 2000 reported more treatment failures in the ivermectin group at two weeks (RR 13.50, 95% CI 1.84 to 99.26; 85 participants), as did Bachewar 2009 at one week follow up (RR 2.90, 95% CI 1.21 to 6.96; 55 participants, Analysis 2.1). Significant heterogeneity was not detected and the trials' combined estimate showed more treatment failures with ivermectin (RR 4.61, 95% CI 2.07 to 10.26, fixed-effect model; 140 participants). Figure 2.

Figure 2. Forest plot of comparison: 2 Ivermectin versus permethrin, outcome: 2.1 Treatment failure in clinically diagnosed cases.
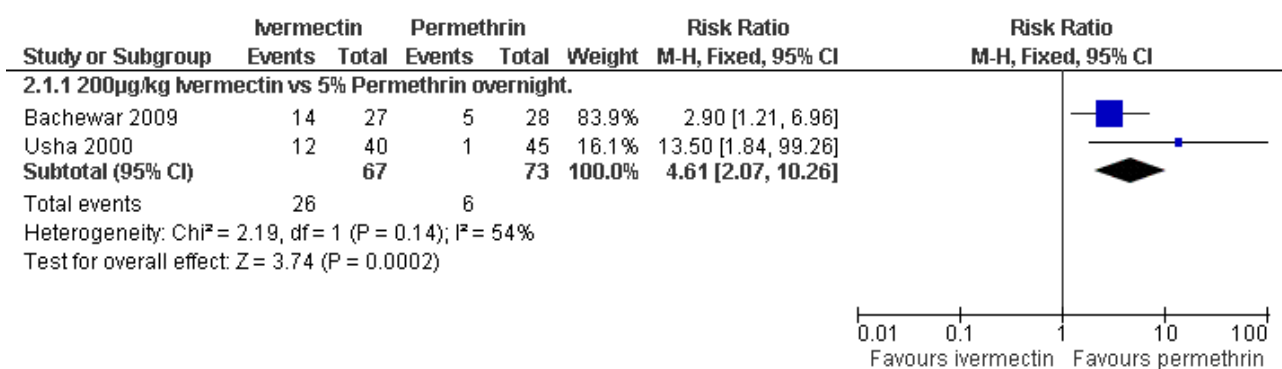
Adverse events

Three of 43 participants in the ivermectin group in the Usha 2000 trial reported aggravation of symptoms. No adverse events were reported in Bachewar 2009 (see Table 2).

1.3. Versus lindane (253 participants, 2 trials)

Chouela 1999 compared 150 µg/kg bodyweight oral ivermectin with 1% topical lindane, while Madan 2001 compared 200 µg/kg ivermectin with 1% lindane.

Treatment failure in clinically diagnosed cases

Chouela 1999 found no significant difference between the groups at 15 days (43 participants), while at four weeks Madan 2001 found that treatment failures were reduced in the ivermectin group

(RR 0.31, 95% CI 0.18 to 0.54; 150 participants, Analysis 3.1). Heterogeneity was not detected and the trials' combined estimate showed a benefit of ivermectin over lindane (RR 0.36, 95% CI 0.23 to 0.58, fixed-effect model; 193 participants). Figure 3.

Figure 3.   Forest plot of comparison: 3 Ivermectin versus lindane, outcome: 3.1 Treatment failure in clinically diagnosed cases.

Study or Subgroup	Ivermectin Events	Total	Lindane Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
3.1.1 150-200µg/kg Ivermectin vs 1% Lindane.						
Chouela 1999	5	19	11	24	19.0%	0.57 [0.24, 1.37]
Madan 2001	12	69	45	81	81.0%	0.31 [0.18, 0.54]
Subtotal (95% CI)		88		105	100.0%	0.36 [0.23, 0.58]
Total events	17		56			

Heterogeneity: Chi² = 1.35, df = 1 (P = 0.25); I² = 26%
Test for overall effect: Z = 4.29 (P < 0.0001)

0.01 0.1 1 10 100
Favours ivermectin   Favours lindane
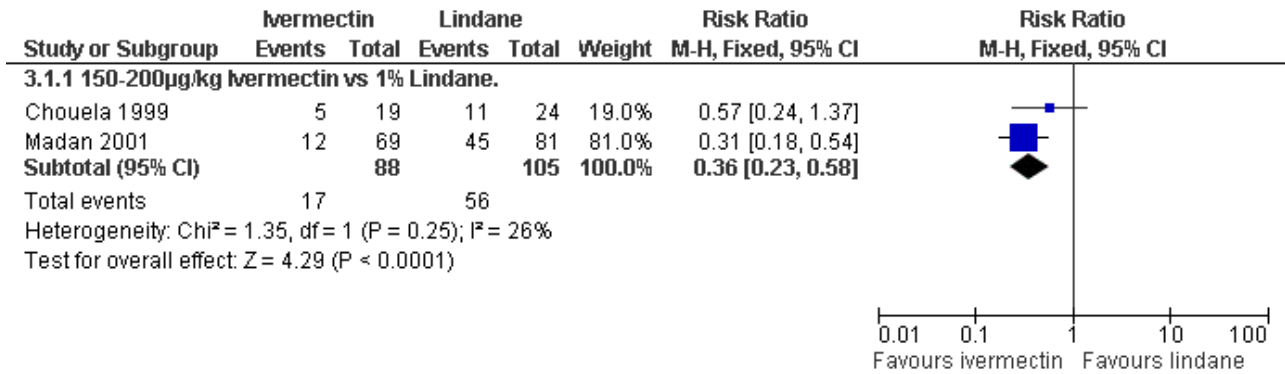
Adverse events

See Table 2. Chouela 1999 reported adverse events in 4/26 participants in the ivermectin group (headache, hypotension, abdominal pain, and vomiting) and in 6/37 participants in the lindane group (headache). Madan 2001 reported an adverse event in 1/100 participants in the ivermectin group (severe headache); there were none in the lindane group.

1.4. Versus benzyl benzoate (462 participants, 5 trials)

Brooks 2002 compared 200 µg/kg bodyweight oral ivermectin with 10% topical benzyl benzoate. Glaziou 1993 compared 100 µg/kg bodyweight ivermectin with 10% benzyl benzoate. Nnoruka 2001 and Bachewar 2009 compared 200 µg/kg bodyweight ivermectin with 25% benzyl benzoate. Ly 2009 compared 150 to 200 µg/kg bodyweight ivermectin with 12.5% benzyl benzoate.

Treatment failure in clinically diagnosed cases

See Analysis 4.1. No significant difference between the two groups was found in Bachewar 2009 at one week follow up (52 participants). After 14 days Ly 2009 found a significant difference in favour of benzyl benzoate compared with ivermectin (RR 2.00, 95% CI 1.47 to 2.72; 162 participants). No significant difference between the two groups was found in Brooks 2002 at three weeks (80 participants) or by Glaziou 1993 at 30 days (44 participants). At 30 days Nnoruka 2001 found a significant difference in favour of ivermectin (RR 0.13, 95% CI 0.03 to 0.53; 58 participants). Heterogenity was detected between the trials (Chi² = 27.97, df = 4, P < 0.0001; I² = 86%; see Figure 4 for forest plot). The differences in drug regimen and length of follow up that exist between the five trials may explain this heterogeneity.

Figure 4.   Forest plot of comparison: 4 Ivermectin versus benzyl benzoate, outcome: 4.1 Treatment failure in clinically diagnosed cases.
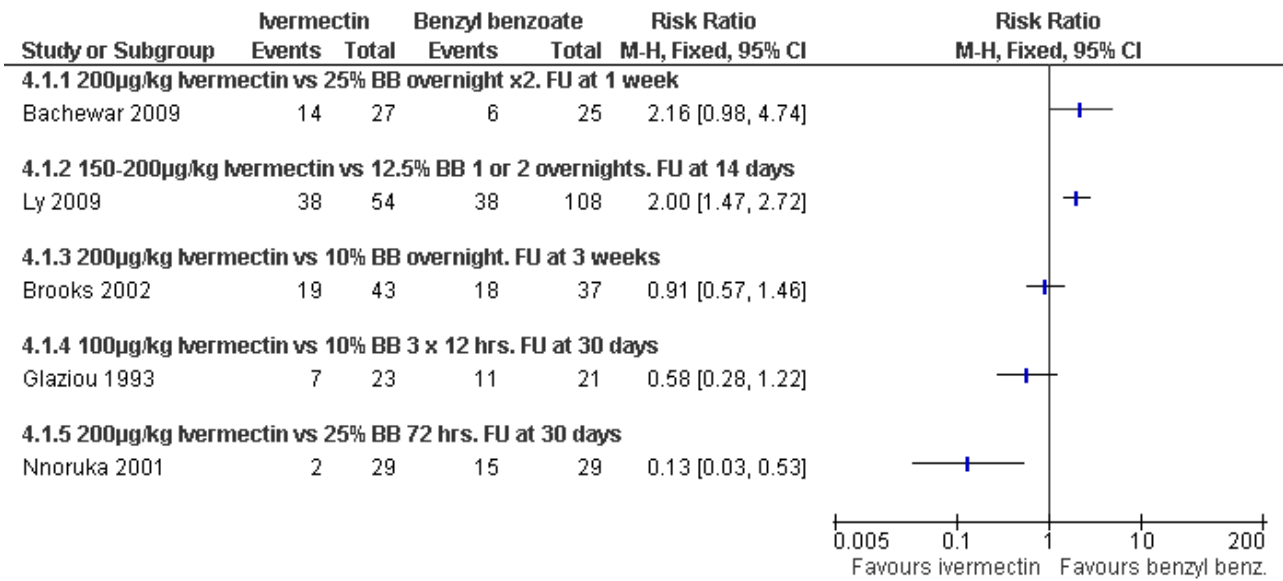
Itch persistence

See Analysis 4.2. Brooks 2002 found no significant difference in the number of participants who reported night-time itch at three weeks (58 participants). Figure 5.

Figure 5.   Forest plot of comparison: 4 Ivermectin versus benzyl benzoate, outcome: 4.2 Itch persistence.
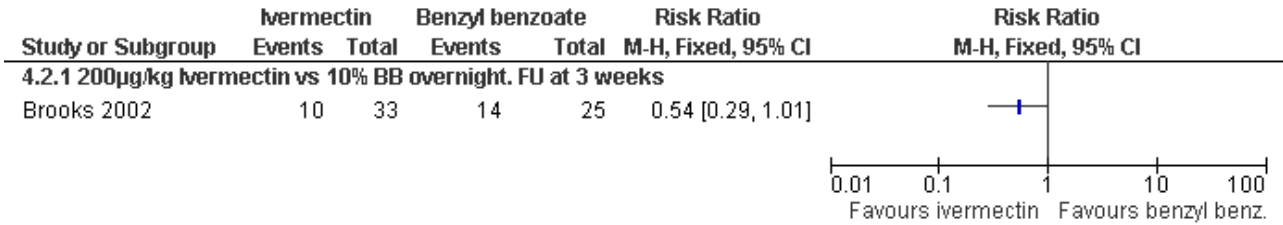
Adverse events

See Table 2. Brooks 2002 reported adverse events in 4/43 participants in the ivermectin group (pustular rash, cellulitis) and in 12/37 participants in the benzyl benzoate group (burning or stinging, dermatitis). Glaziou 1993 and Nnoruka 2001 reported adverse events only in the benzyl benzoate group: 5/21 participants (mild increase in pruritus) in Glaziou 1993; and 7/29 participants (pruritus and irritation) in Nnoruka 2001. Ly 2009 reported adverse events in 7/65 participants in the ivermectin group (abdominal pain, diarrhoea) and in 30/116 participants in the benzyl benzoate groups. Bachewar 2009 reported no adverse events.

2. Permethrin

2.1. Versus crotamiton (196 participants, 2 trials)

Two trials compared 5% permethrin with 10% crotamiton (Taplin 1990; Amer 1992). In Taplin 1990 the drugs were applied for 8 to 10 hours, whereas in Amer 1992 the drugs were applied overnight on two consecutive days.

Treatment failure

See Analysis 5.1 and Analysis 5.2. Participants in both trials had their scabies clinically diagnosed and microscopically confirmed. The comparative treatment failure rates described for clinically diagnosed cases therefore apply equally to microscopically diagnosed cases in these trials. Taplin 1990 found that treatment failure was reduced in the permethrin group after 28 days (RR 0.26, 95% CI 0.11 to 0.65; 94 participants, Analysis 5.1.3). Amer 1992 found no significant difference in outcome between the groups after 28 days (100 participants). Heterogeneity was not detected and a combined estimate showed a benefit of permethrin over crotamiton (RR 0.24, 95% CI 0.10 to 0.55, fixed-effect analysis; 194 participants). Figure 6 and Figure 7.

Figure 6. Forest plot of comparison: 5 Permethrin versus crotamiton, outcome: 5.1 Treatment failure in clinically diagnosed cases.
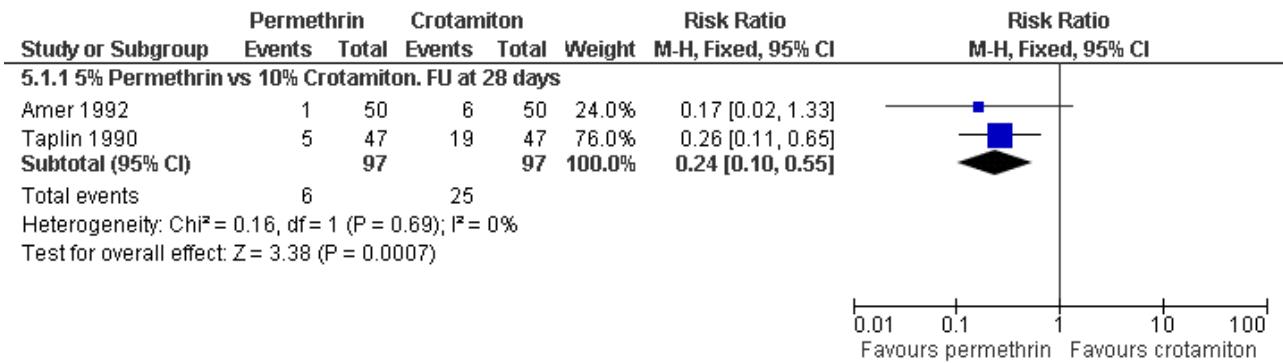
Figure 7. Forest plot of comparison: 5 Permethrin versus crotamiton, outcome: 5.2 Treatment failure in microscopically diagnosed cases.
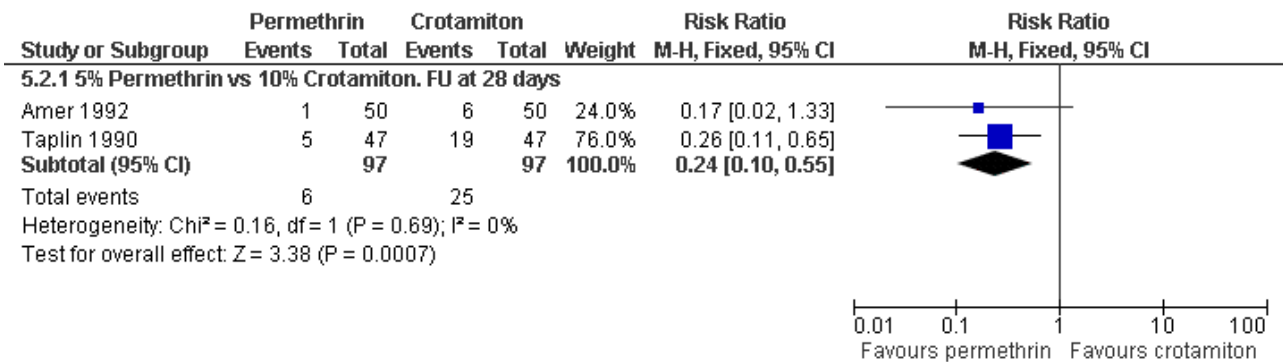
Itch persistence

See Analysis 5.3. Permethrin reduced the number of participants with itch persistence in Taplin 1990 (RR 0.26, 95% CI 0.11 to 0.65; 94 participants). Figure 8.

Figure 8. Forest plot of comparison: 5 Permethrin versus crotamiton, outcome: 5.3 Itch persistence.
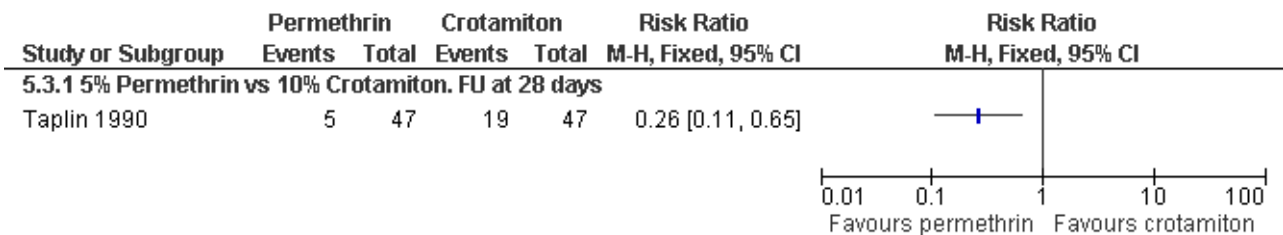
Adverse events

See Table 2. Taplin 1990 reported no adverse events in the permethrin group, but did report adverse events in 10/47 participants in the crotamiton group (worsening of symptoms). Amer 1992 reported no adverse events.

2.2. Versus lindane (835 participants, 5 trials)

Five trials compared 5% topical permethrin with 1% topical lindane (Hansen 1986; Taplin 1986; Schultz 1990; Amer 1992; Zargari 2006).

Treatment failure in clinically diagnosed cases

See Analysis 6.1. Zargari 2006 reported fewer treatment failures in the permethrin group after 14 days (RR 0.15, 95% CI 0.06 to 0.40; 99 participants). At 28 days Amer 1992 found two consecutive overnight applications of permethrin to be superior to two consecutive overnight applications of lindane (RR 0.08, 95% CI 0.01 to 0.57; 100 participants). Three trials compared a single application of permethrin with a single application of lindane, with follow up at 28 days (Hansen 1986, Schultz 1990 and Taplin 1986).

No benefit was found for either treatment by Hansen 1986 (28 days, 99 participants) or Schultz 1990 (28 +/- 7 days, 404 participants), whereas Taplin 1986 found permethrin to be superior (RR 0.22, 95% CI 0.05 to 0.95; 51 participants).

Heterogenity was detected between the results of the five studies (Chi^2 = 11.83, df = 4, P = 0.02; I^2 = 66%; see Figure 9 for forest plot)

so the trials were grouped by drug regimen and length of follow up in order to explore causes of heterogeneity. The pooled effect for the three trials sharing the same drug regimen (single application) and length of follow up (four weeks) showed a significant effect in favour of permethrin (RR 0.59, 95% CI 0.37 to 0.95, fixed-effect model; 554 participants). Statistical heterogeneity was not detected in this group of three trials.

Figure 9. Forest plot of comparison: 6 Permethrin versus lindane, outcome: 6.1 Treatment failure in clinically diagnosed cases.
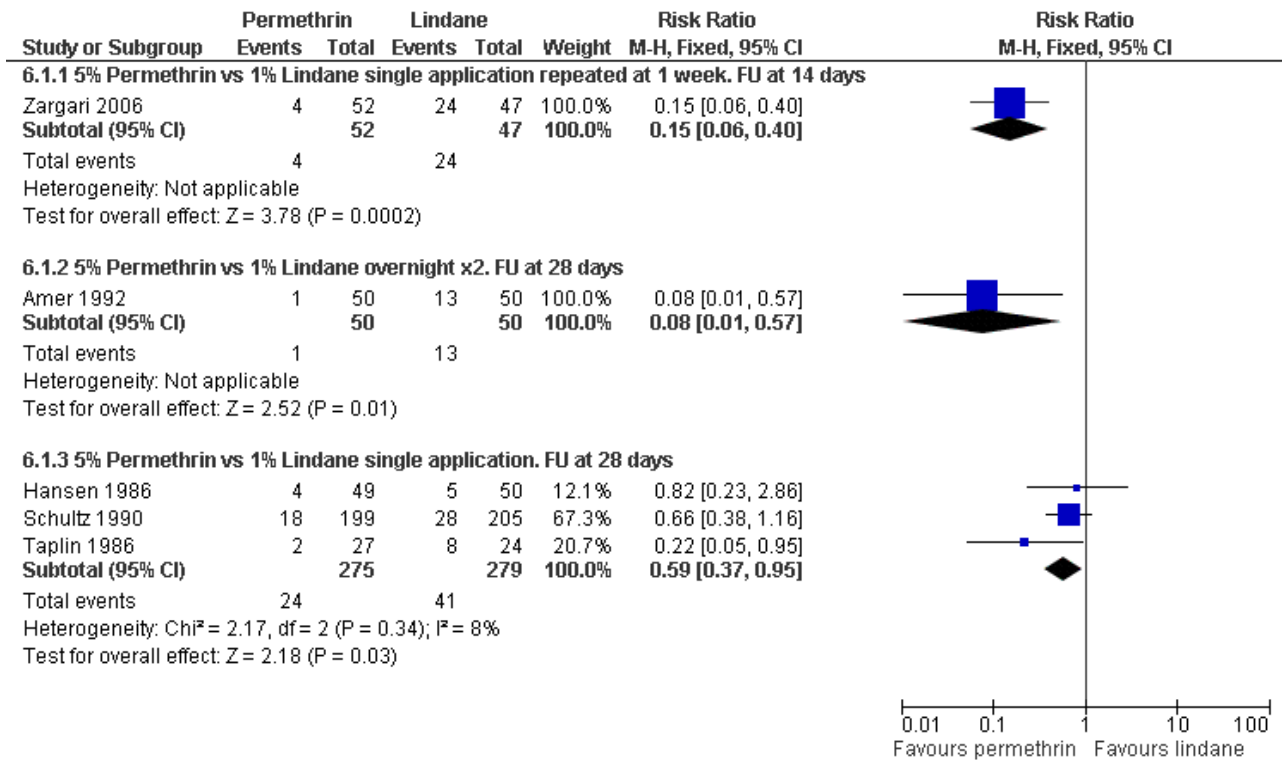
Treatment failure in microscopically confirmed cases

See Analysis 6.2. Two consecutive overnight applications of permethrin was found to be superior to two consecutive overnight applications of lindane after 28 days in Amer 1992 (RR 0.08, 95%

CI 0.01 to 0.57; 100 participants). Taplin 1986 (46 participants) and Schultz 1990 (338 participants) both compared single applications of permethrin and lindane with follow up at 28 days. Neither trial showed a significant difference between the interventions. Figure 10.

Figure 10.   Forest plot of comparison: 6 Permethrin versus lindane, outcome: 6.2 Treatment failure in microscopically diagnosed cases.
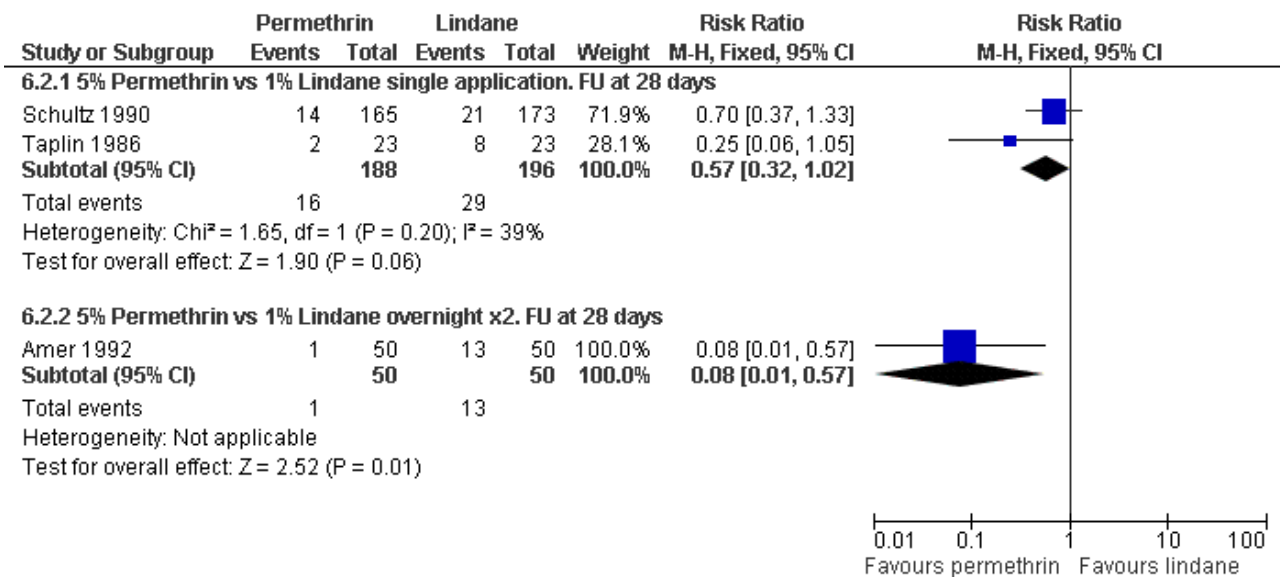
Itch persistence

See Analysis 6.3. The two trials that reported on itch persistence found different effects: Hansen 1986 found no significant difference between the two interventions after 28 days (99 participants),

whereas Schultz 1990 found permethrin to be superior after 28 +/- 7 days (RR 0.56, 95% CI 0.37 to 0.86; 391 participants). Heterogeneity was not detected and a combined estimate showed permethrin to be superior (RR 0.61, 95% CI 0.44 to 0.86, fixed effects model; 490 participants). Figure 11.

Figure 11.   Forest plot of comparison: 6 Permethrin versus lindane, outcome: 6.3 Itch persistence.
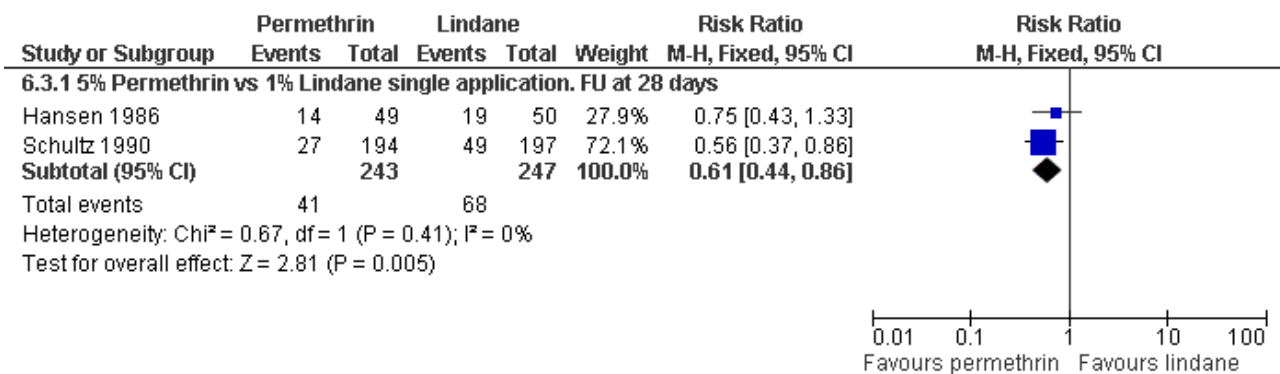
Adverse events

See Table 2. Hansen 1986 recorded mild burning, stinging, or itching in both groups (5/49 participants in the permethrin group, 5/50 participants in the lindane group). Schultz 1990 reported adverse events in 51/234 participants in the permethrin group (burning/stinging, pruritus, erythema, tingling, rash, diarrhoea, persistent excoriation) and in 43/233 participants in the lindane group (burning/stinging, pruritus, tingling, erythema, rash, papular rash, diarrhoea, contact dermatitis, phemphigus). Zargari 2006

reported skin irritation in both groups (2/59 participants in the permethrin group, 1/58 participant in the lindane group). Amer 1992 and Taplin 1986 both reported no adverse events.

2.3 Versus benzyl benzoate (69 participants, 1 trial)

Treatment failure in clinically diagnosed cases

See Analysis 7.1. In Bachewar 2009 there was no significant difference in treatment failure between the two groups after one week (RR 0.74, 95% CI 0.26 to 2.14; 53 participants). Figure 12.

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**Figure 12. Forest plot of comparison: 7 Permethrin versus benzyl benzoate, outcome: 7.1 Treatment failure in clinically diagnosed cases.**

Study or Subgroup	Permethrin Events	Permethrin Total	Benzyl benzoate Events	Benzyl benzoate Total	Risk Ratio M-H, Fixed, 95% CI
7.1.1 5% Permethrin vs 25% BB overnight x2 FU at 1 week					
Bachewar 2009	5	28	6	25	0.74 [0.26, 2.14]

Risk Ratio M-H, Fixed, 95% CI — scale 0.01, 0.1, 1, 10, 100. Favours permethrin / Favours benzyl benz.
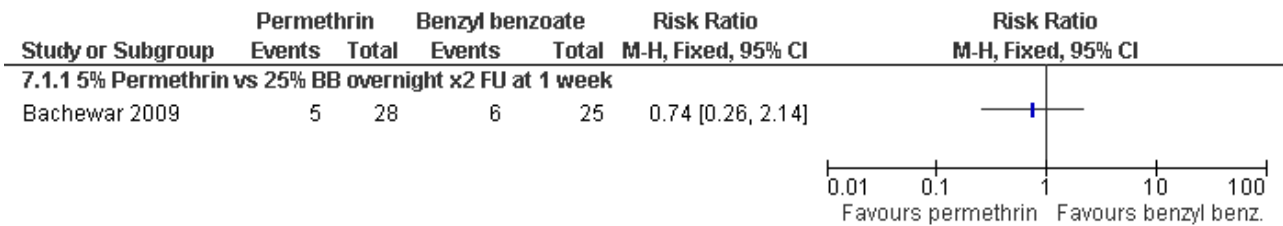
Adverse events

No adverse events were reported in Bachewar 2009.

2.4. Versus synergized natural pyrethrins (40 participants, 1 trial)

Amerio 2003 compared 5% topical permethrin with topical 0.16% natural pyrethrins synergized with 1.65% pyperonil butoxide.

Treatment failure

All participants had their scabies both clinically diagnosed and microscopically confirmed. There were no treatment failures in either group after 28 days (40 participants).

Itch persistence

See Analysis 8.1.There was no significant difference in itch persistence between the two groups after 28 days (40 participants). Figure 13.

Figure 13. Forest plot of comparison: 8 Permethrin versus natural synergized pyrethrins, outcome: 8.1 Itch persistence.

Study or Subgroup	Permethrin Events	Permethrin Total	Synergized pyrethrin Events	Synergized pyrethrin Total	Risk Ratio M-H, Fixed, 95% CI
8.1.1 5% Permethrin vs 0.16% Pyrethrins for 8 hours x2. FU at 4 weeks					
Amerio 2003	4	20	0	20	9.00 [0.52, 156.91]

Risk Ratio M-H, Fixed, 95% CI — scale 0.001, 0.1, 1, 10, 1000. Favours permethrin / Favours pyrethrins
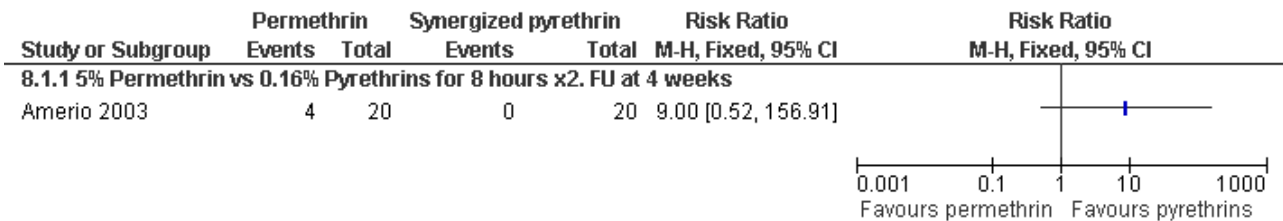
Adverse events

See Table 2. Ten of the 20 participants in the permethrin group and two of the 20 participants in the synergized pyrethrin group were reported as having secondary skin infections requiring antibiotic treatment. It was not clear from the trial report whether this was considered an adverse event or rather a baseline characteristic.

3. Other drug comparisons

3.1. Crotamiton versus lindane (100 participants, 1 trial)

Amer 1992 compared 10% topical crotamiton with 1% topical lindane.

Treatment failure

See Analysis 9.1 and Analysis 9.2. All participants in Amer 1992 had their scabies both clinically diagnosed and microscopically confirmed. There was no significant difference in treatment failure between the two groups after 28 days (100 participants). Figure 14 and Figure 15.

Figure 14. Forest plot of comparison: 9 Crotamiton versus lindane, outcome: 9.1 Treatment failure in clinically diagnosed cases.

Study or Subgroup	Crotamiton Events	Crotamiton Total	Lindane Events	Lindane Total	Risk Ratio M-H, Fixed, 95% CI
9.1.1 10% Crotamiton vs 1% Lindane overnight x2. FU at 28 days					
Amer 1992	6	50	13	50	0.46 [0.19, 1.12]

Risk Ratio M-H, Fixed, 95% CI — scale 0.1, 0.2, 0.5, 1, 2, 5, 10. Favours crotamiton / Favours lindane
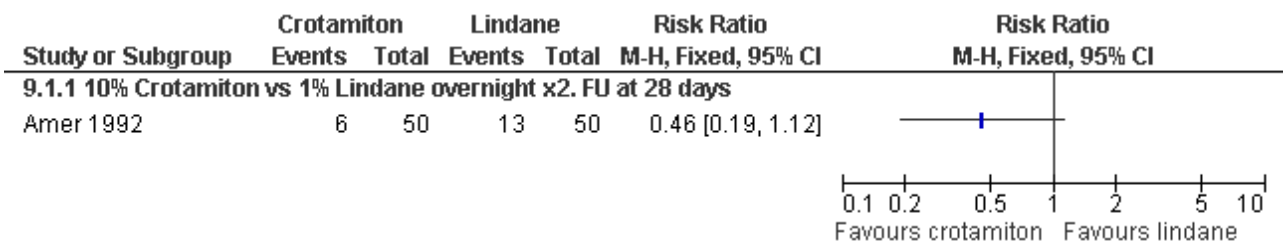
Figure 15. Forest plot of comparison: 9 Crotamiton versus lindane, outcome: 9.2 Treatment failure in microscopically diagnosed cases.
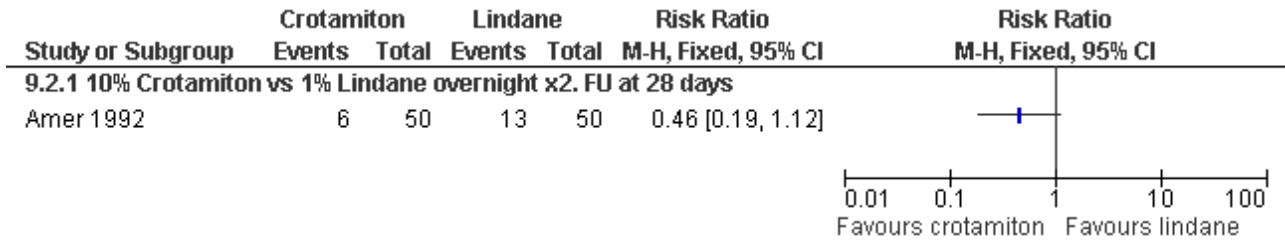
Adverse events

None were reported.

3.2. Lindane versus sulfur (100 participants, 1 trial)

Singalavanija 2003 compared 0.3% topical lindane with 10% topical sulfur.

Treatment failure in clinically diagnosed cases

See Analysis 10.1. There was no significant difference between the two groups after 28 days in Singalavanija 2003 (68 participants). Figure 16.

Figure 16. Forest plot of comparison: 10 Lindane versus sulfur, outcome: 10.1 Treatment failure in clinically diagnosed cases.
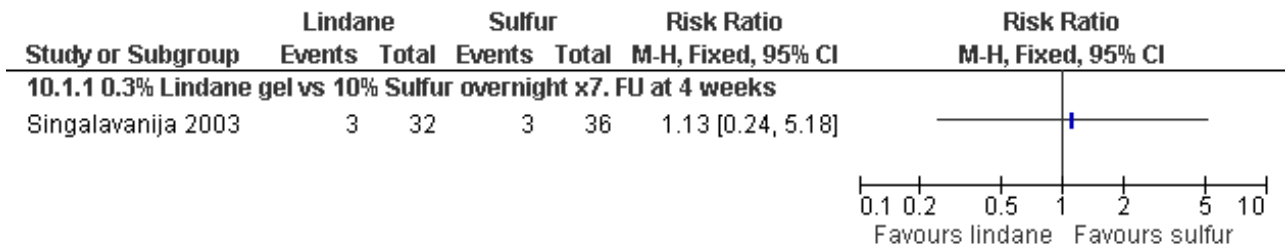
Itch persistence

See Analysis 10.2. There was no significant difference between the groups in the number of participants in whom itch persisted at 28 days (68 participants). Figure 17.

Figure 17. Forest plot of comparison: 10 Lindane versus sulfur, outcome: 10.2 Itch persistence.
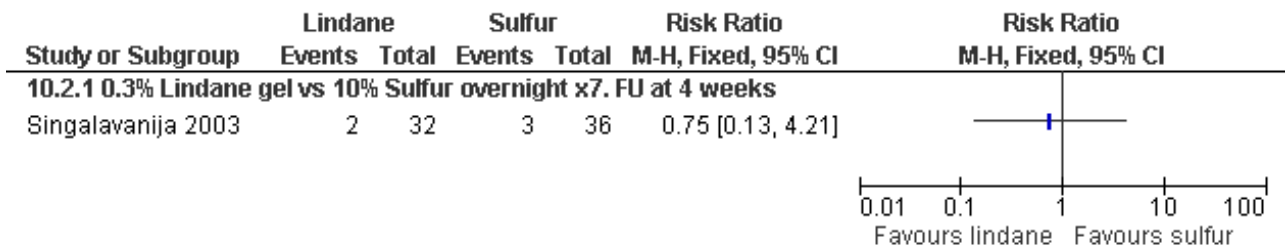
Adverse events

See Table 2. The reported adverse events (foul odour, burning, erythema) occurred in the sulfur group (14/50 participants) and the lindane group (14/50 participants).

3.3. Benzyl benzoate versus sulfur (158 participants, 1 trial)

Gulati 1978 compared 25% topical benzyl benzoate with topical sulfur ointment.

Treatment failure in clinically diagnosed cases

See Analysis 11.1. There was no significant difference between the two groups after 15 days in Gulati 1978 (158 participants). Figure 18.

Figure 18.   Forest plot of comparison: 11 Benzyl benzoate versus sulfur, outcome: 11.1 Treatment failure in clinically diagnosed cases.
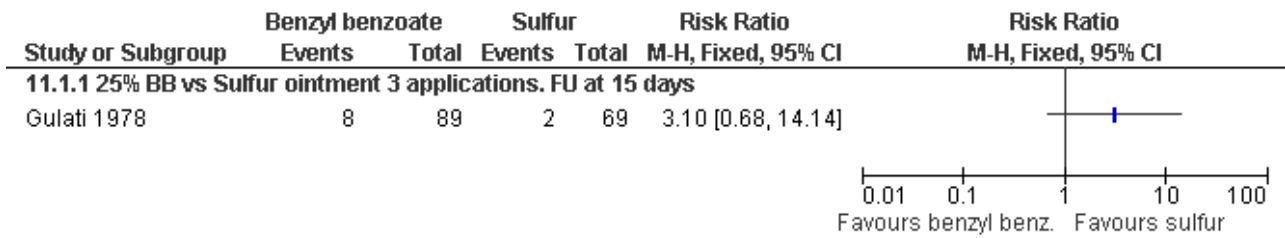
Adverse events

None were reported.

3.4. Benzyl benzoate versus synergized natural pyrethrins (240 participants, 1 trial)

Biele 2006 compared 10% topical benzyl benzoate with topical 0.165% natural pyrethrins synergized with 1.65% pyperonil butoxide.

Treatment failure

See Analysis 12.1 and Analysis 12.2. All participants had their scabies both clinically diagnosed and microscopically confirmed. There was no significant difference in treatment failure between the two groups after four weeks in Biele 2006 (240 participants). Figure 19 and Figure 20.

Figure 19.   Forest plot of comparison: 12 Benzyl benzoate versus natural synergized pyrethrins, outcome: 12.1 Treatment failure in clinically diagnosed cases.
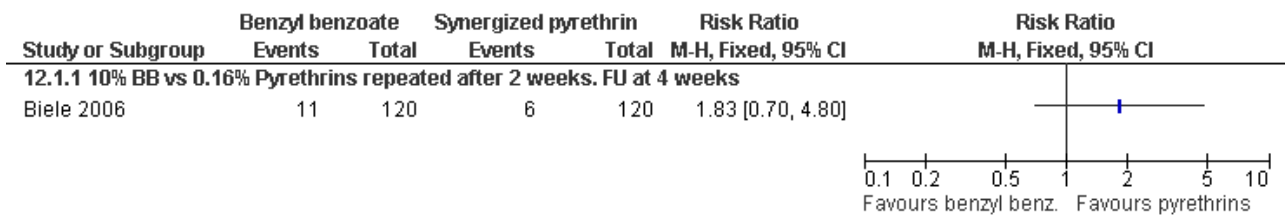
Figure 20.   Forest plot of comparison: 12 Benzyl benzoate versus natural synergized pyrethrins, outcome: 12.2 Treatment failure in microscopically diagnosed cases.
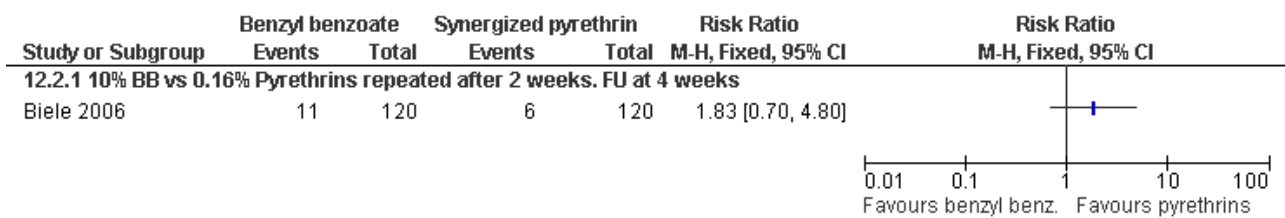
Itch persistence

See Analysis 12.3. There was no significant difference in itch persistence between the two groups after four weeks (240 participants). Figure 21.

Figure 21. Forest plot of comparison: 12 Benzyl benzoate versus natural synergized pyrethrins, outcome: 12.3 Itch persistence.

Study or Subgroup	Benzyl benzoate Events	Total	Synergized pyrethrin Events	Total	Risk Ratio M-H, Fixed, 95% CI	Risk Ratio M-H, Fixed, 95% CI
12.3.1 10% BB vs 0.16% Pyrethrins repeated after 2 weeks. FU at 4 weeks						
Biele 2006	10	120	6	120	1.67 [0.63, 4.44]	

Favours benzyl benz.   Favours pyrethrins
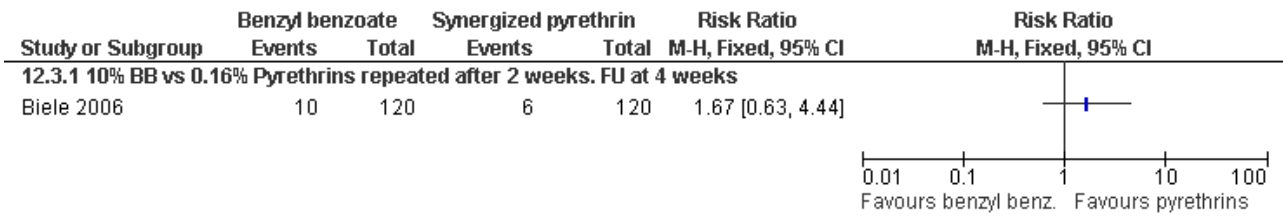
Adverse events

Twenty-two of the 120 participants in the benzyl benzoate group and three of the 120 participants in the synergized natural pyrethrins group experienced skin irritation and burning sensations after drug application (see Table 2).

4. Length of treatment comparisons

4.1. Benzyl benzoate: one overnight application versus two overnight applications (116 participants, 1 trial)

Treatment failure in clinically diagnosed cases.

There was no significant difference in treatment failure between the two groups after 14 days in Ly 2009 (108 participants, Analysis 13.1). Figure 22.

Figure 22. Forest plot of comparison: 13 Benzyl benzoate: one application versus two applications, outcome: 13.1 Treatment failure in clinically diagnosed cases.

Study or Subgroup	One application Events	Total	Two applications Events	Total	Risk Ratio M-H, Fixed, 95% CI	Risk Ratio M-H, Fixed, 95% CI
13.1.1 12.5% BB overnight x1 vs 12.5% BB overnight x2. FU at 14 days						
Ly 2009	23	60	15	48	1.23 [0.72, 2.08]	

Favours one application   Favours two applications
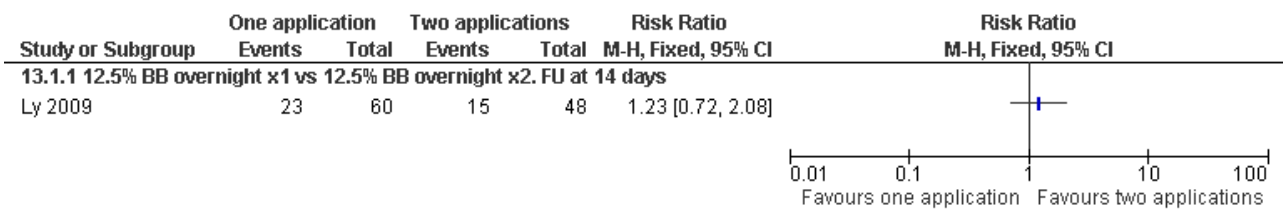
Adverse events

Irritant dermatitis was reported in 30 out of 116 participants (see Table 2).

4.2. Lindane: short application versus long application (87 participants, 1 trial)

Treatment failure

Maggi 1986 did not assess this outcome measure.

Itch persistence

A short application of lindane reduced itch persistence at 14 days (RR 0.34, 95% CI 0.12 to 0.98; 87 participants, Analysis 14.1). However, the trial authors did suggest that the pruritus experienced by the participants could have been due to a lindane-associated contact dermatitis. Figure 23.

Figure 23. Forest plot of comparison: 14 Lindane: short application versus long application, outcome: 14.1 Itch persistence.

Study or Subgroup	Short course lindane Events	Total	Long course lindane Events	Total	Risk Ratio M-H, Fixed, 95% CI	Risk Ratio M-H, Fixed, 95% CI
14.1.1 1% Lindane 2x 1hr applications vs 2x 4 day applications. FU at 14 days						
Maggi 1986	4	45	11	42	0.34 [0.12, 0.98]	

Favours short course   Favours long course
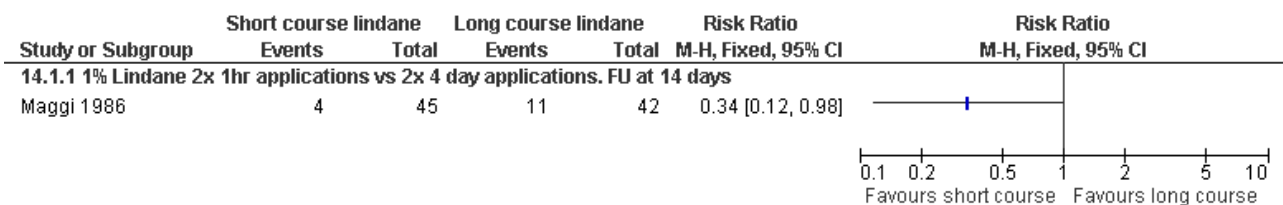
Adverse events

None other than pruritus (see above) were reported.

4.3. Decamethrin: two-day plus two-day application versus four-day application (127 participants, 1 trial)

Treatment failure in clinically diagnosed cases.

There were no treatment failures in either group in Schenone 1986 after 21 days: 0/53 treatment failures in the two-plus-two-day group; and 0/74 treatment failures in the four-day group. Five

participants in each group received a second treatment at seven days due to the presence of active lesions. This second treatment consisted of two applications of 0.02% decamethrin on consecutive days.

Adverse events

Fifteen of 127 participants experienced "moderate skin hotness" after application of decamethrin (see Table 2).

5. Drug vehicle comparisons

5.1. Sulfur: pork fat vehicle versus cold cream vehicle (51 participants, 1 trial)

Treatment failure in clinically diagnosed cases

See Analysis 15.1. There was no significant difference in the number of treatment failures between the two groups after 10 days in Avila-Romay 1991 (51 participants). Figure 24.

Figure 24. Forest plot of comparison: 15 Sulfur: pork fat vehicle versus cold cream vehicle, outcome: 15.1 Treatment failure in clinically diagnosed cases.
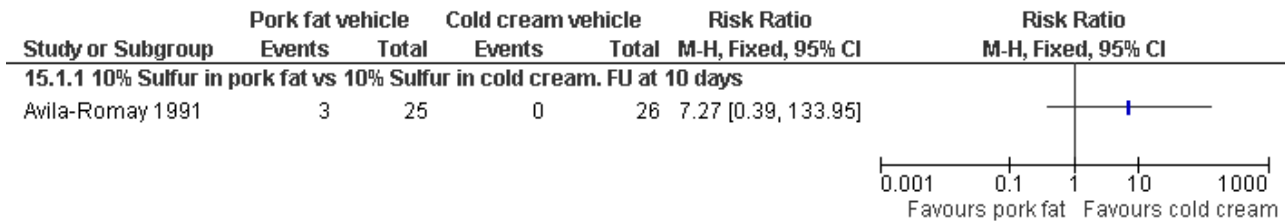
Adverse events

See Table 2. Pruritus, xerosis, burning sensation, and erythema were reported for cases and contacts in both groups. There were adverse events in 68/53 participants in the pork fat vehicle group, including keratosis pilaris. There were adverse events in 45/58 participants in the cold cream vehicle group, including keratosis follicularis.

DISCUSSION

The review's objective was to evaluate the effectiveness of current treatments for scabies in order to inform practice and guide future research. The previous version of this review noted that clinicians faced considerable uncertainty when choosing the best treatment for scabies (Walker 2000). Ten years later the picture is a little clearer, but there are still considerable gaps in our knowledge.

Trial quality

All 22 included trials were designed to test the effectiveness of one or more treatments for scabies. Methodological quality varied between trials. Only two trials described both adequate randomization sequence generation and adequate allocation concealment, and the majority of the reports described neither adequately. The blinding was absent, or the degree of blinding was unclear in ten of the 22 identified trials, and losses to follow up were greater than 20% of the enrolled participants in four of the trials.

Effectiveness

The results of this review suggest that, of the topical treatments for scabies, permethrin is most effective. Permethrin has been tested against topical crotamiton, topical lindane, and oral ivermectin in randomized controlled trials, and it appears to be superior to all three in terms of minimizing treatment failure in participants with a clinical diagnosis of scabies. In the one trial that tested permethrin against topical benzyl benzoate no difference in cure rate was detected, however this trial was small (53 participants) and the data used in the review related only to one week follow up.

In the subgroup of participants with microscopically confirmed scabies, permethrin was again superior to crotamiton, but there is uncertainty as to whether permethrin is superior to lindane. Permethrin also appears to be better at relieving itch than either crotamiton or lindane (itch was not reported as a separate outcome in the ivermectin versus permethrin trial). Unfortunately no trials comparing permethrin with either topical sulfur or topical malathion were identified; permethrin's relative effectiveness against these treatments therefore remains unknown.

In some countries natural pyrethrin-based topical treatments are available as an alternative to permethrin cream (Biele 2006). Pyrethrins are naturally occurring insecticidal compounds found in the *Compositae* family of plants (Wagner 2000), whereas permethrin is a synthetic pyrethroid analogue. Results from the two Italian trials included in this review suggest that pyrethrin is equivalent in effectiveness to both permethrin and benzyl benzoate.

Trials comparing crotamiton with lindane, lindane with sulfur, and sulfur with benzyl benzoate have all produced equivocal results, suggesting that there is no single most effective treatment out of these four topical options. In most countries the choice is in any case restricted, either due to lack of availability, or the lack of a licence for scabies.

Ivermectin is currently the only oral treatment for scabies that is in routine use. It appears to be more effective than both placebo and lindane, but less effective than permethrin. There was significant heterogeneity in the results of the five trials that compared ivermectin and benzyl benzoate, which may be explained by differences in drug regimen and length of follow up between the trials. After stratifying by drug regimen and length of follow up the relative effectiveness of ivermectin appeared to increase with increasing length of follow up. This may mean that ivermectin is slower in achieving cure than topical benzyl benzoate, however, this conclusion is rather speculative given these data.

An advantage of an oral antiscabietic treatment over a topical one is ease of use, particularly in hot humid climates, when engaging in mass treatment, or when treating children. However,

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ivermectin is not presently licensed for the treatment of scabies in most countries. Ivermectin's effectiveness, cost effectiveness, and safety in mass treatment in areas of high endemicity (preferably as a sustainable public health intervention) need to be further evaluated in larger trials of sufficient power.

Topical ivermectin has also been suggested to be effective after success in uncontrolled studies (Yeruham 1998; Victoria 2001). At present there is no commercially available topical ivermectin preparation available for the treatment of scabies, and randomized controlled trials are needed to evaluate this potential new treatment option.

There are still no published reports of randomized controlled trials that test the effectiveness of malathion against either placebo or another drug, despite over 30 years passing by since a non-controlled study first suggested that the drug was effective (Hanna 1978). The 2010 British National Formulary recommends malathion as the treatment of choice if permethrin is inappropriate (BNF 2010), despite the lack of evidence from randomized controlled trials. Such a trial comparing malathion with permethrin is needed to test their relative effectiveness.

We found trials of the herbal remedies toto soap (Alebiosu 2003) and lippia oil (Oladimeji 2000; Oladimeji 2005), but these trials did not meet the review's inclusion criteria. Both treatments look promising, but randomized controlled trials making direct comparisons with the existing best treatments are needed to assess their true relative effectiveness.

Treatment regimen was assessed in two trials. Maggi 1986 found that a one-hour application of lindane reduced itch compared with a much longer four-day application; the authors suggested that the itch may, at least in part, have been due to a dermatitis caused by the lindane treatment itself. Schenone 1986 compared two different regimens using decamethrin, a pyrethroid insecticide in the same class as permethrin. All participants were cured in both groups. Decamethrin is not commercially available for the treatment of scabies and we found no trials that tested its effectiveness against other treatments. Decamethrin (as deltamethrin) is usually used as an agricultural insecticide and its safety as an antiscabietic medication has not been established (WHO 1990).

The formulation of a topically applied product may influence its efficacy. For example, a 1% permethrin formulation marketed for the treatment of head lice appears to be less effective than the conventional antiscabietic 5% preparation, according to case reports (Cox 2000). None of the trials included in this review directly compared different strength formulations of the same treatment.

One trial compared different vehicles for the same drug (Avila-Romay 1991). Cold cream as a treatment vehicle for sulfur may be more effective than pork fat, with fewer adverse events. For resource-poor countries this could be a cheap and safe option, which in some circumstances might also be more culturally acceptable.

This review did not seek to assess the relative cost effectiveness of the various treatments for scabies; however, large cost differences are apparent. In the UK, costs are: permethrin £5.51 per 30 g of cream, benzyl benzoate £0.50 per 100 mL, crotamiton £2.99 per 100 mL, and malathion £2.96 per 100 mL (BNF 2010). When lindane

was marketed in the UK it was a fifth the cost of permethrin per treatment (BNF 1997).

We did not specifically attempt to assess the effectiveness of treatments for crusted scabies, and none of the included trials selected participants with this diagnosis. Caution should therefore be exercised in generalizing the results of this review to the treatment of patients with atypical severe scabies infection. This is an important area where more research is needed.

Caution should also be exercised in generalizing these results, which were obtained from trials that recruited individual participants (mostly in the outpatient setting), to the management of outbreaks in institutions. Given the burden of disease caused by scabies within institutions, such as long-term healthcare facilities, the inclusion of such patients in randomized controlled trials of effectiveness would be beneficial.

Mass treatment of a community in order to eradicate scabies has been tested in two studies (Dunne 1991; Bockarie 2000), both of which used oral ivermectin. Unfortunately neither of these studies met the review's inclusion criteria (Bockarie 2000 was an uncontrolled trial, and Dunne 1991 recruited participants on the basis of a diagnosis of onchocerciasis). Further research is needed to test the effectiveness, safety, and practicality of this approach to the management of scabies, particularly in areas of high prevalence.

Safety

Serious adverse events leading to death or permanent disability were not reported in any of the included or excluded trials. This review did not seek to systematically review the literature on the safety of antiscabietic treatments, but a number of notable reports of serious adverse events that have been published elsewhere are discussed below.

Convulsions and aplastic anaemia have both been reported with the use of lindane (Rauch 1990; Elgart 1996); in some cases this being thought to be due to the application of the drug to non-intact skin. Lindane was withdrawn by the manufacturer from the UK market in 1996, but this was for commercial and not toxicological reasons. In 1995, the US Food and Drug Administration designated lindane as a second-line treatment due to its potential toxicity; only to be used in those who have failed to respond to, or who are intolerant of, other antiscabietic treatments (WHO 2003).

Ivermectin has been very widely used in the treatment of onchocerciasis (predominantly in adults) and even with repeated doses serious adverse effects have been rare (DeSole 1989; Pacque 1990). However, an increased risk of death among a group of elderly patients with scabies in a long-term care facility has been reported (Barkwell 1997). Whether this was due to ivermectin or to interactions with other scabicides, including lindane and permethrin, or other treatments such as psychoactive drugs was not clear and there was considerable discussion of the validity of this report (Bredal 1997; Coyne 1997; Diazgranados 1997; Reintjes 1997).

Rare adverse reactions have been reported with the use of both permethrin (dystonia, Coleman 2005) and natural pyrethrin (fatal asthma, Wagner 2000).

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The relative purity of the active ingredients of certain topical treatments and their isomeric ratios may also affect drug toxicity. In particular, very little is known about the effects of exposure to different isomeric grades of permethrin. Clinical grade material is 25:75 cis isomer:trans isomer and agricultural grade is 40:60. The cis isomer has 10 times the acute toxicity and there could be dangers in people in resource-poor countries using agricultural-grade permethrin for treating human infestations (personal communication from Ian Burgess, Medical Entomology Centre, Cambridge). Similar problems have been reported with the inappropriate use of agricultural grade malathion for treating human infestations (Petros 1990).

A search of the WHO Adverse Drug Reaction Database in 1998 for a previous version of this review found reports of serious adverse drug reactions for convulsions (benzyl benzoate 4, crotamiton 1, lindane 38, malathion 2, permethrin 6) and death (benzyl benzoate 0, crotamiton 1, lindane 1, malathion 0, permethrin 5) (Walker 2000). A search for this update of the review of the UK Medicines and Healthcare Products Regulatory Agency database of suspected drug reactions found reports for convulsions (benzyl benzoate 1, crotamiton 0, lindane 3, malathion 0, permethrin 0, sulfur 0, ivermectin 1) and death (benzyl benzoate 0, crotamiton 0, lindane 1, malathion 0, permethrin 1 (intra uterine death), sulfur 0, ivermectin 3) (MHRA 2006). Extreme caution must be shown in interpreting these reports, as they are clearly influenced by the extent to which the products are used and by the quality of the reporting. Neither can a causal link be assumed for any of the reported events.

AUTHORS' CONCLUSIONS

Implications for practice

On the basis of the available evidence from randomized controlled trials, topical permethrin appears to be the most effective treatment for scabies. Ivermectin appears to be an effective oral treatment, but in many countries it is not licensed for this indication.

Implications for research

Trials are needed to evaluate the relative effectiveness of malathion against permethrin, and the relative effectiveness of herbal treatments against existing treatments. The effectiveness of topical ivermectin also needs to be explored. The most appropriate treatment for the severe crusted form of scabies has not yet been established in randomized controlled trials.

Researchers should ensure that toxicity and safety outcomes are systematically collected in future trials as well as being notified through routine monitoring of adverse events in clinical practice.

Approaches to the control of outbreaks in institutions and public health programmes to control scabies in populations with high prevalence require evaluation.

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CHARACTERISTICS OF STUDIES

Characteristics of included studies [ordered by study ID]

Amer 1992

Methods	Design: randomized controlled trial
	Generation of allocation sequence: "according to code"
	Allocation concealment: unclear
	Blinding: unclear
	Inclusion of randomized participants in the analysis: 100%
Participants	Number: 150 enrolled (all ages; sex not stated)
	Inclusion criteria: clinically diagnosed and microbiologically confirmed scabies
	Exclusion criteria: significant impetiginization

Amer 1992 *(Continued)*

Interventions	1. 5% permethrin (50 participants) 2. 10% crotamiton (50 participants) 3. 1% lindane (50 participants) Each medication applied "neck to toe" on 2 successive nights
Outcomes	1. Number of participants clinically cured (no new lesions and all original lesions healed) at 28 days
Notes	Location: Egypt Date: not stated Colour photographs used for comparison before and after treatment

Amerio 2003

Methods	Design: randomized controlled trial Generation of allocation sequence: computer generated Allocation concealment: phone call-based procedure Blinding: investigators only Inclusion of randomized participants in the analysis: 100%
Participants	Number: 40 enrolled (mean age 44, standard deviation 17; 19 males, 21 females) Inclusion criteria: immunocompetent; aged 18 to 75; microscopically confirmed uncomplicated scabies Exclusion criteria: HIV positive; severe renal failure; liver insufficiency; acute or chronic leukaemia; lymphoma; use of antiscabietic preparations in previous 30 days; pregnancy; breastfeeding
Interventions	1. 5% permethrin cream (20 participants) 2. 0.16% natural pyrethrins synergized with pyperonil butoxide (1.65%) in thermolabile foam ("Milice", Mipharm, Italy) (20 participants) Both medications applied to entire body surface except head for 8 h overnight on 2 consecutive days, and then same treatment repeated after 14 days
Outcomes	1. Number of participants with clearance of lesions at 4 weeks 2. Number of participants with complete relief of itching at 4 weeks Not included in this review: 3. Number of participants with clearance of lesions at 2 weeks 4. Number of participants with complete relief of itching at 2 weeks 5. Clinical grading score (semi-quantitative measure of numbers of lesions) at 2 and 4 weeks 6. Itching score at 2 and 4 weeks 7. Numbers of days taking antihistamine drugs 8. Numbers of participants with secondary skin infection
Notes	Location: Italy Date: March 2001 to October 2001 Trial supported by unrestricted grant from Mipharm SpA

Avila-Romay 1991

Methods	Design: randomized controlled trial
	Generation of allocation sequence: "randomly assigned"
	Allocation concealment: unclear
	Blinding: unclear
	Inclusion of randomized participants in the analysis: 100%
Participants	Number: 51 cases and 60 contacts enrolled (children 6 to 17 years old; sex not stated)
	Inclusion criteria: clinically compatible lesions associated with itching
	Exclusion criteria: secondary infection
Interventions	1. 10% sulfur in pork fat with 1% salicylic acid as preservative (25 cases and 28 contacts) 2. 10% sulfur in cold cream (26 cases and 32 contacts)
	Both medications applied nightly for 3 nights then once 3 nights later, average dose 7 g
	Both medications applied by the patients from shoulders to feet for about 5 minutes, under supervision of a physician
Outcomes	1. Number of participants clinically cured at 10 days (defined as absence of cutaneous lesions and itching) 2. Secondary cutaneous reactions in cases and contacts
	Not included in this review: 3. Patient preference (not further defined)
Notes	Location: Mexico; participants from a house for orphan children
	Date: not stated
	60 contacts also randomly assigned to treatment with sulfur in either pork fat or cold cream

Bachewar 2009

Methods	Design: randomized controlled trial
	Generation of allocation sequence: computer generated
	Allocation concealment: unclear
	Blinding: none
	Inclusion of randomized participants in the analysis: 78% (23/103 lost to follow up)
Participants	Number: 103 enrolled (aged over 12; 63 males, 40 females)
	Inclusion criteria: clinically diagnosed scabies
	Exclusion criteria: pregnancy; lactation; women of child bearing age; abnormal liver or kidney function; thyroid disease; cardiac disorders; nervous system disorders; psychiatric illness; diabetes mellitus; hypertension; chronic infectious disease; any concurrent medication; consuming tobacco, alcohol, or any substance of abuse; any other associated skin disease which could alter the picture of scabies; known/suspected immunocompromised individuals; having scabies with atypical presentations including crusted scabies and scabies incognito; any antiscabetic treatment in the preceding week; non-compliant participants.

Bachewar 2009 *(Continued)*

Interventions	1. 25% benzyl benzoate lotion applied to whole body below neck and left overnight, on 2 consecutive nights (35 participants)
	2. 5% permethrin cream applied to whole body below neck and left overnight (34 participants)
	3. Oral ivermectin 200 µg/kg bodyweight single dose (34 participants)
	Not included in this review:
	4. Second topical application of 25% benzyl benzoate lotion at 1 week for treatment failures in intervention group 1 (benzyl benzoate)
	5. Second topical application of 5% permethrin cream at 1 week for treatment failures in intervention group 2 (permethrin)
	6. Second dose of oral ivermectin at 1 week for treatment failures in intervention group 3 (ivermectin)
Outcomes	1. Number of participants cured at 1 week (defined as absence of new papules, vesicles or classical burrows)
	2. Adverse events
	Not included in this review:
	3. Number of participants cured at 2 weeks (defined as absence of new papules, vesicles or classical burrows)
	4. Itching recorded on visual analogue scale
Notes	Location: Nagpur, India
	Date: March to July 2007
	All family members and close contacts treated at same time as the participant with 25% benzyl benzoate lotion

Biele 2006

Methods	Design: randomized controlled trial
	Generation of allocation sequence: computer generated
	Allocation concealment: unclear
	Blinding: investigators
	Inclusion of randomized participants in the analysis: 100%
Participants	Number: 240 enrolled (aged 18 to 75 years, mean age 31 years (pyrethrin group) and 30 years (benzyl benzoate); males only)
	Inclusion criteria: clinically diagnosed and microscopically confirmed scabies
	Exclusion criteria: treatment for scabies within previous 15 days; renal failure (plasma creatinine > 2.5 mg/dL); liver insufficiency (alanine aminotransferase or aspartate aminotransferase > 3 upper normal limit); acute or chronic leukaemia or lymphoma
Interventions	1. 10% benzyl benzoate lotion ("SCAB", PentaMedical, Milan, Italy), topical application on 5 consecutive days (120 participants)
	2. 0.165% natural pyrethrins synergized with pyperonil butoxide (1.65%) in thermolabile foam ("Milice", Mipharm, Italy), topical application on 3 consecutive days (120 participants)

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Biele 2006 *(Continued)*

Both treatments were applied to all skin surfaces from scalp to soles of feet

Treatment was repeated after 2 weeks if participant was not considered clinically cured

Outcomes	1. Number of participants clinically cured at 4 weeks 2. Number of participants with relief of itching at 4 weeks 3. Adverse events Not included in this review: 4. Number of participants with clearance of lesions at 2 weeks 5. Clinical grading score (semi-quantitative measure of numbers of lesions) at 4 weeks 6. Itching score at 4 weeks
Notes	Location: Italy Date: October 2003 to July 2004

Brooks 2002

Methods	Design: randomized controlled trial Generation of allocation sequence: computer generated Allocation concealment: unclear Blinding: investigators Inclusion of randomized participants in the analysis: 73% (30/110 lost to follow up)
Participants	Number: 110 enrolled (children 6 months to 14 years old; sex not stated) Inclusion criteria: clinically diagnosed scabies Exclusion criteria: treatment for scabies within previous 2 months; major intercurrent illness; history of meningitis or neurological illness
Interventions	1. Oral ivermectin 200 µg/kg bodyweight single dose (55 participants) 2. 10% benzyl benzoate applied neck to toe overnight (55 participants)
Outcomes	1. Number of participants clinically cured at 3 weeks (defined as absence of skin lesions) 2. Number of participants with persistence of night-time itch at 3 weeks 3. Adverse events Not included in this review 4. Itch severity 5. Numbers of lesions
Notes	Location: Vanuatu Date: January to April 2001 Family contacts treated with same drug as the participant Author confirmed equal numbers of participants randomized to each intervention

Chouela 1999

Methods	Design: randomized controlled trial

Chouela 1999 *(Continued)*

Generation of allocation sequence: unclear

Allocation concealment: unclear

Blinding: participants (study described as double blind)

Inclusion of randomized participants in the analysis: 81% (10/53 participants lost to follow up or withdrew)

Participants	Number: 53 enrolled (aged over 18 years with a mean age of 40.8 years; 19 males, 34 females)
	Inclusion criteria: clinical or parasitological signs compatible with scabies
	Exclusion criteria: pregnancy; breastfeeding; treatment for scabies within previous 4 weeks; renal dysfunction; hepatic dysfunction; concomitant antidepressant; anxiolytic or antipruritic drug use; severe immunodeficiency; HIV infection; clinically high risk for HIV; neoplasia affecting immunity; immunosuppressive treatment; gastrointestinal dysfunction; history of convulsions
Interventions	1. Single dose of oral ivermectin, 150 to 200 μg/kg in 6 mg tablets plus single topical application of 60 mL placebo solution (26 participants) 2. Single topical application of 60 mL 1% lindane topical solution plus placebo tablets (27 participants)
	Both placebo and 1% lindane solutions applied neck to toe and kept on for 8 h
	Not included in this review: 3. Second dose of oral ivermectin, 150 to 200 μg/kg in 6 mg tablets plus single topical application of 60 mL placebo solution at 15 days for treatment failures in intervention group 1 (ivermectin) 4. Second topical application of 60 mL 1% lindane topical solution plus placebo tablets at 15 days for treatment failures in intervention group 2 (lindane)
Outcomes	1. Number of participants cured at 15 days (defined as absence of pruritus and clinical lesions or a reduction of signs and symptoms to a score of 1 (mild pruritus and mild lesions)) 2. Adverse events
	Not included in this review 3. Number of participants receiving second dose at 15 days who were cured at 29 days
Notes	Location: Argentina
	Date: April 1996 to February 1997
	Members of the same household who were infested but could not be included in the study treated with 1% lindane (adults) or 6% sulfur cream (infants)

Glaziou 1993

Methods	Design: randomized controlled trial
	Generation of allocation sequence: "randomly allocated"
	Allocation concealment: unclear
	Blinding: outcomes assessor
	Inclusion of randomized participants in the analysis: 100%
Participants	Number: 44 enrolled (aged 5 to 56 years, mean 17.5 years; 23 males, 21 females)
	Inclusion criteria: clinically diagnosed scabies defined as the association of pruritus with at least 1 classical burrow

Glaziou 1993 *(Continued)*

	Exclusion criteria: other disease; pregnancy; abnormal physical examination (except for cutaneous lesions); abnormal laboratory screen; refused consent
Interventions	1. Oral ivermectin 100 μg/kg bodyweight single dose (23 participants) 2. 10% benzyl benzoate applied to entire body except head on 3 occasions 12 h apart (21 participants)
Outcomes	1. Number of participants clinically cured at 30 days (defined as complete disappearance of initial lesions and pruritus) 2. Adverse events Not included in this review: 3. Number of participants clinically cured at 7 days 4. Number of participants clinically cured at 14 days 5. Mean clinical score (based on number and activity of lesions)
Notes	Location: French Polynesia Date: 1992 All household contacts treated at same time as the participant with 10% benzyl benzoate Merck Sharp and Dohme supplied the ivermectin tablets at no cost

Gulati 1978

Methods	Design: randomized controlled trial Generation of allocation sequence: "cases ... divided at random" Allocation concealment: unclear Blinding: unclear Inclusion of randomized participants in the analysis: 100%
Participants	Number: 158 enrolled (mean age 16.6 years; 75 males, 83 females) Inclusion criteria: clinical diagnosis of scabies Exclusion criteria: none stated
Interventions	1. 25% benzyl benzoate emulsion (89 participants) 2. Sulfur ointment (69 participants) Both medications "applied all over the body after a thorough scrub bath with soap and water once in the morning, then again at night and again the next morning" Treatments were repeated in those whose lesions persisted after the 10th day
Outcomes	1. Number of participants with clinically assessed "clearance of lesions" at 15 days Not included in this review: 2. Numbers of participants with clearance of lesions at 3 to 5, 6 to 8, 9 to 11, and 12 to 14 days 3. Number of days until clearance of lesions
Notes	Location: India Date: not stated Family contacts treated concurrently with same drug as the participant

Gulati 1978 *(Continued)*

33% of participants had secondarily infected lesions

Prevalence of scabies in this study was 158/1727 (9.1%)

Hansen 1986

Methods	Design: randomized controlled trial
	Generation of allocation sequence: unclear
	Allocation concealment: unclear
	Blinding: unclear, "single blind"
	Inclusion of randomized participants in the analysis: 95% (5/104 lost to follow up)
Participants	Number: 104 enrolled (aged 2 to 71 years)
	Inclusion criteria: clinical and/or microscopic diagnosis of scabies
	Exclusion criteria: none stated
Interventions	1. 1% lindane lotion (50 participants) 2. 5% permethrin lotion (49 participants)
	Both medications applied as a single application
Outcomes	1. Number of participants with absence of lesions at 28 days 2. Number of participants with persistence of pruritus at 28 days 3. Adverse events
	Not included in this review: 4. Number of participants with absence of lesions at 14 days
Notes	Location: not stated
	Date: not stated
	Data taken from a conference abstract

Ly 2009

Methods	Design: randomized controlled trial
	Generation of allocation sequence: random number table
	Allocation concealment: unclear
	Blinding: none
	Inclusion of randomized participants in the analysis: 90% (19/181 lost to follow up)
Participants	Number: 181 enrolled (mean age 16.5 years; 116 males, 65 females)
	Inclusion criteria: clinical diagnosis of scabies
	Exclusion criteria: pruritus due to insect bites; chickenpox in participant or member of participant's family; treatment for scabies within previous month; under 5 years or over 65 years of age; weight less than 15 kg; pregnancy; breastfeeding; use of bleaching products for cosmetic purposes; crusted sca-

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Ly 2009 *(Continued)*

	bies; diabetes; hypertension; cardiovascular disease; neurological disease; living outside of Dakar district
Interventions	1. Oral ivermectin 150-200 µg/kg bodyweight single dose (65 participants)
	2. 12.5% benzyl benzoate to whole body except head (single application left on for 24 hours, 68 participants; two consecutive 24 hour applications, 48 participants)
	Not included in this review
	4. Second dose of oral ivermectin at 14 days for treatment failures in intervention group 1 (ivermectin)
	5. Second single application of 12.5% benzyl benzoate at 14 days for treatment failures in intervention group 2 (benzyl benzoate single application)
	6. Second double application of 12.5% benzyl benzoate at 14 days for treatment failures in intervention group 3 (benzyl benzoate double application)
Outcomes	1. Number of participants cured at 14 days (defined as complete disappearance of visible lesions and itching)
	2. Adverse events
	Not included in this review
	3. Number of participants cured at 28 days
	4. Number of participants with bacterial superinfection
	5. Compliance with medication regimen
Notes	Location: Dakar, Senegal
	Date: July 2003 to September 2004

Macotela-Ruiz 1993

Methods	Design: randomized controlled trial
	Generation of allocation sequence: unclear
	Allocation concealment: unclear
	Blinding: participants and outcomes assessor
	Inclusion of randomized participants in the analysis: 100%
Participants	Number: 55 enrolled (aged over 5 years;18 males mean age 25 +/- 4 years, 37 females mean age 24 +/- 16 years)
	Inclusion criteria: clinical diagnosis of scabies
	Exclusion criteria: pregnancy; breastfeeding; impaired renal function; impaired liver function; treatment for scabies within previous 3 weeks
Interventions	1. Oral ivermectin 200 µg/kg bodyweight single dose (29 participants)
	2. Placebo (26 participants)
Outcomes	1. Number of participants clinically cured at 7 days (defined as absence of itching and no dermatologically active lesions)

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Macotela-Ruiz 1993 *(Continued)*

	2. Adverse events
Notes	Location: Mexico
	Date: not stated
	Trial stopped at 7 days as ivermectin group significantly clinically better

Madan 2001

Methods	Design: randomized controlled trial
	Generation of allocation sequence: unclear
	Allocation concealment: unclear
	Blinding: outcomes assessor
	Inclusion of randomized participants in the analysis: 75% (50/200 lost to follow up)
Participants	Number: 200 enrolled (aged over 5 years; 132 males, 68 females)
	Inclusion criteria: clinical diagnosis of scabies (defined as nocturnal itching and/or family contact with similar complaint and/or typical lesions)
	Exclusion criteria: pregnancy; breastfeeding; severe cardiovascular, respiratory, or central nervous system disorders
Interventions	1. Oral ivermectin 200 µg/kg bodyweight single dose (100 participants) 2. 1% lindane lotion applied neck to toe and left on overnight (100 participants)
Outcomes	1. Number of participants clinically cured at 4 weeks (defined as no signs or symptoms of scabies) 2. Adverse events
	Not included in this review: 3. Number of participants clinically cured at 2 weeks 4. Number of patients with good improvement at 4 weeks
Notes	Location: India
	Date: not stated
	Microscopic confirmation of diagnosis in 170/200 (85%) of participants
	Family contacts treated with 25% benzyl benzoate lotion for 3 days

Maggi 1986

Methods	Design: randomized controlled trial
	Generation of allocation sequence: "randomly selected"
	Allocation concealment: unclear
	Blinding: unclear
	Inclusion of randomized participants in the analysis: 100%

Maggi 1986 *(Continued)*

Participants	Number: 87 enrolled (children, age range not stated)
	Inclusion criteria: scabies, not further explained
	Exclusion criteria: pyodermatitis
Interventions	1. 1% lindane suspension applied topically from chin to feet; 2 x 1-h applications 7 days apart (45 participants) 2. 1% lindane suspension applied topically from chin to feet; 2 series of 4 daily applications, 7 days apart (42 participants)
Outcomes	1. Number of participants with absence of pruritus at 14 days
	Not included in this review: 2. Number of participants with absence of pruritus at 7 days 3. Numbers of participants with excoriations or burrows at days 7 and 14
Notes	Location: Chile
	Date: March to November 1985

Nnoruka 2001

Methods	Design: randomized controlled trial
	Generation of allocation sequence: random-number table
	Allocation concealment: unclear
	Blinding: unclear
	Inclusion of randomized participants in the analysis: 100%
Participants	Number: 58 enrolled (aged 5 to 63 years, mean 27.9 years; 35 males, 33 females) Inclusion criteria: clinically diagnosed scabies (microbiologically confirmed in 43/58) Exclusion criteria: aged < 5 years
Interventions	1. Oral ivermectin 200 µg/kg bodyweight single dose (29 participants) 2. 25% benzyl benzoate emulsion applied neck to toe and left for 72 h (29 participants)
Outcomes	1. Number of participants clinically cured at 30 days (defined as complete disappearance of initial lesions and pruritus) 2. Adverse events
	Not included in this review: 3. Number of participants clinically cured at 7 days 4. Number of participants clinically cured at 14 days 5. Response of pruritus (graded on subjective scale) at 7, 14, and 30 days 6. Mean clinical score (based on number and activity of lesions)
Notes	Location: Nigeria
	Date: June 1998
	All household contacts treated at same time as the participant (treatment not stated)

Schenone 1986

Methods	Design: randomized controlled trial
	Generation of allocation sequence: unclear
	Allocation concealment: unclear
	Blinding: unclear
	Inclusion of randomized participants in the analysis: 100%
Participants	Number: 127 enrolled (aged 4 to 19 years; 53 males, 74 females)
	Inclusion criteria: clinical diagnosis of scabies
	Exclusion criteria: none stated
Interventions	1. 40 mL of 0.02% decamethrin lotion, applied everywhere except skull and face, daily for 2 days, and repeated on 2 more days 1 week later (53 participants) 2. 40 mL of 0.02% decamethrin lotion, applied everywhere except skull and face, daily for 4 days (74 participants)
Outcomes	1. Number of participants clinically cured at 21 days (defined as no active lesions)
Notes	Location: Chile (18 boarding schools in Santiago)
	Date: 1985
	Prevalence amongst boarding school children (aged 4 to 19): 127/868 (14.6%)
	Contacts treated with single dose of 0.02% decamethrin

Schultz 1990

Methods	Design: randomized controlled trial
	Generation of allocation sequence: unclear
	Allocation concealment: medication supplied to each trial centre in identical coded boxes
	Blinding: outcomes assessor
	Inclusion of randomized participants in the analysis: 87% (63/467 participants not analysed (for primary outcome))
Participants	Number: 467 enrolled (aged 2 months to 75 years, mean age 22.1 years; 297 males, 170 females)
	Inclusion criteria: clinical diagnosis of scabies
	Exclusion criteria: pregnancy; breastfeeding; treatment with ectoparasiticide within previous 3 weeks; renal impairment; hepatic impairment; known allergy to permethrin or lindane
Interventions	1. 5% permethrin cream applied to entire body below ears, single application (234 participants) 2. 1% lindane lotion applied from neck down, single application (233 participants)
Outcomes	1. Number of participants clinically cured at 28 +/- 7 days (defined as all original lesions healed and no new lesions) 2. Number of participants with persistence of itch 3. Adverse events
	Not included in this review:

Schultz 1990 *(Continued)*

	4. Number of participants clinically cured at 14 +/- 3 days 5. Number of microbiologically confirmed cases clinically cured
Notes	Location: USA and Mexico (4 sexually transmitted diseases clinics, 2 dermatology clinics, and 2 family practice clinics, 1 of which was in Mexico and all others in USA) Date: not stated Personal contacts of 85% of participants provided with 1% lindane for their use Study supported in part by a grant from Burroughs Wellcome (manufacturers of permethrin) who also provided statistical assistance

Singalavanija 2003

Methods	Design: randomized controlled trial Generation of allocation sequence: random-number table Allocation concealment: unclear Blinding: unclear Inclusion of randomized participants in the analysis: 68% (32/100 participants lost to follow up)
Participants	Number: 100 enrolled (aged 6 months to 13 years; 60 males, 40 females) Inclusion criteria: clinically diagnosed and microbiologically confirmed scabies Exclusion criteria: resident in an orphanage; serious central nervous system illness; malnutrition; immunodeficiency
Interventions	1. 10% sulfur ointment (50 participants) 2. 0.3% lindane gel (50 participants) Both medications applied neck to toe by parents for 7 consecutive nights
Outcomes	1. Number of participants clinically cured (no new lesions and healing of all old lesions) at 4 weeks 2. Number of participants with decrease or absence of itching at 4 weeks 3. Adverse events Not included in this review: 4. Number of participants clinically cured at 2 weeks (defined as no new lesions and healing of all old lesions) 5. Number of participants with decrease or absence of itching at 2 weeks 6. Number of participants with absence of parasites on skin scraping at 2 and 4 weeks
Notes	Location: Thailand Date: December 1999 to May 2000 Contacts treated with either 25% benzyl benzoate (adults) or 10% sulfur (children)

Taplin 1986

Methods	Design: randomized controlled trial Generation of allocation sequence: "randomized code"

Taplin 1986 *(Continued)*

Allocation concealment: identical coded medication tubes; codes held by sponsor

Blinding: investigators

Inclusion of randomized participants in the analysis: 98% (1/52 participant lost to follow up)

Participants	Number: 52 enrolled (aged 2 to 40 years, mean age 9 years; 22 males, 29 females, 1 gender not stated) Inclusion criteria: clinically diagnosed scabies (confirmed microscopically in 46/52 cases) Exclusion criteria: unwell; febrile; taking any medication; treatment with pediculicides, scabicides, or other topical agent in previous 3 months
Interventions	1. 5% permethrin cream (27 participants) 2. 1% lindane lotion (25 participants) Both medications applied as a single application head to toe
Outcomes	1. Number of participants with no new lesions and healing of all original lesions at 1 month 2. Adverse events Not included in this review: 3. Number of participants with no new lesions and healing of all original lesions at 2 weeks
Notes	Location: Panama Date: not stated All family contacts treated with 1% lindane lotion Photographs taken before and after treatment and distribution of any lesions noted on diagrams Study supported in part by a grant from Burroughs Wellcome (manufacturers of permethrin)

Taplin 1990

Methods	Design: randomized controlled trial Generation of allocation sequence: unclear Allocation concealment: "medications supplied in identical … tubes that were coded and randomized" Blinding: investigators Inclusion of randomized participants in the analysis: 98% (2/96 participants lost to follow up)
Participants	Number: 96 enrolled (aged 2 months to 5 years; 42 males, 54 females) Inclusion criteria: clinical diagnosis and the recovery of at least 1 live mite Exclusion criteria: none stated
Interventions	1. 10% crotamiton cream (48 participants) 2. 5% permethrin cream (48 participants) Both medications applied as single application from head to toe and left for 8 to 10 h
Outcomes	1. Number of participants with no new lesions and all original active lesions healed at 28 days 2. Number of participants with persistence of pruritus at 28 days 3. Adverse events

Taplin 1990 *(Continued)*

	Not included in this review: 4. Number of participants with no new lesions and all original active lesions healed at 14 days 5. Number of participants with persistence of pruritus at 14 days
Notes	Location: Panama Date: 1985 Household contacts were treated with 5% permethrin cream 65/96 (68%) participants had secondary cutaneous infection Study supported in part by a grant from Burroughs Wellcome (manufacturers of permethrin)

Usha 2000

Methods	Design: randomized controlled trial Generation of allocation sequence: computer-generated random-number table Allocation concealment: investigators did not take part in allocation Blinding: none Inclusion of randomized participants in the analysis: 100%
Participants	Number: 88 enrolled (aged over 5 years with a mean age of 21.3 years (ivermectin) and 22.4 years (permethrin); 59 males, 26 females) Inclusion criteria: clinical diagnosis (3 out of burrow/lesions in classical sites/nocturnal itch/family history) or microscopic diagnosis Exclusion criteria: pregnancy; breastfeeding; treatment for scabies within previous 1 month; serious central nervous system, hepatic, cardiac, or renal disease
Interventions	1. Oral ivermectin 200 µg/kg bodyweight single dose (43 participants) 2. 5% permethrin cream applied topically overnight (45 participants) Not included in this review 3. Second dose of oral ivermectin, 200 µg/kg for treatment failures in intervention group 1 (12 participants) 4. Second topical application 5% permethrin cream for treatment failures in intervention group 2 (1 participant)
Outcomes	1. Number of participants clinically cured at 2 weeks (defined as symptom improvement) 2. Adverse events Not included is this review: 3. Number of participants clinically cured at 1, 4, and 8 weeks
Notes	Location: India Date: August 1996 to December 1997 Contacts treated with same drug as the index case, except contacts who were children under 5 or pregnant women; these were treated with 12.5% to 25% benzyl benzoate emulsion Author confirmed randomization method and blinding 3 participants in ivermectin group withdrawn due to using additional treatment

Zargari 2006

Methods	Design: randomized controlled trial
	Generation of allocation sequence: unclear
	Allocation concealment: "drugs ... packaged in identical appearing tubes and randomized and coded by the manufacturer"
	Blinding: participants and investigators
	Inclusion of randomized participants in the analysis: 84.6% (18/117 lost to follow up)
Participants	Number: 117 enrolled (aged 6 to 64 years, mean age 30.2 years +/- 15.3; 55 males and 44 females followed up)
	Inclusion criteria: clinically diagnosed scabies (defined as burrow or typical lesions at classical sites plus nocturnal pruritus plus similar symptoms in contacts) and/or microscopically diagnosed scabies (demonstration of egg, larvae, mite, or faecal material)
	Exclusion criteria: < 5 years of age; treatment with antiscabietic medication or topical steroid in previous 4 weeks; pregnancy; breastfeeding; severe central nervous system, hepatic, or renal problems
Interventions	1. 5% permethrin cream (59 participants) 2. 1% lindane cream (58 participants)
	Both medications applied as a single application head to toe, and repeated 1 week later
Outcomes	1. Number of participants with no new lesions and improvement in itching at 14 days 2. Adverse events
Notes	Location: Iran
	Date: December 2002 to October 2003
	Treatment advised for all family members and close contacts
	Study supported by Gilaranco Company (manufacturers of permethrin and lindane)

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

Study	Reason for exclusion
Abedin 2007	Non-randomized study
Alebiosu 2003	Allocation method inadequate; expressed preference of participants for different interventions taken into account
Amer 1981	Non-randomized study
Bockarie 2000	Non-controlled study
Burgess 1986	Non-randomized study
Cannon 1948	Non-controlled study
Chowdhury 1977	Non-controlled study

Study	Reason for exclusion
Cubela 1978	Non-randomized study
Curiati 1984	Non-randomized study
Damodaran 1979	A trial of iron and folic acid supplementation
Daneshpajooh 2000	Unclear if randomized
Dika 2006	Non-controlled study
Dourmishev 1998	Non-controlled study
Dunne 1991	Study participants selected on basis of having onchocerciasis rather than scabies
Gallegos 1996	Thesis unavailable
Gordon 1944	Non-randomized study
Grabner 1970	Non-randomized study
Hamm 2006	Non-controlled study
Hanna 1978	Non-controlled study
Haustein 1989	Non-randomized study
Henderson 1991	Non-randomized study
Henderson 1992	Non-randomized study
Kar 1994	Case study
Kaur 1980	Non-randomized study
Kenawi 1993	Non-randomized study
Khan 2007	Non-randomized study
Konstantinov 1979	Non-randomized study
Landegren 1979	Non-randomized study
López 2003	Non-randomized study
Macotela-Ruiz 1996	Not truly randomized; unbalanced groups
Mapar 2008	Non-randomized study
Meinking 1995b	Non-controlled study
Mellanby 1945	Non-randomized study
Mozgunov 1978	Non-controlled study
Nag 1995	Non-randomized study

Study	Reason for exclusion
Neto 1984	Non-randomized study
Oberoi 2007	Non-randomized study; cure not assessed
Oladimeji 2000	Participants randomized to 1 of 3 treatments (lippia oil, benzyl benzoate, or liquid paraffin) but no clear randomization within these groups to 36 separate treatment schedule subgroups
Oladimeji 2005	Trial design inadequate with control group consisting of participants excluded from intervention arms
Oyelami 2009	Non-controlled study
Paasch 2000	Non-randomized study
Paschoal 1985	Not a trial of scabies treatment effectiveness
Pierce 1951	Non-randomized study
Regis 2003	Outcome is reinfestation not treatment failure
Reid 1990	Non-controlled study
Sehgal 1972	No assessment of any outcomes were reported
Srinivas 1996	Randomization unclear; comparison of lindane applied by bath, paint brush, and spray
Srivastava 1980	Allocation made on a "random basis and on availability of drugs"
Sule 2007	Non-randomized study
Suvanprakorn 1987	Non-controlled study
Taplin 1983a	Non-randomized study
Taplin 1983b	Non-controlled study
Taplin 1991	Non-controlled study
Tausch 1999	Comparison between 2 different brands of the same drug (10% crotamiton lotion)
Thianprasit 1984	Non-controlled study
Woolridge 1948	Non-controlled study
Yonkonsky 1990	Non-controlled study

Characteristics of ongoing studies [ordered by study ID]

Naeyaert ongoing

Trial name or title	"A randomised, double blind, double dummy study to compare the efficacy and safety of a single administration of ivermectin to a single administration of permethrin for the treatment of scabies"

Naeyaert ongoing *(Continued)*

Methods	—
Participants	Expected enrolment: 160 Minimum age: 5 years Both genders Inclusion criteria: at least 1 of scabies tunnels or positive microscopic examination (acarids, faeces, or ova); at least two of non-specific injuries with a typical distribution pattern, serious itching which increases during the night, or family or contacts with similar complaints Exclusion criteria: treatment for scabies < 4 weeks ago; treatment with corticoids < 1 week ago; pregnancy; breastfeeding; HIV; serious immunodepressive patients; sensitivity or allergy to 1 of the components of the study medication; damage of the central nerve system
Interventions	Administration of ivermectin or permethrin on day 0
Outcomes	Primary: clinical healing of the skin injuries on day 28 Secondary: decrease of itching on day 28; amelioration of the life quality on day 28; number and gravity of adverse events
Starting date	July 2004
Contact information	Jean-Marie Naeyaert, Principal Investigator, University Hospital Ghent, Ghent 9000, Belgium
Notes	ClinicalTrials.gov identifier: NCT00262418

DATA AND ANALYSES

Comparison 1. Ivermectin versus placebo

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Treatment failure in clinically diagnosed cases	1		Risk Ratio (M-H, Fixed, 95% CI)	Totals not selected
1.1 200µg/kg Ivermectin vs placebo. Follow up at 7 days	1		Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]

Analysis 1.1. Comparison 1 Ivermectin versus placebo, Outcome 1 Treatment failure in clinically diagnosed cases.

Study or subgroup	Ivermectin n/N	Placebo n/N	Risk Ratio M-H, Fixed, 95% CI	Risk Ratio M-H, Fixed, 95% CI
1.1.1 200µg/kg Ivermectin vs placebo. Follow up at 7 days				
Macotela-Ruiz 1993	6/29	22/26		0.24[0.12,0.51]

Favours ivermectin 0.01 0.1 1 10 100 Favours placebo
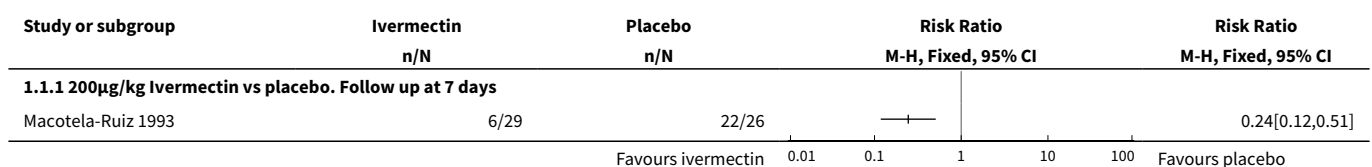
Comparison 2.   Ivermectin versus permethrin

Outcome or subgroup title	No. of studies	No. of partici-pants	Statistical method	Effect size
1 Treatment failure in clinically diagnosed cas-es	2		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
1.1 200µg/kg Ivermectin vs 5% Permethrin overnight.	2	140	Risk Ratio (M-H, Fixed, 95% CI)	4.61 [2.07, 10.26]

Analysis 2.1.   Comparison 2 Ivermectin versus permethrin, Outcome 1 Treatment failure in clinically diagnosed cases.
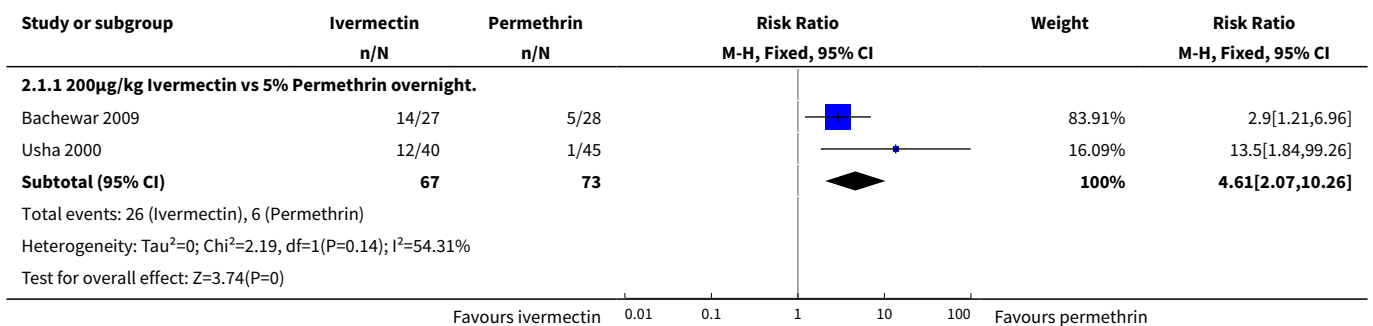
Study or subgroup	Ivermectin n/N	Permethrin n/N	Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
2.1.1 200µg/kg Ivermectin vs 5% Permethrin overnight.					
Bachewar 2009	14/27	5/28		83.91%	2.9[1.21,6.96]
Usha 2000	12/40	1/45		16.09%	13.5[1.84,99.26]
Subtotal (95% CI)	**67**	**73**		**100%**	**4.61[2.07,10.26]**
Total events: 26 (Ivermectin), 6 (Permethrin)					
Heterogeneity: Tau²=0; Chi²=2.19, df=1(P=0.14); I²=54.31%					
Test for overall effect: Z=3.74(P=0)					

Favours ivermectin   0.01   0.1   1   10   100   Favours permethrin

Comparison 3.   Ivermectin versus lindane

Outcome or subgroup title	No. of studies	No. of partici-pants	Statistical method	Effect size
1 Treatment failure in clinically diagnosed cases	2		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
1.1 150-200µg/kg Ivermectin vs 1% Lindane.	2	193	Risk Ratio (M-H, Fixed, 95% CI)	0.36 [0.23, 0.58]

Analysis 3.1.   Comparison 3 Ivermectin versus lindane, Outcome 1 Treatment failure in clinically diagnosed cases.

Study or subgroup	Ivermectin n/N	Lindane n/N	Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
3.1.1 150-200µg/kg Ivermectin vs 1% Lindane.					
Chouela 1999	5/19	11/24		19.02%	0.57[0.24,1.37]
Madan 2001	12/69	45/81		80.98%	0.31[0.18,0.54]
Subtotal (95% CI)	**88**	**105**		**100%**	**0.36[0.23,0.58]**
Total events: 17 (Ivermectin), 56 (Lindane)					
Heterogeneity: Tau²=0; Chi²=1.35, df=1(P=0.25); I²=25.85%					
Test for overall effect: Z=4.29(P<0.0001)					

Favours ivermectin   0.01   0.1   1   10   100   Favours lindane

Comparison 4. Ivermectin versus benzyl benzoate

Outcome or subgroup title	No. of studies	No. of partici-pants	Statistical method	Effect size
1 Treatment failure in clinically diagnosed cases	5		Risk Ratio (M-H, Fixed, 95% CI)	Totals not select-ed
1.1 200µg/kg Ivermectin vs 25% BB overnight x2. FU at 1 week	1		Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
1.2 150-200µg/kg Ivermectin vs 12.5% BB 1 or 2 overnights. FU at 14 days	1		Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
1.3 200µg/kg Ivermectin vs 10% BB overnight. FU at 3 weeks	1		Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
1.4 100µg/kg Ivermectin vs 10% BB 3 x 12 hrs. FU at 30 days	1		Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
1.5 200µg/kg Ivermectin vs 25% BB 72 hrs. FU at 30 days	1		Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
2 Itch persistence	1		Risk Ratio (M-H, Fixed, 95% CI)	Totals not select-ed
2.1 200µg/kg Ivermectin vs 10% BB overnight. FU at 3 weeks	1		Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]

Analysis 4.1. Comparison 4 Ivermectin versus benzyl benzoate, Outcome 1 Treatment failure in clinically diagnosed cases.

Study or subgroup	Ivermectin n/N	Benzyl benzoate n/N	Risk Ratio M-H, Fixed, 95% CI	Risk Ratio M-H, Fixed, 95% CI
4.1.1 200µg/kg Ivermectin vs 25% BB overnight x2. FU at 1 week				
Bachewar 2009	14/27	6/25		2.16[0.98,4.74]
4.1.2 150-200µg/kg Ivermectin vs 12.5% BB 1 or 2 overnights. FU at 14 days				
Ly 2009	38/54	38/108		2[1.47,2.72]
4.1.3 200µg/kg Ivermectin vs 10% BB overnight. FU at 3 weeks				
Brooks 2002	19/43	18/37		0.91[0.57,1.46]
4.1.4 100µg/kg Ivermectin vs 10% BB 3 x 12 hrs. FU at 30 days				
Glaziou 1993	7/23	11/21		0.58[0.28,1.22]
4.1.5 200µg/kg Ivermectin vs 25% BB 72 hrs. FU at 30 days				
Nnoruka 2001	2/29	15/29		0.13[0.03,0.53]

Favours ivermectin 0.005 0.1 1 10 200 Favours benzyl benz.

Analysis 4.2. Comparison 4 Ivermectin versus benzyl benzoate, Outcome 2 Itch persistence.

Study or subgroup	Ivermectin	Benzyl benzoate	Risk Ratio	Risk Ratio
	n/N	n/N	M-H, Fixed, 95% CI	M-H, Fixed, 95% CI
4.2.1 200µg/kg Ivermectin vs 10% BB overnight. FU at 3 weeks				
Brooks 2002	10/33	14/25		0.54[0.29,1.01]

Favours ivermectin 0.01 0.1 1 10 100 Favours benzyl benz.

Comparison 5. Permethrin versus crotamiton

Outcome or subgroup title	No. of studies	No. of partici- pants	Statistical method	Effect size
1 Treatment failure in clinically diag- nosed cases	2		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
1.1 5% Permethrin vs 10% Crotamiton. FU at 28 days	2	194	Risk Ratio (M-H, Fixed, 95% CI)	0.24 [0.10, 0.55]
2 Treatment failure in microscopically di- agnosed cases	2		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
2.1 5% Permethrin vs 10% Crotamiton. FU at 28 days	2	194	Risk Ratio (M-H, Fixed, 95% CI)	0.24 [0.10, 0.55]
3 Itch persistence	1		Risk Ratio (M-H, Fixed, 95% CI)	Totals not select- ed
3.1 5% Permethrin vs 10% Crotamiton. FU at 28 days	1		Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]

Analysis 5.1. Comparison 5 Permethrin versus crotamiton, Outcome 1 Treatment failure in clinically diagnosed cases.

Study or subgroup	Permethrin	Crotamiton	Risk Ratio	Weight	Risk Ratio
	n/N	n/N	M-H, Fixed, 95% CI		M-H, Fixed, 95% CI
5.1.1 5% Permethrin vs 10% Crotamiton. FU at 28 days					
Amer 1992	1/50	6/50		24%	0.17[0.02,1.33]
Taplin 1990	5/47	19/47		76%	0.26[0.11,0.65]
Subtotal (95% CI)	**97**	**97**		**100%**	**0.24[0.1,0.55]**
Total events: 6 (Permethrin), 25 (Crotamiton)					
Heterogeneity: Tau²=0; Chi²=0.16, df=1(P=0.69); I²=0%					
Test for overall effect: Z=3.38(P=0)					

Favours permethrin 0.01 0.1 1 10 100 Favours crotamiton

Analysis 5.2. Comparison 5 Permethrin versus crotamiton, Outcome 2 Treatment failure in microscopically diagnosed cases.

Study or subgroup	Permethrin n/N	Crotamiton n/N	Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
5.2.1 5% Permethrin vs 10% Crotamiton. FU at 28 days					
Amer 1992	1/50	6/50		24%	0.17[0.02,1.33]
Taplin 1990	5/47	19/47		76%	0.26[0.11,0.65]
Subtotal (95% CI)	**97**	**97**		**100%**	**0.24[0.1,0.55]**
Total events: 6 (Permethrin), 25 (Crotamiton)					
Heterogeneity: Tau²=0; Chi²=0.16, df=1(P=0.69); I²=0%					
Test for overall effect: Z=3.38(P=0)					

Favours permethrin 0.01 0.1 1 10 100 Favours crotamiton

Analysis 5.3. Comparison 5 Permethrin versus crotamiton, Outcome 3 Itch persistence.

Study or subgroup	Permethrin n/N	Crotamiton n/N	Risk Ratio M-H, Fixed, 95% CI	Risk Ratio M-H, Fixed, 95% CI
5.3.1 5% Permethrin vs 10% Crotamiton. FU at 28 days				
Taplin 1990	5/47	19/47		0.26[0.11,0.65]

Favours permethrin 0.01 0.1 1 10 100 Favours crotamiton

Comparison 6. Permethrin versus lindane

Outcome or subgroup title	No. of studies	No. of partici-pants	Statistical method	Effect size
1 Treatment failure in clinically diagnosed cases	5		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
1.1 5% Permethrin vs 1% Lindane single application repeated at 1 week. FU at 14 days	1	99	Risk Ratio (M-H, Fixed, 95% CI)	0.15 [0.06, 0.40]
1.2 5% Permethrin vs 1% Lindane overnight x2. FU at 28 days	1	100	Risk Ratio (M-H, Fixed, 95% CI)	0.08 [0.01, 0.57]
1.3 5% Permethrin vs 1% Lindane single application. FU at 28 days	3	554	Risk Ratio (M-H, Fixed, 95% CI)	0.59 [0.37, 0.95]
2 Treatment failure in microscopically diagnosed cases	3		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
2.1 5% Permethrin vs 1% Lindane single application. FU at 28 days	2	384	Risk Ratio (M-H, Fixed, 95% CI)	0.57 [0.32, 1.02]
2.2 5% Permethrin vs 1% Lindane overnight x2. FU at 28 days	1	100	Risk Ratio (M-H, Fixed, 95% CI)	0.08 [0.01, 0.57]
3 Itch persistence	2		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only

Outcome or subgroup title	No. of studies	No. of partici- pants	Statistical method	Effect size
3.1 5% Permethrin vs 1% Lindane single appli- cation. FU at 28 days	2	490	Risk Ratio (M-H, Fixed, 95% CI)	0.61 [0.44, 0.86]

Analysis 6.1. Comparison 6 Permethrin versus lindane, Outcome 1 Treatment failure in clinically diagnosed cases.

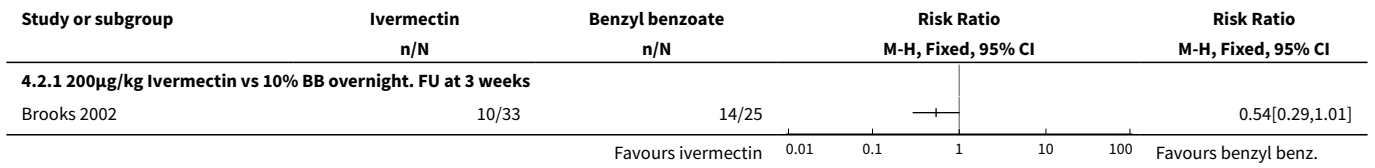| Study or subgroup	Permethrin n/N	Lindane n/N	Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
6.1.1 5% Permethrin vs 1% Lindane single application repeated at 1 week. FU at 14 days					
Zargari 2006	4/52	24/47		100%	0.15[0.06,0.4]
Subtotal (95% CI)	**52**	**47**		**100%**	**0.15[0.06,0.4]**
Total events: 4 (Permethrin), 24 (Lindane)					
Heterogeneity: Not applicable					
Test for overall effect: Z=3.78(P=0)					
6.1.2 5% Permethrin vs 1% Lindane overnight x2. FU at 28 days					
Amer 1992	1/50	13/50		100%	0.08[0.01,0.57]
Subtotal (95% CI)	**50**	**50**		**100%**	**0.08[0.01,0.57]**
Total events: 1 (Permethrin), 13 (Lindane)					
Heterogeneity: Not applicable					
Test for overall effect: Z=2.52(P=0.01)					
6.1.3 5% Permethrin vs 1% Lindane single application. FU at 28 days					
Hansen 1986	4/49	5/50		12.07%	0.82[0.23,2.86]
Schultz 1990	18/199	28/205		67.27%	0.66[0.38,1.16]
Taplin 1986	2/27	8/24		20.66%	0.22[0.05,0.95]
Subtotal (95% CI)	**275**	**279**		**100%**	**0.59[0.37,0.95]**
Total events: 24 (Permethrin), 41 (Lindane)					
Heterogeneity: Tau²=0; Chi²=2.17, df=2(P=0.34); I²=7.69%					
Test for overall effect: Z=2.18(P=0.03)					

Favours permethrin 0.01 0.1 1 10 100 Favours lindane

Analysis 6.2. Comparison 6 Permethrin versus lindane, Outcome 2 Treatment failure in microscopically diagnosed cases.

Study or subgroup	Permethrin n/N	Lindane n/N	Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
6.2.1 5% Permethrin vs 1% Lindane single application. FU at 28 days					
Schultz 1990	14/165	21/173		71.93%	0.7[0.37,1.33]
Taplin 1986	2/23	8/23		28.07%	0.25[0.06,1.05]
Subtotal (95% CI)	**188**	**196**		**100%**	**0.57[0.32,1.02]**
Total events: 16 (Permethrin), 29 (Lindane)					
Heterogeneity: Tau²=0; Chi²=1.65, df=1(P=0.2); I²=39.29%					
Test for overall effect: Z=1.9(P=0.06)					

Favours permethrin 0.01 0.1 1 10 100 Favours lindane

Study or subgroup	Permethrin n/N	Lindane n/N	Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
6.2.2 5% Permethrin vs 1% Lindane overnight x2. FU at 28 days					
Amer 1992	1/50	13/50		100%	0.08[0.01,0.57]
Subtotal (95% CI)	**50**	**50**		**100%**	**0.08[0.01,0.57]**
Total events: 1 (Permethrin), 13 (Lindane)					
Heterogeneity: Not applicable					
Test for overall effect: Z=2.52(P=0.01)					

Favours permethrin 0.01 0.1 1 10 100 Favours lindane

Analysis 6.3. Comparison 6 Permethrin versus lindane, Outcome 3 Itch persistence.

Study or subgroup	Permethrin n/N	Lindane n/N	Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
6.3.1 5% Permethrin vs 1% Lindane single application. FU at 28 days					
Hansen 1986	14/49	19/50		27.89%	0.75[0.43,1.33]
Schultz 1990	27/194	49/197		72.11%	0.56[0.37,0.86]
Subtotal (95% CI)	**243**	**247**		**100%**	**0.61[0.44,0.86]**
Total events: 41 (Permethrin), 68 (Lindane)					
Heterogeneity: Tau²=0; Chi²=0.67, df=1(P=0.41); I²=0%					
Test for overall effect: Z=2.81(P=0.01)					

Favours permethrin 0.01 0.1 1 10 100 Favours lindane

Comparison 7. Permethrin versus benzyl benzoate

Outcome or subgroup title	No. of studies	No. of partici-pants	Statistical method	Effect size
1 Treatment failure in clinically diagnosed cas-es	1		Risk Ratio (M-H, Fixed, 95% CI)	Totals not select-ed
1.1 5% Permethrin vs 25% BB overnight x2 FU at 1 week	1		Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]

Analysis 7.1. Comparison 7 Permethrin versus benzyl benzoate, Outcome 1 Treatment failure in clinically diagnosed cases.
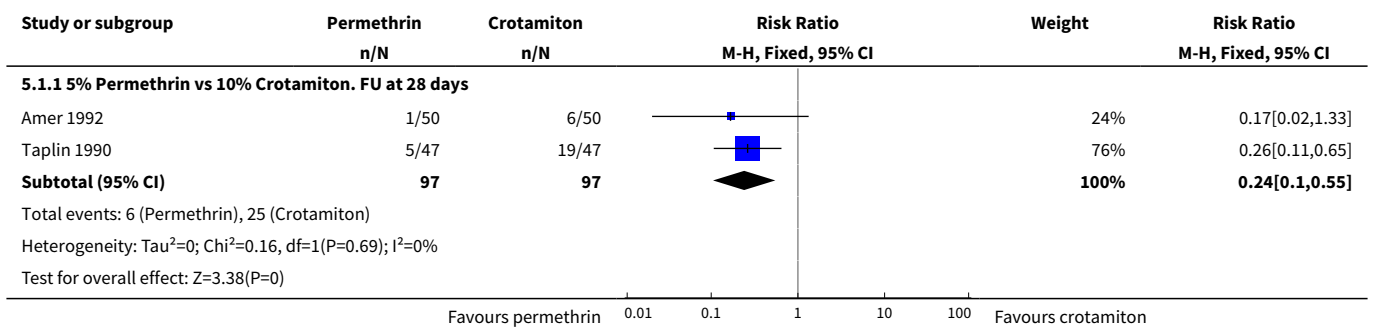
Study or subgroup	Permethrin n/N	Benzyl benzoate n/N	Risk Ratio M-H, Fixed, 95% CI	Risk Ratio M-H, Fixed, 95% CI
7.1.1 5% Permethrin vs 25% BB overnight x2 FU at 1 week				
Bachewar 2009	5/28	6/25		0.74[0.26,2.14]

Favours permethrin 0.01 0.1 1 10 100 Favours benzyl benz.

Comparison 8.   Permethrin versus natural synergized pyrethrins

Outcome or subgroup title	No. of studies	No. of partici-pants	Statistical method	Effect size
1 Itch persistence	1		Risk Ratio (M-H, Fixed, 95% CI)	Totals not select-ed
1.1 5% Permethrin vs 0.16% Pyrethrins for 8 hours x2. FU at 4 weeks	1		Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]

Analysis 8.1.   Comparison 8 Permethrin versus natural synergized pyrethrins, Outcome 1 Itch persistence.
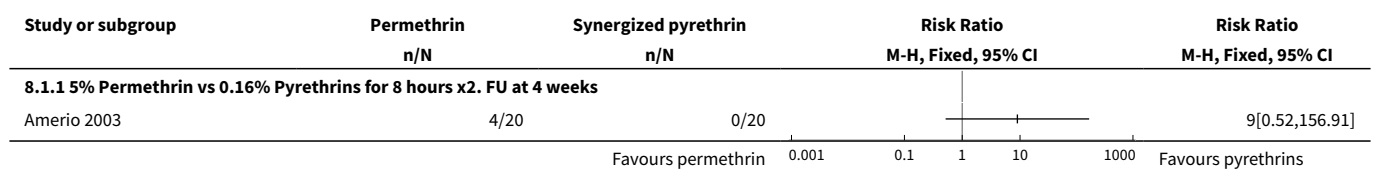
Study or subgroup	Permethrin n/N	Synergized pyrethrin n/N	Risk Ratio M-H, Fixed, 95% CI	Risk Ratio M-H, Fixed, 95% CI
8.1.1 5% Permethrin vs 0.16% Pyrethrins for 8 hours x2. FU at 4 weeks				
Amerio 2003	4/20	0/20		9[0.52,156.91]

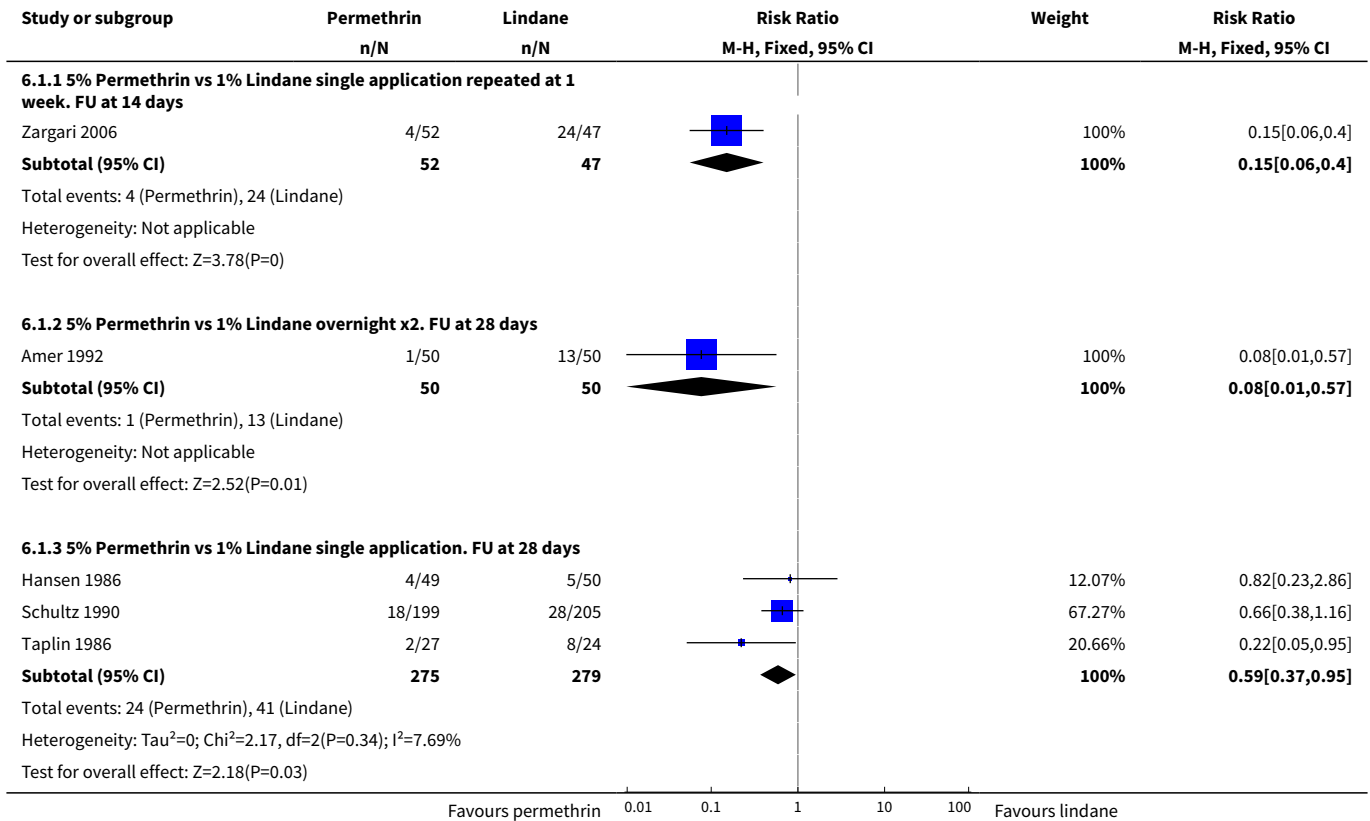Favours permethrin 0.001 0.1 1 10 1000 Favours pyrethrins

Comparison 9.   Crotamiton versus lindane

Outcome or subgroup title	No. of studies	No. of partici-pants	Statistical method	Effect size
1 Treatment failure in clinically diagnosed cas-es	1		Risk Ratio (M-H, Fixed, 95% CI)	Totals not select-ed
1.1 10% Crotamiton vs 1% Lindane overnight x2. FU at 28 days	1		Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
2 Treatment failure in microscopically diag-nosed cases	1		Risk Ratio (M-H, Fixed, 95% CI)	Totals not select-ed
2.1 10% Crotamiton vs 1% Lindane overnight x2. FU at 28 days	1		Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]

Analysis 9.1.   Comparison 9 Crotamiton versus lindane, Outcome 1 Treatment failure in clinically diagnosed cases.

Study or subgroup	Crotamiton n/N	Lindane n/N	Risk Ratio M-H, Fixed, 95% CI	Risk Ratio M-H, Fixed, 95% CI
9.1.1 10% Crotamiton vs 1% Lindane overnight x2. FU at 28 days				
Amer 1992	6/50	13/50		0.46[0.19,1.12]

Favours crotamiton 0.1 0.2 0.5 1 2 5 10 Favours lindane
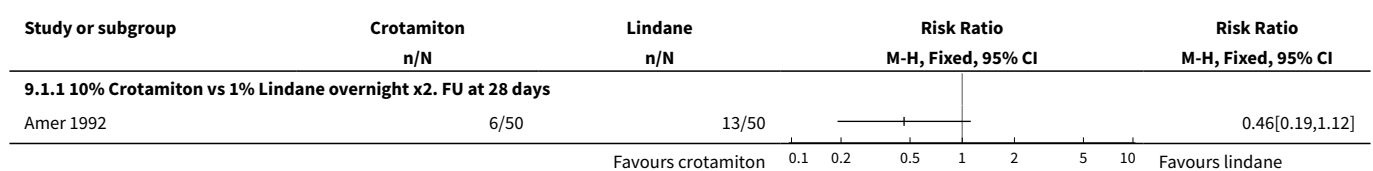
Analysis 9.2. Comparison 9 Crotamiton versus lindane, Outcome 2 Treatment failure in microscopically diagnosed cases.

Study or subgroup	Crotamiton n/N	Lindane n/N	Risk Ratio M-H, Fixed, 95% CI	Risk Ratio M-H, Fixed, 95% CI
9.2.1 10% Crotamiton vs 1% Lindane overnight x2. FU at 28 days				
Amer 1992	6/50	13/50		0.46[0.19,1.12]

Favours crotamiton 0.01 0.1 1 10 100 Favours lindane
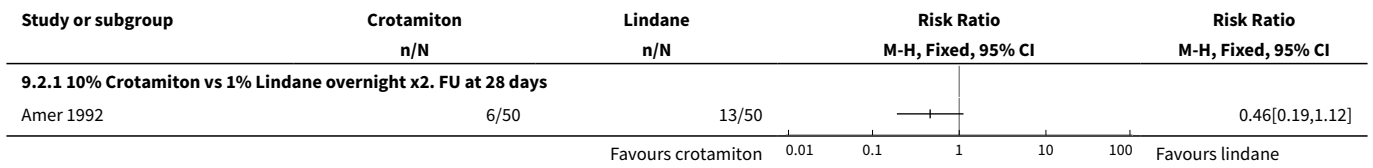
Comparison 10.   Lindane versus sulfur

Outcome or subgroup title	No. of studies	No. of partici-pants	Statistical method	Effect size
1 Treatment failure in clinically diagnosed cases	1		Risk Ratio (M-H, Fixed, 95% CI)	Totals not select-ed
1.1 0.3% Lindane gel vs 10% Sulfur overnight x7. FU at 4 weeks	1		Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
2 Itch persistence	1		Risk Ratio (M-H, Fixed, 95% CI)	Totals not select-ed
2.1 0.3% Lindane gel vs 10% Sulfur overnight x7. FU at 4 weeks	1		Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]

Analysis 10.1.   Comparison 10 Lindane versus sulfur, Outcome 1 Treatment failure in clinically diagnosed cases.

Study or subgroup	Lindane n/N	Sulfur n/N	Risk Ratio M-H, Fixed, 95% CI	Risk Ratio M-H, Fixed, 95% CI
10.1.1 0.3% Lindane gel vs 10% Sulfur overnight x7. FU at 4 weeks				
Singalavanija 2003	3/32	3/36		1.13[0.24,5.18]

Favours lindane 0.1 0.2 0.5 1 2 5 10 Favours sulfur
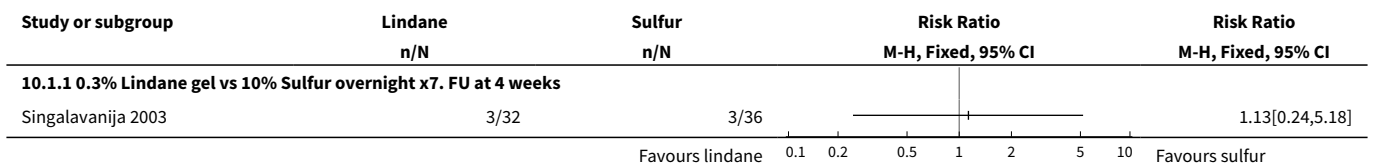
Analysis 10.2.   Comparison 10 Lindane versus sulfur, Outcome 2 Itch persistence.
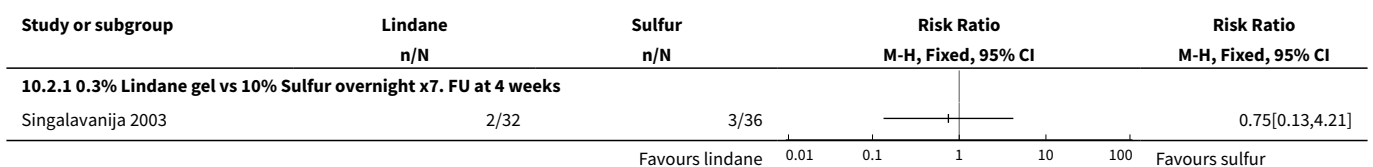
Study or subgroup	Lindane n/N	Sulfur n/N	Risk Ratio M-H, Fixed, 95% CI	Risk Ratio M-H, Fixed, 95% CI
10.2.1 0.3% Lindane gel vs 10% Sulfur overnight x7. FU at 4 weeks				
Singalavanija 2003	2/32	3/36		0.75[0.13,4.21]

Favours lindane 0.01 0.1 1 10 100 Favours sulfur

Comparison 11. Benzyl benzoate versus sulfur

Outcome or subgroup title	No. of studies	No. of partici-pants	Statistical method	Effect size
1 Treatment failure in clinically diagnosed cases	1		Risk Ratio (M-H, Fixed, 95% CI)	Totals not select-ed
1.1 25% BB vs Sulfur ointment 3 applications. FU at 15 days	1		Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]

Analysis 11.1. Comparison 11 Benzyl benzoate versus sulfur, Outcome 1 Treatment failure in clinically diagnosed cases.

Study or subgroup	Benzyl benzoate n/N	Sulfur n/N	Risk Ratio M-H, Fixed, 95% CI	Risk Ratio M-H, Fixed, 95% CI
11.1.1 25% BB vs Sulfur ointment 3 applications. FU at 15 days				
Gulati 1978	8/89	2/69		3.1[0.68,14.14]

Favours benzyl benz.   0.01   0.1   1   10   100   Favours sulfur
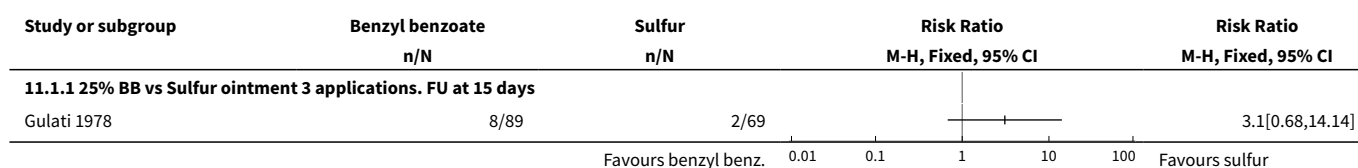
Comparison 12. Benzyl benzoate versus natural synergized pyrethrins

Outcome or subgroup title	No. of studies	No. of partici-pants	Statistical method	Effect size
1 Treatment failure in clinically diagnosed cases	1		Risk Ratio (M-H, Fixed, 95% CI)	Totals not select-ed
1.1 10% BB vs 0.16% Pyrethrins repeated af-ter 2 weeks. FU at 4 weeks	1		Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
2 Treatment failure in microscopically diag-nosed cases	1		Risk Ratio (M-H, Fixed, 95% CI)	Totals not select-ed
2.1 10% BB vs 0.16% Pyrethrins repeated af-ter 2 weeks. FU at 4 weeks	1		Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
3 Itch persistence	1		Risk Ratio (M-H, Fixed, 95% CI)	Totals not select-ed
3.1 10% BB vs 0.16% Pyrethrins repeated af-ter 2 weeks. FU at 4 weeks	1		Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]

Analysis 12.1. Comparison 12 Benzyl benzoate versus natural synergized pyrethrins, Outcome 1 Treatment failure in clinically diagnosed cases.

Study or subgroup	Benzyl benzoate n/N	Synergized pyrethrin n/N	Risk Ratio M-H, Fixed, 95% CI	Risk Ratio M-H, Fixed, 95% CI
12.1.1 10% BB vs 0.16% Pyrethrins repeated after 2 weeks. FU at 4 weeks				
Biele 2006	11/120	6/120		1.83[0.7,4.8]

Favours benzyl benz. 0.1 0.2 0.5 1 2 5 10 Favours pyrethrins
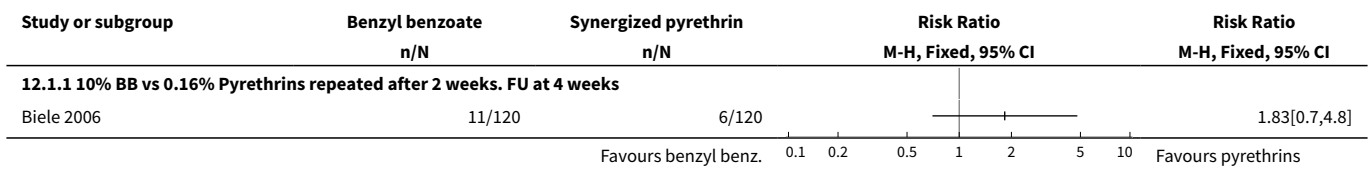
Analysis 12.2. Comparison 12 Benzyl benzoate versus natural synergized pyrethrins, Outcome 2 Treatment failure in microscopically diagnosed cases.

Study or subgroup	Benzyl benzoate n/N	Synergized pyrethrin n/N	Risk Ratio M-H, Fixed, 95% CI	Risk Ratio M-H, Fixed, 95% CI
12.2.1 10% BB vs 0.16% Pyrethrins repeated after 2 weeks. FU at 4 weeks				
Biele 2006	11/120	6/120		1.83[0.7,4.8]

Favours benzyl benz. 0.01 0.1 1 10 100 Favours pyrethrins
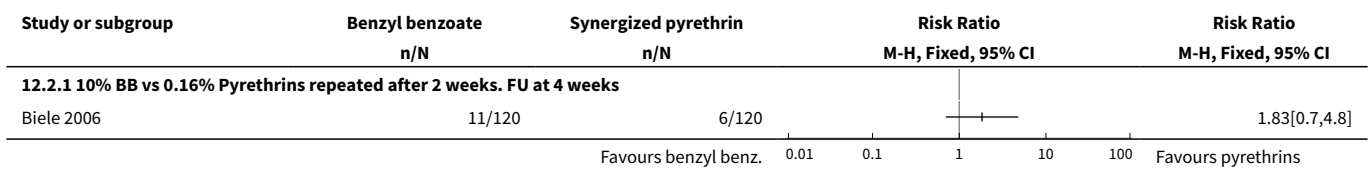
Analysis 12.3. Comparison 12 Benzyl benzoate versus natural synergized pyrethrins, Outcome 3 Itch persistence.

Study or subgroup	Benzyl benzoate n/N	Synergized pyrethrin n/N	Risk Ratio M-H, Fixed, 95% CI	Risk Ratio M-H, Fixed, 95% CI
12.3.1 10% BB vs 0.16% Pyrethrins repeated after 2 weeks. FU at 4 weeks				
Biele 2006	10/120	6/120		1.67[0.63,4.44]

Favours benzyl benz. 0.01 0.1 1 10 100 Favours pyrethrins
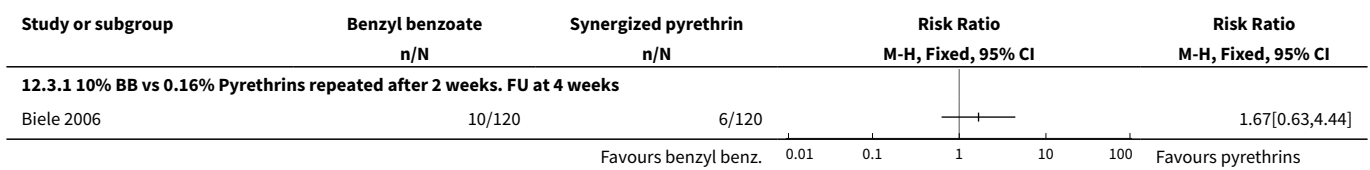
Comparison 13. Benzyl benzoate: one application versus two applications

Outcome or subgroup title	No. of studies	No. of partici-pants	Statistical method	Effect size
1 Treatment failure in clinically diagnosed cases	1		Risk Ratio (M-H, Fixed, 95% CI)	Totals not select-ed
1.1 12.5% BB overnight x1 vs 12.5% BB overnight x2. FU at 14 days	1		Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]

Analysis 13.1. Comparison 13 Benzyl benzoate: one application versus two applications, Outcome 1 Treatment failure in clinically diagnosed cases.

Study or subgroup	One application n/N	Two applications n/N	Risk Ratio M-H, Fixed, 95% CI	Risk Ratio M-H, Fixed, 95% CI
13.1.1 12.5% BB overnight x1 vs 12.5% BB overnight x2. FU at 14 days				
Ly 2009	23/60	15/48		1.23[0.72,2.08]

Favours one application 0.01 0.1 1 10 100 Favours two applications
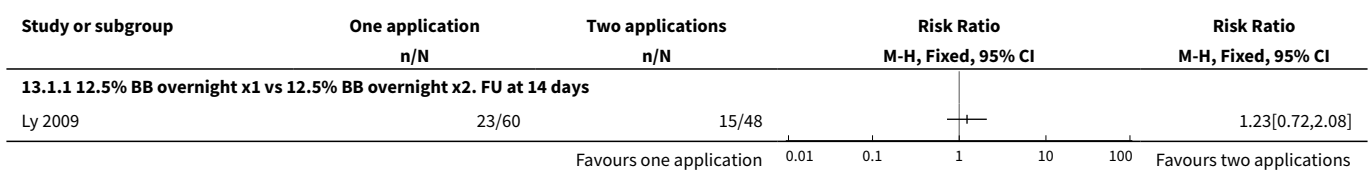
Comparison 14.   Lindane: short application versus long application

Outcome or subgroup title	No. of studies	No. of partici-pants	Statistical method	Effect size
1 Itch persistence	1		Risk Ratio (M-H, Fixed, 95% CI)	Totals not select-ed
1.1 1% Lindane 2x 1hr applications vs 2x 4 day applications. FU at 14 days	1		Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]

Analysis 14.1.   Comparison 14 Lindane: short application versus long application, Outcome 1 Itch persistence.

Study or subgroup	Short course lindane n/N	Long course lindane n/N	Risk Ratio M-H, Fixed, 95% CI	Risk Ratio M-H, Fixed, 95% CI
14.1.1 1% Lindane 2x 1hr applications vs 2x 4 day applications. FU at 14 days				
Maggi 1986	4/45	11/42		0.34[0.12,0.98]

Favours short course 0.1 0.2 0.5 1 2 5 10 Favours long course
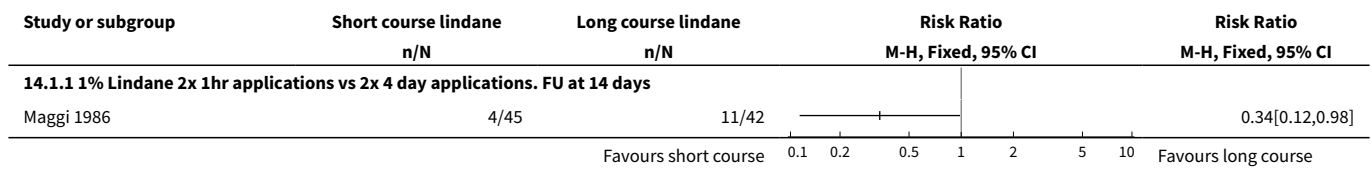
Comparison 15.   Sulfur: pork fat vehicle versus cold cream vehicle

Outcome or subgroup title	No. of studies	No. of partici-pants	Statistical method	Effect size
1 Treatment failure in clinically diagnosed cases	1		Risk Ratio (M-H, Fixed, 95% CI)	Totals not select-ed
1.1 10% Sulfur in pork fat vs 10% Sulfur in cold cream. FU at 10 days	1		Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]

Analysis 15.1.   Comparison 15 Sulfur: pork fat vehicle versus cold cream vehicle, Outcome 1 Treatment failure in clinically diagnosed cases.

Study or subgroup	Pork fat vehicle n/N	Cold cream vehicle n/N	Risk Ratio M-H, Fixed, 95% CI	Risk Ratio M-H, Fixed, 95% CI
15.1.1 10% Sulfur in pork fat vs 10% Sulfur in cold cream. FU at 10 days				
Avila-Romay 1991	3/25	0/26		7.27[0.39,133.95]

Favours pork fat 0.001 0.1 1 10 1000 Favours cold cream
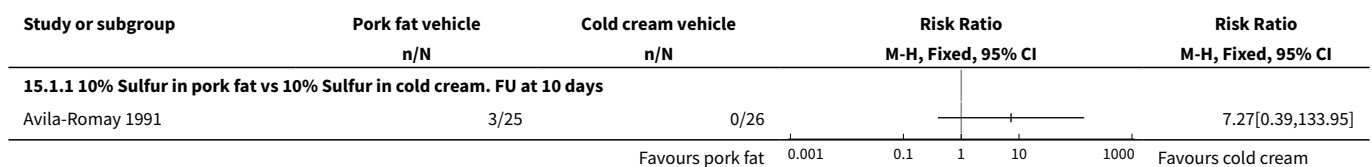
ADDITIONAL TABLES

Table 1. Quality assessment

Trial	Allocation sequence generation	Allocation concealment	Blinding	Inclusion[a]
Amer 1992	Unclear	Unclear	Unclear	Adequate
Amerio 2003	Adequate	Adequate	Investigators	Adequate
Avila-Romay 1991	Unclear	Unclear	Unclear	Adequate
Bachewar 2009	Adequate	Unclear	None	Inadequate
Biele 2006	Adequate	Unclear	Investigators	Adequate
Brooks 2002	Adequate	Unclear	Investigators	Inadequate
Chouela 1999	Unclear	Unclear	Described as "double blind"; participants blinded	Adequate
Glaziou 1993	Unclear	Unclear	Outcomes assessor	Adequate
Gulati 1978	Unclear	Unclear	Unclear	Adequate
Hansen 1986	Unclear	Unclear	"Single blind", unclear who was blinded	Adequate
Ly 2009	Adequate	Unclear	None	Adequate
Macotela-Ruiz 1993	Unclear	Unclear	Participant and outcomes assessor	Adequate
Madan 2001	Unclear	Unclear	Outcomes assessor	Inadequate
Maggi 1986	Unclear	Unclear	Unclear	Adequate
Nnoruka 2001	Adequate	Unclear	Unclear	Adequate
Schenone 1986	Unclear	Unclear	Unclear	Adequate
Schultz 1990	Unclear	Adequate	Outcomes assessor	Adequate
Singalavanija 2003	Adequate	Unclear	Unclear	Inadequate
Taplin 1986	Unclear	Adequate	Investigators	Adequate
Taplin 1990	Unclear	Adequate	Investigators	Adequate
Usha 2000	Adequate	Adequate	None	Adequate
Zargari 2006	Unclear	Adequate	Investigators and participants	Adequate

[a]Inclusion of randomized participants in analysis.

Table 2. Adverse events

Comparison	Trial	Adverse event	Intervention	n/N[a]	Intervention	n/N[a]

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Table 2. Adverse events *(Continued)*

Comparison	Study	Event					
Ivermectin vs placebo	Macotela-Ruiz 1993	None recorded	Ivermectin	—	Placebo	—
Ivermectin vs permethrin	Usha 2000	Aggravation of symptoms	Ivermectin	3/43	Permethrin	0/45
	Bachewar 2009	None recorded	Ivermectin	—	Permethrin	—
Ivermectin vs lindane	Chouela 1999	Headache	Ivermectin	1/26	Lindane	6/27
		Headache	Ivermectin	1/26	Lindane	0/27
		Hypotension	Ivermectin	1/26	Lindane	0/27
		Abdominal pain	Ivermectin	1/26	Lindane	0/27
		Vomiting	Ivermectin	1/26	Lindane	0/27
	Madan 2001	Severe headache	Ivermectin	1/100	Lindane	0/100
Ivermectin vs benzyl benzoate	Glaziou 1993	Mild increase in pruritus	Ivermectin	0/23	Benzyl benzoate	5/21
	Nnoruka 2001	Pruritus and irritation	Ivermectin	0/29	Benzyl benzoate	7/29
	Brooks 2002	Pustular rash	Ivermectin	3/43	Benzyl benzoate	0/37
		Cellulitis	Ivermectin	1/43	Benzyl benzoate	0/37
		Burning or stinging	Ivermectin	0/43	Benzyl benzoate	6/37
		Dermatitis	Ivermectin	0/43	Benzyl benzoate	6/37
	Bachewar 2009	None recorded	Ivermectin	—	Benzyl benzoate	—
	Ly 2009	Abdominal pain	Ivermectin	5/65	Benzyl benzoate	0/116
		Mild diarrhoea	Ivermectin	2/65	Benzyl benzoate	0/116
		Irritant dermatitis	Ivermectin	0/65	Benzyl benzoate	30/116
Permethrin vs crotamiton	Taplin 1990	Worsening of symptoms	Permethrin	0/48	Crotamiton	10/48
	Amer 1992	None recorded	Permethrin	—	Crotamiton	—
Permethrin vs lindane	Hansen 1986	Mild burning, stinging, or itching	Permethrin	5/49	Lindane	5/50

Table 2. Adverse events *(Continued)*

	Taplin 1986	None recorded	Permethrin	—	Lindane	—
	Schultz 1990	Burning/stinging	Permethrin	23/234	Lindane	12/233
		Pruritus	Permethrin	15/234	Lindane	17/233
		Erythema	Permethrin	5/234	Lindane	3/233
		Tingling	Permethrin	4/234	Lindane	5/233
		Rash	Permethrin	2/234	Lindane	2/233
		Diarrhoea	Permethrin	1/234	Lindane	1/233
		Persistent excoriation	Permethrin	1/234	Lindane	0/233
		Contact dermatitis	Permethrin	0/234	Lindane	1/233
		Phemphigus	Permethrin	0/234	Lindane	1/233
		Papular rash	Permethrin	0/234	Lindane	1/233
	Amer 1992	None recorded	Permethrin	—	Lindane	—
	Zargari 2006	Skin irritation	Permethrin	2/59	Lindane	1/58
Permethrin versus benzyl benzoate	Bachewar 2009	None recorded	Permethrin	—	Benzyl benzoate	—
Permethrin vs synergized natural pyrethrins	Amerio 2003	Secondary skin infection	Permethrin	10/20	Synergized pyrethrins	2/20
Crotamiton vs lindane	Amer 1992	None recorded	Lindane	—	Crotamiton	—
Lindane vs sulfur	Singalavanija 2003	Foul odour	Lindane	3/50	Sulfur	10/50
		Burning	Lindane	6/50	Sulfur	2/50
		Erythema	Lindane	5/50	Sulfur	2/50
Benzyl benzoate vs sulfur	Gulati 1978	None recorded	Benzyl benzoate	—	Sulfur	—
Benzyl benzoate vs synergized natural pyrethrins	Biele 2006	Skin irritation and burning sensations	Benzyl benzoate	22/120	Synergized pyrethrins	3/120
Lindane: short vs long application	Maggi 1986	None recorded	Lindane (short course)	—	Lindane (long course)	—

Table 2. Adverse events *(Continued)*

Decamethrin: 2-day + 2-day vs 4-day application	Schenone 1986	Moderate skin hotness	Decamethrin (both regimens)	15/127		
Sulfur: pork fat vehicle vs cold cream vehicle	Avila-Romay 1991	Pruritus	Sulfur/salicylic acid in pork fat	32/53	Sulfur in cold cream	18/58
		Xerosis	Sulfur/salicylic acid in pork fat	18/53	Sulfur in cold cream	14/58
		Burning sensations	Sulfur/salicylic acid in pork fat	9/53	Sulfur in cold cream	6/58
		Keratosis pilaris	Sulfur/salicylic acid in pork fat	8/53	Sulfur in cold cream	0/58
		Erythema	Sulfur/salicylic acid in pork fat	1/53	Sulfur in cold cream	6/58
		Keratosis follicularis		0/53	Sulfur in cold cream	1/58

[a]No. participants reporting event/total no. participants.

A P P E N D I C E S

Appendix 1. Search methods: detailed search strategies

Search set	CIDG SR[a]	CENTRAL	MEDLINE/EMBASE[b]	LILACS[b]	INDMED
1	scabies	scabies	scabies	scabies	scabies
2	—	Sarcoptes scabiei	SCABIES	treatment	Sarcoptes scabiei
3	—	1 or 2	1 or 2	1 and 2	1 or 2
4	—	—	treatment	—	—
5	—	—	benzyl benzoate	—	—
6	—	—	crotamiton	—	—
7	—	—	lindane	—	—
8	—	—	malathion	—	—
9	—	—	permethrin	—	—
10	—	—	ivermectin	—	—

(Continued)

11	—	—	sulphur	—	—
12	—	—	hexachlorocyclohexane	—	—
13	—	—	gamma benzene hexachloride	—	—
14	—	—	4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13	—	—
15	—	—	3 and 14	—	—
16	—	—	Limit 15 to human	—	—

aCochrane Infectious Diseases Group Specialized Register.

bSearch terms used in combination with the search strategy for retrieving trials developed by The Cochrane Collaboration (Higgins 2006); upper case: MeSH or EMTREE heading; lower case: free text term.

WHAT'S NEW

Date	Event	Description
11 August 2010	New search has been performed	Two new trials Bachewar 2009 and Ly 2009 added. Trials now stratified according to drug regimen and length of follow up if heterogeneity detected. Removal of meta-analyses where heterogeneity detected. Minor changes to conclusion regarding effectiveness of ivermectin compared with benzyl benzoate.

HISTORY

Protocol first published: Issue 2, 1996
Review first published: Issue 4, 1997

Date	Event	Description
18 August 2008	Amended	Converted to new review format with minor editing.
30 April 2007	New citation required and conclusions have changed	2007, Issue 3: A substantive update with new authors. We included nine new trials and excluded two studies (Dunne 1991 and Macotela-Ruiz 1996) included in Walker 2000 after re-evaluation, as noted in the 'Characteristics of excluded studies'. The review has been rewritten and reformatted throughout, and the conclusions of the review have been updated to reflect the new trial evidence. We used more precise definitions in the 'Types of interventions' and separated the 'Types of outcome measures' into primary, secondary, and adverse events. Treatment failure in those clinically diagnosed and treatment failure in those microscopically confirmed are considered as separate outcome measures, while parasitological cure is no longer an outcome measure. We reformatted the search strategy section, but did not attempt to systematically search literature for adverse events. For data analysis, we used relative risks rather than odds ratios, and used a random-effects model for meta-analysis if significant het-

Date	Event	Description
		erogeneity was present. We used available-case analyses rather than intention-to-treat analyses using imputed data.
1 February 2006	New search has been performed	New studies found and included or excluded.
1 January 2000	New search has been performed	2000, Issue 3: Revised, synopsis added, and updated with new studies (Walker 2000).
1 January 1999	New search has been performed	1999, Issue 3: Revised and updated with new studies (Walker 1999b).
1 January 1999	New search has been performed	Revised with new title 'Interventions for treating scabies' (Walker 1999a).

CONTRIBUTIONS OF AUTHORS

Mark Strong and Paul Johnstone jointly authored this review update.

DECLARATIONS OF INTEREST

None known.

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Internal sources

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INDEX TERMS

Medical Subject Headings (MeSH)

Benzoates [therapeutic use]; Hexachlorocyclohexane [therapeutic use]; Insecticides [therapeutic use]; Ivermectin [therapeutic use]; Pyrethrins [therapeutic use]; Scabies [drug therapy] [*therapy]; Sulfur [therapeutic use]; Toluidines [therapeutic use]

MeSH check words

Adult; Child; Humans