Efficacy and safety of antiscabietic agents: A systematic review and network meta-analysis of randomized controlled trials

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Background: Many drugs have been used to treat scabies, but it is unclear which of them is the most efficacious.

Objective: To evaluate the comparative efficacy and safety of antiscabietic agents.

Methods: A systematic review of randomized controlled trials was conducted. Direct and network meta-analyses were applied to 13 antiscabietic agents on 3 outcomes (cure, persistent itching, and adverse events). Their probability of having highest efficacy and safety was estimated and ranked.

Results: A network meta-analysis of 52 trials including 9917 patients indicated that permethrin (the reference treatment) had a significantly higher cure rate than sulfur, malathion, lindane, crotamiton, and benzyl benzoate. Combination permethrin plus oral ivermectin had a nonsignificantly higher cure rate than permethrin. Combination permethrin plus oral ivermectin was ranked highest in terms of cure, topical ivermectin in terms of persistent itching, and synergized pyrethrins in terms of adverse events. On the basis of clustered ranking, permethrin, oral ivermectin, and synergized pyrethrins seemed to retain balance between cure and adverse events.

Limitations: There are small numbers of trials and patients in some comparisons and a high risk of bias in some trials.

Conclusion: There is no 1 treatment that ranked highest in all aspects. Physicians should consider the drug's efficacy and safety profiles, along with ease of administration. (J Am Acad Dermatol 2019;80:1435-44.)

Key words: antiscabietic; benzyl benzoate; crotamiton; herbal medicine; ivermectin; lindane; malathion; meta-analysis; network meta-analysis; permethrin; pyrethrins; scabies; sulfur; systematic review.

Scabies is a highly contagious, parasitic infestation of the skin caused by *Sarcoptes scabiei* variety *hominis* mites. It is very common worldwide, particularly in tropical countries, with a global prevalence ranging 0.2%-71.4%.[1] Although serious complications are rare, scabies causes intense itching, decreases quality of life,[2] and might lead to secondary

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bacterial skin infection and acute poststreptococcal glomerulonephritis.[3]

Many topical and oral medications with different efficacies are used for killing scabietic mites, including sulfur, benzyl benzoate, γ-hexachlorocyclohexane or lindane, malathion, crotamiton, permethrin, ivermectin, and synergized pyrethrins.[4] Some medications are used off-label for scabies, and others are not available in some countries. Therefore, practitioners need guidance regarding which ones are the most efficacious therapeutic options.

CAPSULE SUMMARY

- Network meta-analysis indicated that combination permethrin plus oral ivermectin, topical ivermectin, and synergized pyrethrins had the strongest evidence for highest cure, lowest persistent itching, and lowest adverse events, respectively.
- There is no one treatment that ranked highest in all aspects. Physicians should consider an easy-to-use treatment with a balance between efficacy and safety.

Through the search strategy we used, we found 4 systematic reviews on treatments for scabies.[4-7] However, the authors of these reviews did not apply meta-analysis or only applied direct meta-analysis for a limited number of medications; thus, they insufficiently summarized the information, considering there are so many possible treatments. Network meta-analysis, the synthesis of evidence for all possible pairwise comparisons across multiple interventions through the information from direct comparisons with common comparators,[8] has never been performed on antiscabietic agents. In addtion, some treatments (ie, malathion, combination permethrin plus oral ivermectin, and herbal medicine) have never been included in previous systematic reviews. Therefore, we conducted a systematic review and network meta-analysis to estimate the comparative treatment efficacy (ie, clinical or microscopic cure, persistent itching, and re-infestation) and adverse events (AE) for currently available treatments of scabies. The probability a treatment had the highest efficacy or safety was estimated and ranked accordingly.

METHODS

This study was reported following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses statement extension for network meta-analysis[9] and registered with PROSPERO (CRD42016044022). We had no funding sources.

Literature search

Studies were identified from MEDLINE via PubMed, Scopus, and Cochrane Central Register of Controlled Trials, as well as some additional databases (Supplemental Table I; available at https://med.mahidol.ac.th/ceb/sites/default/files/public/pdf/AntiscabieticsNMAsupplement.pdf) from inception to September 14, 2017. Reference lists of selected articles were also explored.

Selection of studies

Study selection was performed independently by 2 reviewers (Dr Thadanipon and Dr Anothaisintawee); disagreement was resolved by consensus with a supervisor (Dr Thakkinstian). Titles and abstracts of identified studies were screened, and the full-texts were reviewed if the abstract was incomplete. Randomized controlled trials (RCTs) were eligible if they included individual patients with scabies; compared a pair of treatments (sulfur, benzyl benzoate, lindane, malathion, crotamiton, permethrin, oral/topical ivermectin, synergized pyrethrins, herbal medicine, placebo/no treatment); and described ≥1 outcomes of interest (ie, clinical or microscopic cure, persistent itching, re-infestation, and AEs). Studies were excluded if they exclusively compared a single drug in different dosages or formulations.

Outcomes of interest

The primary outcome of interest was either clinical cure or microscopic/parasitic cure, as determined by using the definition of each original study. Both were defined regardless of evaluation time. If cure was on an ordinal scale, it was dichotomized as cure versus all other categories combined.

The 3 secondary outcomes of interest were persistent itching, re-infestation, and AEs. Persistent itching was originally defined in studies as presence of itch/pruritus or nocturnal itch/pruritus that did not improve or, in some studies, as itch/pruritus that did not improve by at least 50%. Ordinal persistent itching scales were recategorized as absence versus presence at any degree. Re-infestation was defined by recurrence of scabies after having been cured. AEs consisted of cutaneous (eg, irritation, dermatitis, skin infection) and systemic (eg, headache, abdominal pain, diarrhea) reactions.

Data extraction and risk of bias assessment

Data extraction was performed independently by 2 reviewers (Dr Thadanipon and Dr Anothaisintawee) who used a standardized data

Abbreviations used:

AE: adverse event
CI: confidence interval
RCT: randomized controlled trial
RR: risk ratio
SUCRA: surface under the cumulative ranking curve

extraction form (Supplemental Appendix). Risk of bias was assessed by using the Cochrane Collaboration tool.[10] Disagreement was resolved by consensus with a supervisor (Dr Thakkinstian).

Statistical analysis

Intention-to-treat analysis was carried out for the entire quantitative synthesis. The number of patients initially enrolled was used as the total number of patients being assessed. Nonresponder imputation[11] was applied to all missing outcome data.

Direct meta-analysis of each treatment pair was performed by pooling risk ratios (RRs) if there were at least 3 studies. The Q test and I^2 statistic were applied to assess heterogeneity (ie, variation in outcome between the studies) to indicate how data should be pooled in each meta-analysis. The DerSimonian and Laird method was used for pooling RRs if heterogeneity was present ($P < .1$ or $I^2 \geq 25\%$), otherwise, the inverse variance method was used. Sources of heterogeneity were explored by using meta-regression. Subgroup analysis was subsequently performed by study or treatment characteristic regarded as a source of heterogeneity.

A 2-stage network meta-analysis[12,13] was applied to estimate the relative treatment effects (RRs) of all treatments by using information from the comparisons with common comparators to gain more power of test by integrating direct and indirect comparisons. First, the natural logarithm of the RR (the natural logarithm is required for modelling ratios such as RRs) and its variance-covariance were estimated for each individual study by using permethrin as the reference (standard treatment, approved treatment for scabies worldwide). Second, the natural logarithms of the RRs were pooled across studies by using a multivariate meta-analysis with consistency model; subsequently, multiple treatment comparisons were performed. The probability the treatment had the highest efficacy or safety was estimated and ranked using surface under the cumulative ranking curve (SUCRA), which indicates the percentage of efficacy or safety each treatment has compared with a hypothetical, ideal treatment. A clustered ranking plot that displayed benefit and risk simultaneously was constructed by plotting SUCRA for highest cure versus lowest AEs.

The consistency assumption (ie, agreement between estimates from direct and indirect evidence) was assessed by using a design-by-treatment interaction model.[14,15] Publication bias was assessed by using comparison-adjusted funnel plots.[16]

All analyses were performed using Stata version 15.0.[17] A 2-sided P value of $<.05$ was considered statistically significant, except for the heterogeneity test, in which a P value of $<.1$ was used.

RESULTS

Study selection and characteristics of included studies

A total of 2574 records were identified from all sources (Fig 1). After duplicates were removed and records screened, 75 full-text articles were assessed for eligibility; 22 of these records were excluded (Supplemental Table II), resulting in 53 eligible studies. One of these studies was a registered trial with a completed recruitment status but no results have been provided.[18] Consequently, 52 RCTs[19-70] were included in quantitative synthesis. Most of these trials were hospital-based and conducted in Asia. Forty-two RCTs were conducted in children and adults, 3 in children only,[39,41,49] and 7 in adults only.[37,40,45,52-54,57] In 24 RCTs reporting severity of scabies at baseline, severe cases ranged 1.7%-100%, with a median of 55%. Forty RCTs used microscopic examination for diagnosing scabies, and the remaining RCTs used only clinical examination; none used dermoscopy (Supplemental Table III). Treatment of the patient's contacts or family members was reported in 65.4% of the studies, and the prevention of fomite transmission in 26.9% (Supplemental Table IV).

Thirteen treatments were used in 52 RCTs: placebo (1 RCT), white soft paraffin (1 RCT), sulfur (5 RCTs), benzyl benzoate (including Tenutex; Bioglan, Malmö, Sweden) (14 RCTs), lindane (16 RCTs), malathion (1 RCT), crotamiton (6 RCTs), permethrin (30 RCTs), oral ivermectin (31 RCTs), combination permethrin plus oral ivermectin (1 RCT), topical ivermectin (5 RCTs), synergized pyrethrins (2 RCTs), and herbal medicine (4 RCTs). Their formulations, dosages, and treatment schedules, including both single and repeated administrations, are described in Supplemental Table V. Fifty-one RCTs reported the number of patients with cure at different time points, which were grouped into 1-2 weeks and 3-6 weeks, whereas 18 reported persistent itching. The terms and definitions used for cure and persistent itching

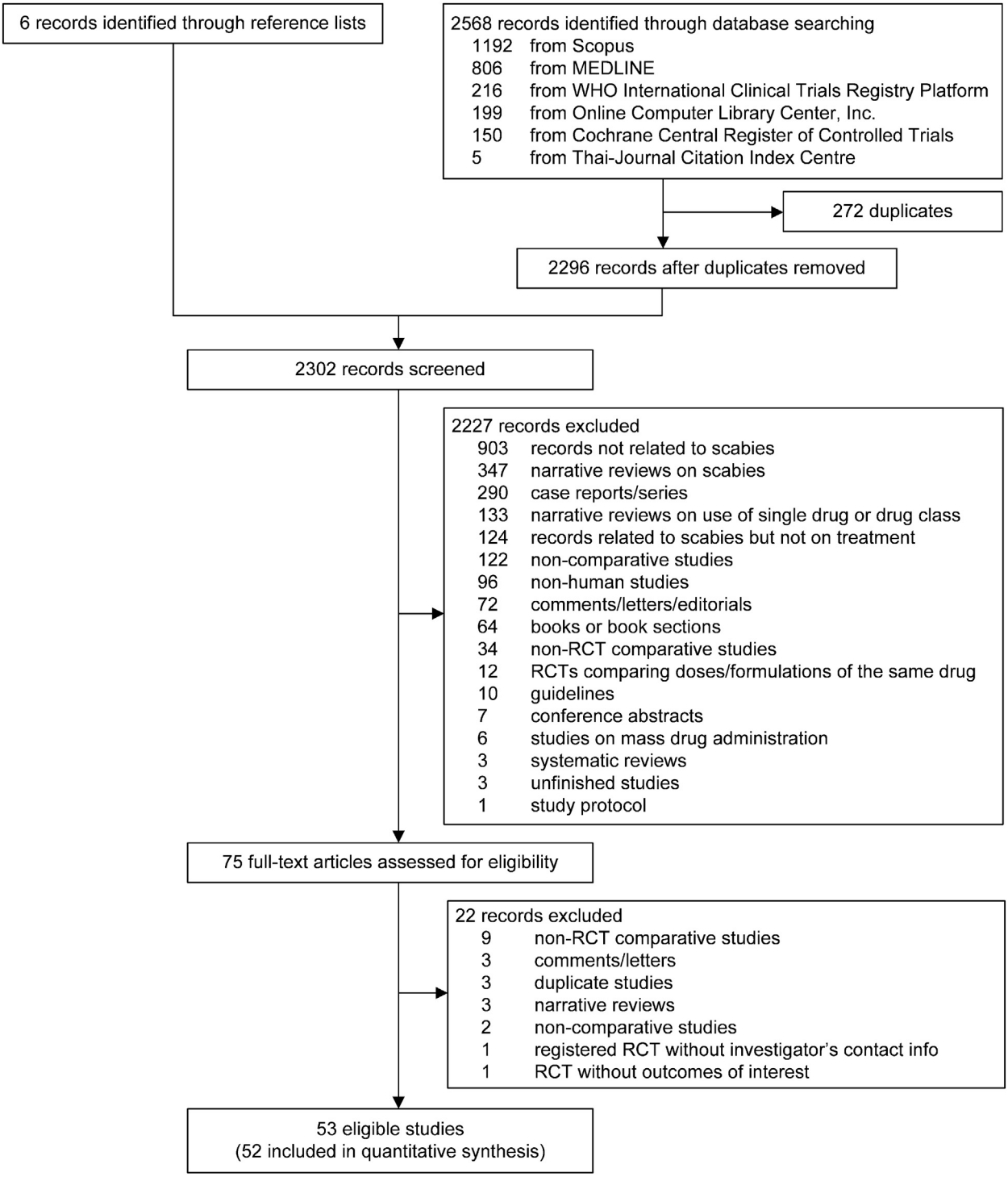

Fig 1. Systematic review flow diagram. *RCT*, Randomized controlled trial; *WHO*, World Health Organization.

outcomes in each study are listed in Supplemental Table VI. In 9 RCTs, re-infestation rates ranging 0%-20% were reported (Supplemental Table VII). Re-infestation was not included in meta-analyses because a limited number of studies provided data regarding this outcome. Thirty-six RCTs reported AEs (Supplemental Tables VIII-X). Due to the scarcity of each AE, a composite of AEs was used, considering

the highest number among all individual events. The results of risk of bias assessment are shown in Supplemental Table XI.

Direct meta-analysis

The results of the direct meta-analysis for cure at 1-2 weeks and 3-6 weeks, persistent itching, and AE outcomes are presented in Supplemental Tables XII-XV, along with subgroup analyses by covariables shown to be potential sources of heterogeneity. In brief, permethrin was significantly better than oral ivermectin, lindane, and crotamiton, and oral ivermectin was significantly better than lindane in achieving cure at both 1-2 weeks and 3-6 weeks. Permethrin was also better than benzyl benzoate for cure at 1-2 weeks. For persistent itching, oral ivermectin was significantly better than benzyl benzoate and lindane; permethrin was also significantly better than lindane for persistent itching. None of the treatments showed a significant difference in AEs in direct meta-analysis.

Network meta-analysis

Treatment comparisons for cure at 1-2 weeks and 3-6 weeks, persistent itching, and composite AEs were mapped (Supplemental Fig 1). The results of the network consistency models are discussed.

Cure. Data from 46 studies (n = 8951) consisting of 25 direct comparisons among 12 treatments were pooled for cure at 1-2 weeks, and data from 37 studies (n = 8110) consisting of 22 direct comparisons among 11 treatments were pooled for cure at 3-6 weeks (Supplemental Fig 1, *A* and *B*). At 3-6 weeks, sulfur, malathion, lindane, crotamiton, and benzyl benzoate had significantly lower cure rates than permethrin (Table I). Mixed treatment comparisons indicated that 13 additional pairs were statistically significant. The highest probability of cure at 3-6 weeks, as indicated by the highest SUCRA, was associated with combination treatment with permethrin and oral ivermectin, followed by permethrin and topical ivermectin (Table II). For cure at 1-2 weeks, permethrin was significantly better than oral ivermectin, placebo, sulfur, malathion, lindane, crotamiton, and benzyl benzoate (Supplemental Table XVI). The treatment ranking for cure at 1-2 weeks was reasonably consistent with that at 3-6 weeks (Table II). No evidence of inconsistency was shown for cure at 1-2 weeks (P = .990) or 3-6 weeks (P = .993).

Persistent itching. Sixteen direct comparisons of 9 treatments (18 studies, 2878 patients) were pooled (Supplemental Fig 1, *C*). Permethrin showed a significantly lower risk for persistent itching than sulfur, lindane, crotamiton, and benzyl benzoate but a significantly higher risk than topical ivermectin (Supplemental Table XVI). An additional 7 mixed treatment comparisons were statistically significant. Topical ivermectin was associated with significantly lower itch compared with all other agents except synergized pyrethrins. The lowest probability of persistent itch was with topical ivermectin, followed by permethrin and synergized pyrethrins (Table II). There was no evidence of inconsistency (P = .972).

Composite AEs. Data from 36 studies (n = 7718) with 26 direct comparisons among 12 treatments were pooled (Supplemental Fig 1, *D*). Permethrin use has a significantly lower risk for AEs than sulfur but a higher risk for AEs than synergized pyrethrins (Table I). Seventeen additional effects were statistically significant. Synergized pyrethrins showed a significantly lower risk for AEs, and sulfur showed a significantly higher risk for AEs than most other agents. The lowest probability for AEs was found with synergized pyrethrins, followed by malathion and oral ivermectin (Table II). No evidence of inconsistency was found (P = .511).

Cure versus AEs. Clustered ranking was applied to cure at 3-6 weeks and AEs (Fig 2). Combination permethrin plus oral ivermectin and topical ivermectin were ranked high for cure (SUCRA 93.1 and 76.2, respectively) but considerably lower for AEs. Synergized pyrethrins had the highest standing for AEs (SUCRA 98) but was slightly lower for cure (SUCRA 60.3). Permethrin and oral ivermectin were ranked high for cure (SUCRA 80.6 and 70.2, respectively) and moderate for AEs. Malathion ranked second for AEs (SUCRA 83.3) but lowest for cure. The remaining treatments did not stand out on either outcome.

Publication bias. Publication bias of the networks was assessed by comparison-adjusted funnel plots (Supplemental Figs 2-5). They were symmetrical, suggesting no evidence of publication bias.

DISCUSSION

The network meta-analysis performed in this systematic review enabled treatment ranking, which can be used to support clinicians' decisions regarding treatment choices. Clustered ranking was applied and revealed that no 1 treatment ranked highest for both cure and AE outcomes. Permethrin, oral ivermectin, and synergized pyrethrins, which were closer to the right upper corner of the clustered ranking plot than other treatments, seemed to provide the best balance between these 2 outcomes. However, because the AEs reported in these trials are not serious adverse reactions, such as hospitalization or death, they could be reasonably given less weight

Table I. Results of network meta-analysis of cure at 3-6 weeks and composite adverse events outcomes

		Composite adverse events										
Cure at 3-6 weeks	*Toplverm*	**6.88 (2.36-20.05)**	**0.27 (0.14-0.52)**	1.29 (0.05-33.07)	1.29 (0.84-1.96)	0.70 (0.13-3.81)	1.42 (0.91-2.22)	**2.40 (1.04-5.55)**	1.17 (0.70-1.93)	1.43 (0.66-3.08)	1.34 (0.84-2.16)	0.99 (0.62-1.57)
	1.07 (0.86-1.32)	*SynPyrethr*	**0.04 (0.01-0.12)**	0.19 (0.01-5.46)	**0.19 (0.07-0.51)**	**0.10 (0.01-0.70)**	**0.21 (0.07-0.58)**	0.35 (0.10-1.22)	**0.17 (0.06-0.48)**	**0.21 (0.06-0.69)**	**0.20 (0.07-0.58)**	**0.14 (0.05-0.39)**
	1.26 (0.97-1.64)	1.18 (0.88-1.60)	*Sulfur*	4.77 (0.18-125.09)	**4.77 (2.69-8.48)**	2.60 (0.46-14.75)	**5.27 (3.00-9.26)**	**8.91 (3.60-22.05)**	**4.33 (2.39-7.82)**	**5.30 (2.24-12.52)**	**4.99 (2.51-9.91)**	**3.67 (2.05-6.55)**
	-	-	-	*Paraffin*	1.00 (0.04-25.12)	0.55 (0.01-20.28)	1.10 (0.04-27.77)	1.87 (0.07-50.68)	0.91 (0.04-22.80)	1.11 (0.04-29.81)	1.05 (0.04-26.92)	0.77 (0.03-19.56)
	0.99 (0.87-1.11)	0.92 (0.77-1.11)	**0.78 (0.61-0.99)**	-	*Permethrin*	0.55 (0.11-2.83)	1.10 (0.83-1.48)	1.87 (0.87-4.02)	0.91 (0.66-1.25)	1.11 (0.57-2.16)	1.05 (0.67-1.62)	0.77 (0.54-1.10)
	0.88 (0.68-1.13)	0.83 (0.62-1.11)	**0.70 (0.50-0.97)**	-	0.89 (0.71-1.12)	*Perm+ Orallverm*	2.03 (0.39-10.60)	3.42 (0.57-20.72)	1.66 (0.31-8.83)	2.04 (0.35-11.99)	1.92 (0.35-10.46)	1.41 (0.26-7.54)
	1.02 (0.90-1.15)	0.95 (0.79-1.16)	0.81 (0.64-1.02)	-	1.03 (0.96-1.11)	1.15 (0.92-1.45)	*Orallverm*	1.69 (0.83-3.44)	0.82 (0.59-1.14)	1.00 (0.50-2.04)	0.95 (0.60-1.49)	0.70 (0.49-1.00)
	1.41 (1.04-1.90)	1.32 (0.94-1.85)	1.11 (0.78-1.60)	-	**1.43 (1.07-1.90)**	**1.59 (1.11-2.28)**	**1.38 (1.05-1.82)**	*Malathion*	0.49 (0.22-1.06)	0.59 (0.22-1.62)	0.56 (0.24-1.30)	**0.41 (0.19-0.91)**
	1.22 (1.06-1.41)	1.15 (0.93-1.41)	0.97 (0.76-1.23)	-	**1.24 (1.13-1.36)**	**1.39 (1.09-1.77)**	**1.20 (1.09-1.32)**	0.87 (0.65-1.16)	*Lindane*	1.23 (0.59-2.56)	1.15 (0.69-1.93)	0.85 (0.56-1.29)
	1.10 (0.82-1.47)	1.03 (0.75-1.41)	0.87 (0.60-1.24)	-	1.11 (0.84-1.47)	1.24 (0.87-1.78)	1.08 (0.81-1.43)	0.78 (0.53-1.16)	0.90 (0.67-1.20)	*Herb*	0.94 (0.43-2.06)	0.69 (0.33-1.43)
	1.27 (1.09-1.48)	1.19 (0.95-1.49)	1.01 (0.77-1.31)	-	**1.29 (1.13-1.47)**	**1.44 (1.11-1.86)**	**1.25 (1.09-1.43)**	0.90 (0.66-1.23)	1.04 (0.90-1.21)	1.16 (0.86-1.57)	*Crotamiton*	0.74 (0.44-1.23)
	1.20 (1.03-1.40)	1.13 (0.94-1.36)	0.95 (0.73-1.24)	-	**1.22 (1.07-1.38)**	**1.36 (1.05-1.76)**	**1.18 (1.03-1.35)**	0.85 (0.63-1.16)	0.98 (0.85-1.14)	1.10 (0.84-1.42)	0.95 (0.80-1.13)	*BenzylB*

Results are risk ratios (95% confidence intervals) between each pair of treatments from network meta-analysis. Comparisons are read from left to right. Bold font indicates statistical significance. Italic font indicates a treatment. Results for cure at 3-6 weeks outcome are presented below treatment names and those for composite adverse events outcome above treatment names.
BenzylB, Benzyl benzoate; *Herb*, herbal medicine; *Orallverm*, oral ivermectin; *Paraffin*, white soft paraffin; *Perm+Orallverm*, combination permethrin plus oral ivermectin; *SynPyrethr*, synergized pyrethrins; *Toplverm*, topical ivermectin.

Table II. Results of treatment ranking from network meta-analysis of cure, persistent itching, and adverse events outcomes

	Cure at 1-2 weeks		Cure at 3-6 weeks		Persistent itching		Adverse events	
Rank	Treatment	SUCRA	Treatment	SUCRA	Treatment	SUCRA	Treatment	SUCRA
1	Perm+Orallverm	93.4	Perm+Orallverm	93.1	Toplverm	98.4	SynPyrethr	98.0
2	Toplverm	85.1	Permethrin	80.6	Permethrin	79.2	Malathion	83.3
3	Permethrin	81.9	Toplverm	76.2	SynPyrethr	73.4	Orallverm	63.8
4	SynPyrethr	71.6	Orallverm	70.2	Orallverm	64.6	Herb	59.1
5	Orallverm	61.3	SynPyrethr	60.3	Lindane	39.3	Crotamiton	57.2
6	Herb	59.7	Herb	52.8	BenzylB	29.7	Permethrin	54.5
7	BenzylB	47.5	BenzylB	32.5	Sulfur	25.7	Paraffin	50.3
8	Lindane	33.7	Lindane	29.1	Herb	20.7	Lindane	43.4
9	Crotamiton	24.2	Sulfur	24.0	Crotamiton	19.0	Toplverm	30.9
10	Malathion	21.0	Crotamiton	19.8			BenzylB	28.8
11	Sulfur	20.3	Malathion	11.4			Perm+Orallverm	28.0
12	Placebo	0.2					Sulfur	2.8

BenzylB, Benzyl benzoate; *Herb*, herbal medicine; *Orallverm*, oral ivermectin; *Paraffin*, white soft paraffin; *Perm+Orallverm*, combination permethrin plus oral ivermectin; *SUCRA*, surface under the cumulative ranking curve; *SynPyrethr*, synergized pyrethrins; *Toplverm*, topical ivermectin.

than cure. As a result, combination permethrin plus oral ivermectin and topical ivermectin, which ranked first and third, respectively, in terms of cure, should still be acceptable.

Of the treatments never included in meta-analyses, malathion ranked low (11th) for the cure outcome but high (second) for AEs. Although more studies on malathion might be needed to yield more robust results, malathion has been classified by the International Agency for Research on Cancer as probably carcinogenic to humans (group 2A),[71] so this drug probably should not be studied any further in clinical trials. In contrast, combination permethrin plus oral ivermectin ranked highest for cure but second lowest for AEs. Despite that, this treatment combination was present in only 1 RCT; therefore, further studies are needed to confirm this finding. Herbal medicine showed moderate results, as reflected by its middle ranks. However, one might not be able to infer these findings to all herbal medicines; those included in this review were a diverse group consisting of 4 individual herbal medicines studied in 4 trials.

Some antiscabietic agents are associated with significant safety concerns. Although the only systemic AE of lindane reported in the 16 studies included in our review was headache in 6 patients from 1 study, lindane has been found to have serious AEs, including death and seizure.[72] It was also recently classified by the International Agency for Research on Cancer as carcinogenic to humans (group 1),[73] hence should be avoided. Oral ivermectin is generally considered as safe, but it has also been reported to lead to rare occurrence of serious AEs, including encephalopathy and death, in loiasis and onchocerciasis patients.[74,75] These serious AEs are possibly linked to high microfilarial load, co-infection with other bloodborne parasites, or genetic predisposition.[76]

When prescribing an antiscabietic medication, one should consider not only its efficacy and safety but also the ease of administration, which can in turn affect the patient's compliance and is therefore very important. The ease of administration ranging from highest to lowest might be seen with oral medication, lotion, cream, and ointment, respectively. Repeated doses or applications should also be given to eradicate the mites emerging from eggs spared by the first dose or application. Furthermore, as scabies is highly contagious via physical contact, concurrent treatment of family members and contacts regardless of their symptoms and prevention of fomite transmission should also be implemented.[77]

Strengths and limitations

Our systematic review included treatments which were absent from previous reviews. Application of network meta-analysis enabled the comparison and ranking of all treatments. The treatment's probability of providing the highest benefit (ie, cure) and lowest risk (ie, AEs) was simultaneously considered. However, there are also some limitations in the present review. Some comparisons had small numbers of studies and participants and, consequently, less precise estimates. Also, many studies were associated with a high risk of bias, especially older studies. In meta-analyses, some characteristics were shown to be sources of heterogeneity, and working with aggregated data was not as flexible as working with individual patient

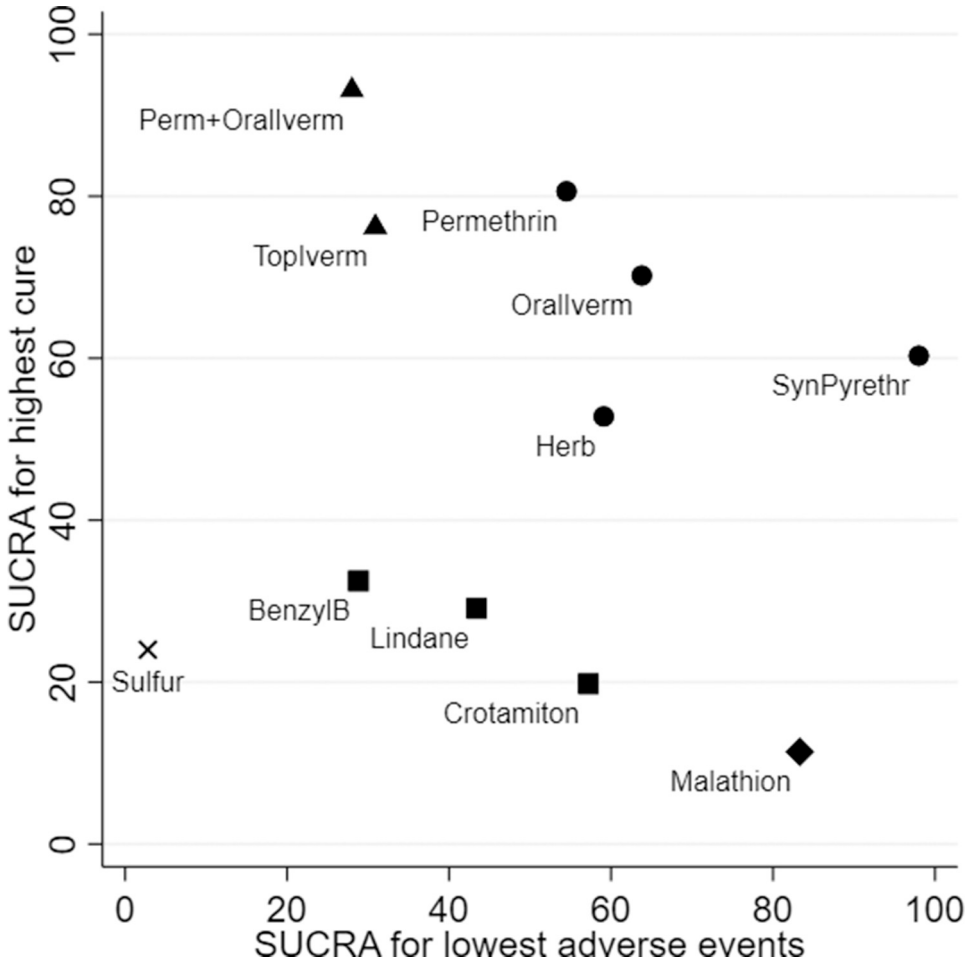

Fig 2. Clustered ranking plot of antiscabietic agents showing their SUCRA values for highest probability of cure at 3-6 weeks versus SUCRA values for lowest probability of adverse events. Each symbol represents a group of treatments in each cluster. Treatments lying in right upper corner are associated with higher probability of cure and lower probability of adverse events. *BenzylB*, Benzyl benzoate; *Herb*, herbal medicine; *Oralverm*, oral ivermectin; *Perm+Oralverm*, combination permethrin plus oral ivermectin; *SUCRA*, surface under the cumulative ranking curve; *SynPyrethr*, synergized pyrethrins; *Topiverm*, topical ivermectin.

data. Last, because most studies did not include crusted scabies patients, the applicability of our findings to crusted scabies is still questionable.

Conclusion

Combination permethrin plus oral ivermectin, topical ivermectin, and synergized pyrethrins had the strongest evidence for highest cure, lowest chance of persistent itching, and lowest adverse reactions, respectively. There was no 1 treatment that ranked highest in all aspects. Physicians should not only consider the efficacy and safety profiles of the medication, but also its ease of administration. Treatment of contacts and prevention of fomite transmission should also be implemented.

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