

Comparative Efficacy and Safety of Oral Ivermectin, Topical Permethrin, and Its Combination in the Treatment of Scabies: A Systematic Literature Review

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INTRODUCTION




- *Sarcptes scabiei* var *hominis* mite
- WHO Skin neglected tropical disease (skin NTD)
- Contagious and extremely itchy parasitic skin infection
- Burrows + papules + nocturnal itch




PERMETHRIN

5% Cream/Lotion




IVERMECTIN

12mg tablet



DESCRIPTION

- synthetic pyrethroid similar to naturally occurring pyrethrins extracted from the chrysanthemum flower
- Mechanism of Action
 - neurotoxic: blocks sodium channels and delay repolarization in scabies mite
 - works for all stages in the life cycle of the mite, including the eggs



DOSE

- apply to cool dry skin
- cover from the neck down to the toes, including under the fingernails
- Wash off after 8-14 hours
- Repeat after 1 week

PRECAUTION

2 MONTHS

*But suggested to be highly effective and to have an acceptable safety profile in infantile scabies (in a recent systematic review)

COST

1 course of treatment (60-kg adult) = ~173-230 Php


EFFECTIVENESS (AT WEEK 4) = ~93%

Rosumeck 2018

RISKS AND SIDE EFFECTS


Mild & temporary (1 in 25%):

- itching
- burning/stinging
- numbness/tingling
- rash/erythema/ eczema
- localized edema



DESCRIPTION

- Philippine FDA-approved drug against intestinal worms
- Given off-label to:
 - humans with scabies
 - communities where scabies is very common
- Mechanism of Action
 - blocks channels in the nervous and muscular systems of the mite leading to paralysis and death
 - active only against stages that are capable of moving (larva, nymphs, adults)



DOSE

- 200 mcg/kg, taken by mouth, 30 minutes before meal to ensure absorption
- Repeat dose after 2 weeks, when all eggs have hatched

PRECAUTION

15 KG

COST

2 doses (for a 60-kg adult) = ~48 Php

EFFECTIVENESS (AT WEEK 4) = ~85%

Rosumeck 2018


RISKS AND SIDE EFFECTS

Mild (1 in 20):

- aggravation of symptoms
- irritation
- headache
- nausea
- pustular rash
- cellulitis
- abdominal pain
- mild diarrhea

Serious (rare):

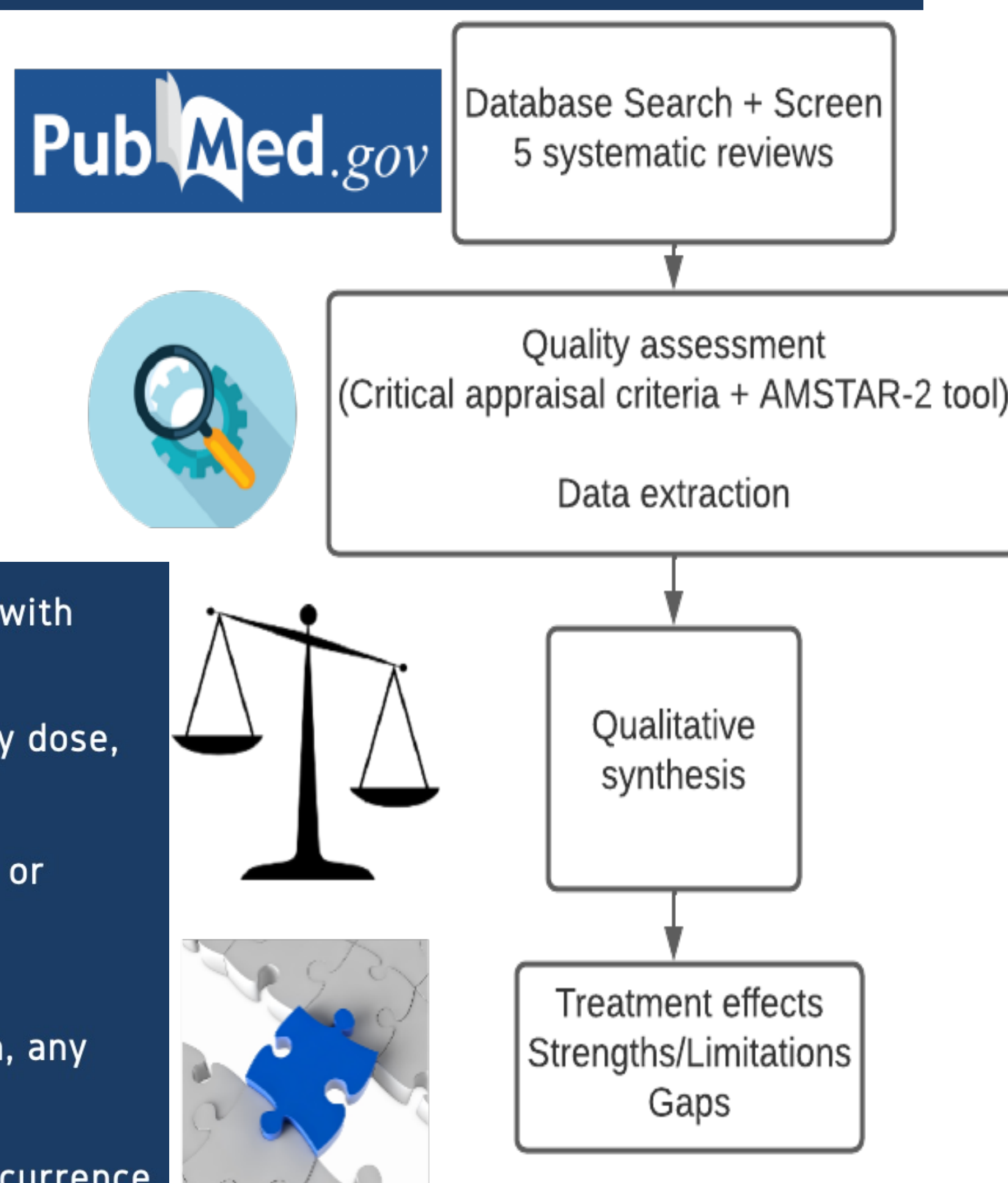
- neurological events
- may be attributed to drug-drug interactions



METHODS

• Search date: January 1, 2016 up to August 7, 2021

• Search strategy: (("scabi*" [All Fields] OR "scabies" [MeSH Terms] OR "sarcptes scabiei" [MeSH Terms] OR "antiscab*" [All Fields]) AND "therapy" [MeSH Subheading]) AND ((y_5 [Filter]) AND (meta-analysis [Filter] OR review [Filter] OR systematicreview [Filter]) AND (humans [Filter]))).



P (POPULATION)	Individual patients with classic scabies
I (INTERVENTION)	Oral ivermectin, any dose, any regimen
C (COMPARATOR)	Topical permethrin or combination oral ivermectin/topical permethrin, any dose/concentration, any regimen;
O (OUTCOMES)	Cure, itch relief, recurrence, adverse events, quality of life, other patient-reported outcomes
S (STUDY DESIGN)	Systematic reviews, with or without meta-analysis

RESULTS

ROSUMECK 2018

Favors PER over oral IVM (1-2 wks.)

Wk 1: RR: 0.65 (95% CI 0.54-0.78) (6 RCTs, N=613; I²=35% low certainty evidence)

Wk 2: RR: 0.91 (95% CI 0.76-1.08) (5 RCTs, N=459; I²=61%; low certainty evidence)

No difference (4 wks.)

a. 1-dose IVM vs 1-application PER

RR 1.00 (95% CI 0.86-1.16) (1 RCT, N=60; high certainty evidence)

b. 2-dose IVM vs 1-application PER

RR 0.97 (95% CI 0.83, 1.14) (1 RCT, N=55; moderate certainty evidence)

THADANIPON 2019

Favors PER (1-2 wks.)

Network RR 1.16 [1.05, 1.27]; P for inconsistency = 0.99

No difference at 3-6 wks.

Network RR 1.03 [0.96, 1.11]; P for inconsistency = 0.99

Combination PER + oral IVM had highest probability of cure at 1-2 weeks (SUCRA: 93.4) over PER (81.9) and oral IVM (61.3)

*No quality assessment or certainty of evidence rating

ADVERSE EVENTS

No significant difference (4 wks.)

RR: 1.30 (95% CI 0.35-4.83) (4 RCTs, N=502; low certainty evidence)

Few, minor, transient AEs

No difference bet. permethrin vs oral ivermectin (3-6 wks.)

Network RR 1.10 [0.83, 1.48]

Oral IVM had highest safety rank (SUCRA: 63.8), over PER (54.5) and combination oral IVM and PER (28.0)

CONCLUSION

Permethrin did not differ from oral ivermectin in cure rate at the 3- to 6- week timepoint, but had an earlier cure at 1-2 weeks. Adverse effects did not significantly differ and were few, mild and transient with both treatments. The evidence ranged widely from low to high certainty. Combination oral ivermectin and topical permethrin was ranked higher in efficacy but lower in safety compared to either drug alone in one moderate validity network meta-analysis.

There is varying certainty of evidence suggesting comparable efficacy and safety of oral ivermectin versus topical permethrin. Limited evidence suggest higher efficacy and lower safety of combination oral ivermectin and topical permethrin compared to either drug alone. An updated systematic review and network meta-analysis is warranted.

REFERENCES

1. Rosumeck S, Nast A, Dressler C. Ivermectin and permethrin for treating scabies. *Cochrane Database Syst Rev.* 2018;2018(4).
2. Thadanipon K, Anothaisintawee T, Rattanasiri S, Thakkinstant A, Attia J. Efficacy and safety of antiscabietic agents: A systematic review and network meta-analysis of randomized controlled trials. *J Am Acad Dermatol.* 2019;80(5):1435-1444.
3. May PJ, Tong SYC, Steer AC, et al. Treatment, prevention and public health management of impetigo, scabies, crusted scabies and fungal skin infections in endemic populations: a systematic review. *Trop Med Int Heal.* 2019;24(3):280-293.
4. Dressler C, Rosumeck S, Sunderkötter C, Werner RN, Nast A. The Treatment of Scabies: A Systematic Review of Randomized Controlled Trials. *Dtsch Arztebl Int.* 2016;113(45):757-762.
5. Dhana A, Yen H, Okhovat JP, Cho E, Keum NN, Khumalo NP. Ivermectin versus permethrin in the treatment of scabies: A systematic review and meta-analysis of randomized controlled trials. *J Am Acad Dermatol.* 2018;78(1):194-198.

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