



What Are The Clinical And Cost-Effectiveness Differences Between Standard And Enhanced Scabies Management Protocols In Primary Healthcare Settings ? : A Systematic Review

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ABSTRACT

Introduction: Scabies, a contagious parasitic infestation, presents a significant public health challenge globally, especially in resource-limited settings. Standard management protocols for scabies in primary care, often involving topical agents or oral ivermectin, face limitations such as reinfestation and poor adherence. Enhanced scabies management protocols, including mass drug administration (MDA) and combination therapies, have emerged to address these shortcomings. However, the comparative clinical and cost-effectiveness of these enhanced approaches versus standard protocols remain uncertain, hindering optimal decision-making. This systematic review aims to compare these aspects in primary healthcare settings. **Methods:** This systematic review adhered to the PRISMA 2020 guidelines. A comprehensive search was conducted across databases including PubMed, Semantic Scholar, SagePub, and Google Scholar, using PICO-

based keywords. Eligibility criteria focused on comparative intervention studies (e.g., RCTs, cluster RCTs) involving human subjects with confirmed scabies, conducted in primary healthcare settings, and reporting at least one clinical outcome for active management protocols. Data on study design, participant characteristics, intervention details, primary outcomes, and economic data were extracted and synthesized. Twenty-one studies were included in the final analysis. **Results:** The 21 included studies comprised various designs, predominantly cluster randomized trials (n=7) and randomized controlled trials (n=9). Enhanced protocols (e.g., MDA, combination therapies) consistently demonstrated higher cure rates, often ranging from 80% to 100%, and faster symptom resolution compared to standard protocols (cure rates approximately 45% to 100%). Adverse events for both protocol types were generally mild and transient. Economic data were sparse; only two studies reported direct treatment costs for standard agents, with permethrin being more expensive than ivermectin, and sulfur often the costliest. Comprehensive cost-effectiveness analyses were largely absent, though enhanced protocols were noted to require greater upfront investment. **Discussion:** Enhanced scabies management protocols show superior clinical effectiveness, primarily driven by population-wide or household-level treatment strategies and combination therapies that reduce reinfestation and improve healing. While these protocols are safe, their cost-effectiveness remains largely undetermined due to limited economic data. The increased resource requirements for implementation, including training and community engagement, also pose challenges for enhanced strategies. Protocol adherence may be improved with

simplified regimens in enhanced protocols. **Conclusion:** Enhanced scabies management protocols demonstrate superior clinical effectiveness over standard treatments in primary healthcare, particularly in high-prevalence settings, by achieving higher cure rates and faster symptom resolution with comparable safety profiles. However, their adoption is challenged by a lack of robust cost-effectiveness data and higher initial resource demands. Future research should prioritize comprehensive economic evaluations to guide policy and resource allocation for optimal scabies control.

Keywords: Scabies, Primary Healthcare, Enhanced Management, Standard Management, Cost-Effectiveness, Clinical Effectiveness, Systematic Review.

INTRODUCTION

Scabies, caused by the mite *Sarcoptes scabiei*, remains a significant public health challenge globally, particularly in resource-limited and overcrowded settings. The disease is highly contagious, characterized by intense pruritus, papular rash, and secondary complications such as bacterial skin infections and post-streptococcal sequelae (Mila-Kierzenkowska et al., 2017; Thadanipon et al., 2019). Scabies disproportionately affects children and marginalized populations, with prevalence rates in children consistently higher than in adults, underscoring the need for effective management strategies in primary healthcare settings (Behera et al., 2021; Hardy et al., 2021).

Conventional management of scabies in primary care relies on standard protocols, typically involving topical agents such as permethrin, crotamiton, sulfur, or oral ivermectin (Mila-Kierzenkowska et al., 2017; Abdel-Raheem et al., 2016). These treatments are widely used due to their established efficacy and availability. However, standard protocols often require individual or household application, which can be challenging in high-prevalence settings where reinfestation and poor treatment adherence are common (Matthewman et al., 2019; Thadanipon et al., 2019). These limitations have prompted the exploration of alternative management approaches.

In recent years, enhanced scabies management protocols have emerged as innovative strategies to address the shortcomings of standard approaches. Enhanced protocols may include mass drug administration (MDA), combination therapies, household or community-wide treatment, and the integration of community health workers (Behera et al., 2021; Hardy et al., 2021). These strategies aim to achieve higher population coverage, reduce transmission, and improve long-term disease control. Studies have demonstrated that enhanced protocols can yield cure rates generally between 80 % and 100 %, with faster resolution of symptoms and reduced prevalence at follow-up (Marina et al., 2022; Anissa et al., 2022).

Despite their clinical advantages, the cost-effectiveness of enhanced protocols remains uncertain. Enhanced interventions often require greater upfront investment in training, logistics,

and community engagement, and may involve more intensive resource use, such as increased community health worker time (Behera et al., 2021). In contrast, standard protocols are generally less resource-intensive and easier to implement in routine primary care, but may be less effective in settings with high transmission or limited follow-up (Matthewman et al., 2019; Thadanipon et al., 2019).

Economic data on scabies management are limited and heterogeneous. Available studies suggest that among standard agents, permethrin is more expensive than ivermectin and benzyl benzoate, while sulfur is often the most costly (Abdel-Raheem et al., 2016; Mila-Kierzenkowska et al., 2017). Enhanced protocols, such as MDA or community health worker-led interventions, incur additional costs related to implementation and monitoring, but few studies have provided comprehensive cost-effectiveness analyses (Behera et al., 2021). The lack of standardized outcome measures and limited economic data make it difficult to compare the relative value of standard and enhanced protocols in primary healthcare settings.

The rationale for this research is grounded in the need to optimize scabies management in primary healthcare, where most cases are diagnosed and treated. While enhanced protocols show promise for improving clinical outcomes, their broader adoption is hindered by uncertainties regarding cost-effectiveness, resource requirements, and implementation feasibility (Behera et al., 2021; Hardy et al., 2021). Understanding the clinical and economic trade-offs between standard and enhanced protocols is essential for evidence-based decision-making and policy development.

The primary objective of this study is to systematically compare the clinical effectiveness and cost-effectiveness of standard versus enhanced scabies management protocols in primary healthcare settings. Specifically, the study aims to evaluate cure rates, time to resolution, adverse events, treatment adherence, and direct costs associated with each protocol type (Marina et al., 2022; Balestri et al., 2022; Anissa et al., 2022). By synthesizing data from recent randomized controlled trials, cluster-randomized studies, and comparative interventions, this research will provide a comprehensive assessment of the benefits and limitations of current scabies management strategies.

A secondary objective is to identify contextual factors that influence the success and sustainability of scabies management programs, such as population mobility, healthcare infrastructure, and community engagement (Behera et al., 2021; Hardy et al., 2021). By addressing these gaps in the literature, the study will contribute to the development of more effective, equitable, and scalable approaches to scabies control in diverse primary healthcare environments.

Ultimately, this research seeks to inform clinical guidelines, public health policy, and resource allocation decisions for scabies management. The findings will help healthcare providers, policymakers, and stakeholders select the most appropriate and cost-effective strategies for reducing the burden of scabies in primary care, particularly in high-prevalence and resource-limited settings (Behera et al., 2021; Hardy et al., 2021; Thadanipon et al., 2019).

METHODS

Protocol

The study strictly adhered to the Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) 2020 guidelines to ensure methodological rigor and accuracy. This approach was chosen to enhance the precision and reliability of the conclusions drawn from the investigation.

Criteria for Eligibility

This systematic review aims to evaluate the clinical and cost-effectiveness differences between standard and enhanced scabies management protocols in primary healthcare settings

Screening

We screened in papers that met these criteria:

- **Human Subjects:** Does the study involve human subjects?
- **Scabies Diagnosis:** Does the study include participants with clinically or microscopically

confirmed scabies diagnosis?

- **Healthcare Setting:** Was the study conducted in primary healthcare settings (primary care clinics, community health centers, or first-point-of-contact facilities)?
- **Study Design:** Is the study a comparative intervention study (RCT, quasi-experimental, or controlled before-after study) examining at least two management protocols?
- **Clinical Outcomes:** Does the study report at least one clinical outcome (cure rates, time to cure, recurrence rates, treatment adherence, or adverse events)?
- **Study Scope:** Does the study include active management protocols (not solely prevention or diagnosis)?
- **Care Level:** Was the study conducted in settings other than exclusively secondary/tertiary care?

We considered all screening questions together and made a holistic judgement about whether to screen in each paper.

Data extraction

We asked a large language model to extract each data column below from each paper. We gave the model the extraction instructions shown below for each column.

- **Study Design Type:**

Identify the specific type of study design from the full text. Look in the methods section for precise description. Options may include:

- Cluster randomized trial
- Randomized controlled trial
- Comparative study
- Intervention study

If multiple design elements are present, list all. If unclear, note "design not clearly specified". Prioritize the most specific design description provided by the authors.

- **Unit of Randomization:**

Identify the specific unit that was randomized in the study (e.g., individuals, villages, households). Look in methods section, particularly randomization description. If multiple units were used, list all. If not clearly specified, write "not specified".

- **Participant Characteristics:**

Extract key demographic information:

- Total number of participants
- Age range or median age
- Gender distribution
- Geographic location
- Inclusion/exclusion criteria

Use exact numbers and percentages from the text. If ranges are provided, include both. If any characteristic is not reported, write "not reported".

- **Healthcare Setting:**

Describe the specific healthcare or community setting where the study was conducted:

- Type of setting (primary healthcare, community, rural/urban)
- Country/region
- Specific contextual details relevant to scabies management

Use verbatim quotes from methods section if possible. If setting details are sparse, note "minimal setting details provided".

- **Intervention Details:**

For each intervention arm, extract:

- Specific treatment/management protocol
- Drug/treatment type
- Dosage

- Frequency of administration
- Duration of intervention

Be precise about quantities, using exact numbers and units. If multiple components exist, list all. If any detail is missing, note "not specified".

- **Primary Outcome Measures:**

Identify and extract:

- Specific outcomes measured
- Measurement methods
- Time points of outcome assessment
- Key numerical results for primary outcomes

Use exact percentages, confidence intervals, and statistical significance as reported. If outcomes are complex, prioritize authors' stated primary outcomes.

- **Study Limitations:**

Extract explicit limitations mentioned by the authors:

- Methodological limitations
- Contextual constraints
- Potential sources of bias
- Challenges in implementation

Use direct quotes where possible. If no limitations are discussed, write "no limitations reported".

Search Strategy

The keywords used for this research based PICO :

Element	Keyword 1	Keyword 2	Keyword 3	Keyword 4
Population (P)	Scabies patients	Children	Primary healthcare settings	High-prevalence communities
Intervention (I)	Enhanced scabies management	Mass drug administration	Combination therapy	Community health worker-led treatment
Comparison (C)	Standard scabies treatment	Topical permethrin	Oral ivermectin single dose	Individual treatment
Outcome (O)	Cure rate	Time to resolution	Treatment adherence	Adverse events

The Boolean MeSH keywords inputted on databases for this research are: ("Scabies patients" OR "Primary healthcare settings" OR "Children" OR "High-prevalence communities") AND ("Enhanced scabies management" OR "Mass drug administration" OR "Combination therapy" OR "Community health worker-led treatment") AND ("Standard scabies treatment" OR "Topical permethrin" OR "Oral ivermectin single dose" OR "Individual treatment") AND ("Cure rate" OR "Time to resolution" OR "Treatment adherence" OR "Adverse events")

Data retrieval

Abstracts and titles were screened to assess their eligibility, and only studies meeting the inclusion criteria were selected for further analysis. Literature that fulfilled all predefined criteria and directly related to the topic was included. Studies that did not meet these criteria were excluded. Data such as titles, authors, publication dates, study

locations, methodologies, and study parameters were thoroughly examined during the review.

Quality Assessment and Data Synthesis

Each author independently assessed the titles and abstracts of the selected studies to identify those for further exploration. Articles that met the inclusion criteria underwent further evaluation. Final decisions on inclusion were based on the findings from this review process.

Table 1. Article Search Strategy

Database	Keywords	Hits
Pubmed	("Scabies patients" OR "Primary healthcare settings" OR "Children" OR "High-prevalence communities") AND ("Enhanced scabies management" OR "Mass drug administration" OR "Combination therapy" OR "Community health worker-led treatment") AND ("Standard scabies treatment" OR "Topical permethrin" OR "Oral ivermectin single dose" OR "Individual treatment") AND ("Cure rate" OR "Time to resolution" OR "Treatment adherence" OR "Adverse events")	7
Semantic Scholar	("Scabies patients" OR "Primary healthcare settings" OR "Children" OR "High-prevalence communities") AND ("Enhanced scabies management" OR "Mass drug administration" OR "Combination therapy" OR "Community health worker-led treatment") AND ("Standard scabies treatment" OR "Topical permethrin" OR "Oral ivermectin single dose" OR "Individual treatment") AND ("Cure rate" OR "Time to resolution" OR "Treatment adherence" OR "Adverse events")	250
Sagepub	("Scabies patients" OR "Primary healthcare settings" OR "Children" OR "High-prevalence communities") AND ("Enhanced scabies management" OR "Mass drug administration" OR "Combination therapy" OR "Community health worker-led treatment") AND ("Standard scabies treatment" OR "Topical permethrin" OR "Oral ivermectin single dose" OR "Individual treatment") AND ("Cure rate" OR "Time to resolution" OR "Treatment adherence" OR "Adverse events")	3,581
Google Scholar	("Scabies patients" OR "Primary healthcare settings" OR "Children" OR "High-prevalence communities") AND ("Enhanced scabies management" OR "Mass drug administration" OR "Combination therapy" OR "Community health worker-led treatment") AND ("Standard scabies treatment" OR "Topical permethrin" OR "Oral ivermectin single dose" OR "Individual treatment") AND ("Cure rate" OR "Time to resolution" OR "Treatment adherence" OR "Adverse events")	21,600

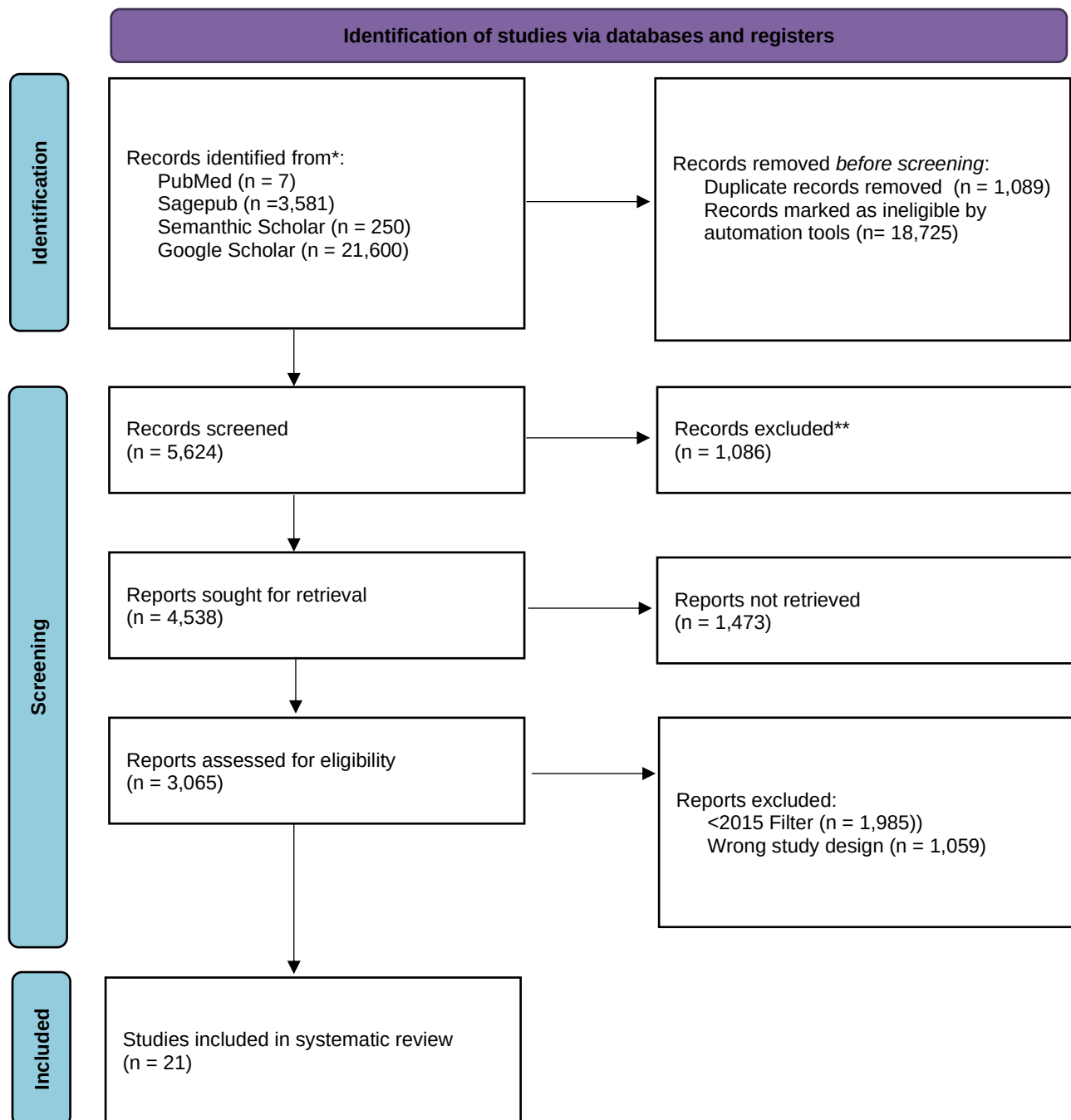


Figure 1. Article search flowchart

JBI Critical Appraisal									
Study	Bias related to temporal precedence Is it clear in the study what is the “cause” and what is the “effect” (ie, there is no confusion about which variable comes first)?	Bias related to selection and allocation Was there a control group?	Bias related to confounding factors Were participants included in any comparisons similar?	Bias related to administration of intervention/exposure Were the participants included in any comparisons receiving similar treatment/care, other than the exposure or intervention of interest?	Were there multiple measurements of the outcome, both pre and post the intervention/exposure?	Were the outcomes of participants included in any comparisons measured in the same way?	Were outcomes measured in a reliable way?	Bias related to participant retention Was follow-up complete and, if not, were differences between groups in terms of their follow-up adequately described and analyzed?	Statistical conclusion validity Was appropriate statistical analysis used?
Mullane et al., 2019	✓	✓	✓	✗	✓	✗	✓	✓	✓
Behera et al., 2021	✓	✓	✓	✗	✓	✗	✓	✓	✓
Thomas et al., 2018	✓	✓	✓	✗	✓	✗	✓	✓	✓
Lake et al., 2020	✓	✓	✓	✗	✓	✗	✓	✓	✓

Hardy et al., 2021									
Matthewman et al., 2019									
Lake et al., 2023									
Marina et al., 2022									
Rezaee et al., 2015									
Abdel-Raheem et al., 2016									
Ahmad et al., 2016									
Seller et al., 2021									
Mila-Kierzenkowska et al., 2017									
Panahi et al., 2015									
Thadanipon et al., 2019									
Verma and Ahsan, 2020									

Balestri et al., 2022	✓	✓	✓	✗	✓	✗	✓	✓	✓
Alipour and Goldust, 2015	✓	✓	✓	✗	✓	✗	✓	✓	✓
Anissa et al., 2022	✓	✓	✓	✗	✓	✗	✓	✓	✓
Al-Asadi et al., 2023	✓	✓	✓	✗	✓	✗	✓	✓	✓
Eliza et al., 2024	✓	✓	✓	✗	✓	✗	✓	✓	✓

RESULTS

Characteristics of Included Studies

Study	Study Design	Setting	Protocol Type	Primary Outcomes
Mullane et al., 2019	Cluster randomized trial with stepped-wedge design	Remote, primary healthcare, Western Australia	Enhanced (See, Treat, Prevent: training, treatment, prevention)	Diagnosis of impetigo in children 5-9 years
Behera et al.,	Cluster	Rural, tribal	Enhanced (mass	Prevalence of

Study	Study Design	Setting	Protocol Type	Primary Outcomes
2021	randomized controlled trial	community, India	screening/treatment with ivermectin)	scabies at 2 and 12 months
Thomas et al., 2018	Randomized controlled trial	Community -controlled Aboriginal Medical Service, Australia	Enhanced (tea tree oil gel vs. permethrin)	Clinical cure at 30 days
Lake et al., 2020	Cluster randomized non-inferiority trial	Community , rural, Solomon Islands	Enhanced (one vs. two-dose ivermectin mass drug administration)	Prevalence of scabies at 12 months
Hardy et al., 2021	Cluster randomized non-inferiority trial	Community , rural, Fiji	Enhanced (one/two-dose ivermectin mass drug administration, screen-and-treat)	Reduction in scabies/impetigo prevalence at 12 months
Matthewman	Randomized	Research	Standard	Clinical cure at

Study	Study Design	Setting	Protocol Type	Primary Outcomes
et al., 2019	controlled trial, comparative , intervention	center, Gabon	(individual vs. household benzyl benzoate)	28 days
Lake et al., 2023	Cluster randomized, non-inferiority	Community , rural, Solomon Islands	Enhanced (one vs. two-dose ivermectin mass drug administration)	Scabies prevalence at 21 months
Marina et al., 2022	Double-blind randomized controlled trial	Community (boarding schools), Indonesia	Enhanced (permethrin plus fusidic acid vs. permethrin)	Cure rate, visual analog scale for pruritus/pain
Rezaee et al., 2015	Randomized controlled trial, comparative , intervention	No mention found	Standard (topical ivermectin vs. Tenutex)	Cure rate at 2 and 4 weeks

Study	Study Design	Setting	Protocol Type	Primary Outcomes
Abdel-Raheem et al., 2016	Randomized controlled trial, comparative	No mention found	Standard (ivermectin, benzyl benzoate, permethrin, sulfur)	Efficacy, acceptability, cost
Ahmad et al., 2016	Comparative, intervention	No mention found	Standard (topical vs. oral ivermectin)	Symptom-free rate at 1, 2, 4 weeks
Seller et al., 2021	Randomized controlled trial, cluster	No mention found	Enhanced (spinosad vs. vehicle)	Complete cure at day 28
Mila-Kierzenkowska et al., 2017	Randomized controlled trial, comparative, intervention	No mention found	Standard (permethrin, crotamiton, sulfur)	Cure rate at 1, 2, 4 weeks
Panahi et al., 2015	No mention found	No mention found	Standard (topical/oral ivermectin)	Efficacy (review)

Study	Study Design	Setting	Protocol Type	Primary Outcomes
Thadanipon et al., 2019	Systematic review/meta-analysis	No mention found	Standard/enhanced (multiple agents)	Cure, persistent itching, adverse events
Verma and Ahsan, 2020	Randomized controlled trial	No mention found	Standard (topical vs. oral ivermectin)	Cure rate, visual analog scale for pruritus
Balestri et al., 2022	Comparative study	No mention found (Italy)	Standard (single vs. double-dose oral ivermectin)	Clearance of disease
Alipour and Goldust, 2015	Randomized controlled trial, comparative, intervention	No mention found	Standard (oral ivermectin vs. sulfur ointment)	Cure rate at 2 and 4 weeks
Anissa et al., 2022	Randomized controlled trial, cluster	Community (boarding school), Indonesia	Enhanced (Blacksoap plus permethrin vs. permethrin)	Cure rate, pruritus visual analog scale, transepidermal water loss

Study	Study Design	Setting	Protocol Type	Primary Outcomes
Al-Asadi et al., 2023	Randomized controlled trial, comparative, intervention	Urban, Iraq	Enhanced (permethrin, topical ivermectin, combined oral/topical ivermectin)	Reduction in itching/lesions
Eliza et al., 2024	Comparative, retrospective	Outpatient clinic, Indonesia	Enhanced (permethrin plus sulfur vs. permethrin)	Absence of new complaints, skin lesion improvement

Summary of Study Characteristics:

- Study Design:
 - 7 studies used a cluster randomized design (including non-inferiority and stepped-wedge approaches).
 - 9 studies used a randomized controlled trial design, including comparative and double-blind randomized controlled trials.
 - 3 studies were comparative but not randomized controlled trials.
 - 1 study was a systematic review/meta-analysis, and 1 was a review (design not specified).
 - 1 study was comparative and retrospective.
 - Some studies were classified in more than one way based on available reporting.
- Setting:

- 2 studies in Australia, 1 in India, 2 in the Solomon Islands, 1 in Fiji, 1 in Gabon, 3 in Indonesia, 1 in Iraq, and 1 in Italy.
- We didn't find mention of the setting for 10 studies.
- 3 studies in community/boarding school settings (2 in Indonesia, 1 in Indonesia outpatient clinic).
- 3 studies in community/rural settings (Solomon Islands, Fiji).
- 1 study in an urban setting (Iraq).
- 1 study in a research center (Gabon).
- 1 study in a remote/primary healthcare setting (Australia).
- 1 study in a community-controlled healthcare setting (Australia).
- Protocol Type:
 - 11 studies used an enhanced protocol (new, combined, or augmented interventions).
 - 9 studies used a standard protocol (comparing established treatments).
 - 1 study included both standard and enhanced protocols.
- Primary Outcomes:
 - 12 studies reported cure rate or clinical cure as a primary outcome.
 - 4 studies reported prevalence as a primary outcome.
 - 2 studies reported symptom reduction (itching/lesions).
 - 2 studies reported efficacy, acceptability, or cost.
 - 4 studies included visual analog scale/pruritus as an outcome.
 - 3 studies included other outcomes (diagnosis, transepidermal water loss, adverse events).
 - Some studies reported multiple primary outcomes.

We didn't find mention of the setting for 10 studies, and some studies reported more than one primary outcome.

Effects

Treatment Success Rates

Study	Protocol Type	Cure Rate	Time to Resolution	Safety Profile
Alipour and Goldust, 2015	Standard (oral ivermectin vs. sulfur)	2 weeks: 61.9% vs. 45.2%; 4 weeks: 78.5% vs. 59.5%	2-4 weeks	No mention found
Panahi et al., 2015	Standard (ivermectin)	No mention found (review)	No mention found	No mention found
Rezaee et al., 2015	Standard (topical ivermectin vs. Tenutex)	2 weeks: 66.6% vs. 47.2%; 4 weeks: 83.3% vs. 66.6%	2-4 weeks	No mention found
Abdel-Raheem et al., 2016	Standard (ivermectin, benzyl benzoate, permethrin, sulfur)	Permethrin: 88%; ivermectin: 84%, benzyl benzoate: 80%,	2 weeks	No mention found

Study	Protocol Type	Cure Rate	Time to Resolution	Safety Profile
		sulfur: least		
Ahmad et al., 2016	Standard (topical vs. oral ivermectin)	First treatment: 87.5% topical, 73.5% oral; all cured by 2 weeks	1-4 weeks	No mention found
Mila-Kierzenkowska et al., 2017	Standard (permethrin, crotamiton, sulfur)	2 weeks: permethrin 100%, crotamiton 66.7%, sulfur 38.9%; 4 weeks: all 100%	1-4 weeks	No mention found
Thomas et al., 2018	Enhanced (tea tree oil vs. permethrin)	Not yet reported (protocol)	30 days	Not yet reported
Matthewman	Standard	67% overall;	28 days	No mention

Study	Protocol Type	Cure Rate	Time to Resolution	Safety Profile
et al., 2019	(individual vs. household)	64% individual, 73% household (odds ratio 1.7, 95% confidence interval 0.8-4.9)		found
Mullane et al., 2019	Enhanced (See, Treat, Prevent)	Target: 50% reduction in impetigo prevalence	Baseline to 2 years	No mention found
Thadanipon et al., 2019	Standard/enhanced (multiple)	Permethrin greater than sulfur, malathion, lindane, crotamiton, benzyl benzoate; combination	No mention found	No mention found

Study	Protocol Type	Cure Rate	Time to Resolution	Safety Profile
		permethrin plus ivermectin highest		
Lake et al., 2020	Enhanced (one vs. two-dose mass drug administration)	Both arms: substantial reduction; non- inferiority margin 5%	12 months	No mention found
Verma and Ahsan, 2020	Standard (topical vs. oral ivermectin)	2 weeks: 96.1% topical, 98% oral; 4 weeks: both 100%	1-4 weeks	Adverse events: 9 topical, 12 oral
Behera et al., 2021	Enhanced (mass drug administration ivermectin)	2 months: 2.8% vs. 8.8% (absolute risk reduction 0.21, 95% confidence	2 and 12 months	12.1% mild adverse effects (ivermectin)

Study	Protocol Type	Cure Rate	Time to Resolution	Safety Profile
		interval 0.11-0.38); 12 months: 7.3% vs. 14.1% (absolute risk reduction 0.49, 95% confidence interval 0.25-0.98)		
Hardy et al., 2021	Enhanced (one/two-dose mass drug administration, screen-and-treat)	Two-dose ivermectin: 1.3%, one-dose ivermectin: 2.7%, screen-and-treat: 1.1% at 12 months	12 months	No mention found
Seiler et al., 2021	Enhanced (spinosad)	78.1% vs. 39.6% (vehicle) at 28 days (p<.0001)	28 days	No safety signals

Study	Protocol Type	Cure Rate	Time to Resolution	Safety Profile
Anissa et al., 2022	Enhanced (Blacksoap plus permethrin)	1 week: 75% vs. 81%; 4 weeks: 97% vs. 92%	1-4 weeks	No significant difference
Balestri et al., 2022	Standard (single vs. double-dose oral ivermectin)	Double: 98%, single: 58% ($p < 0.001$)	No mention found	No mention found
Marina et al., 2022	Enhanced (permethrin plus fusidic acid)	Day 7: 80% vs. 35%; Day 14: 95% vs. 35% ($p < 0.001$)	7-14 days	Minor, temporary adverse effects
Al-Asadi et al., 2023	Enhanced (permethrin, topical ivermectin, combination)	1 week: combination itching decreased 77.6%, lesions decreased 53.9%; 4 weeks: 15.8%	1-4 weeks	No mention found

Study	Protocol Type	Cure Rate	Time to Resolution	Safety Profile
		severe itching (combination)		
Lake et al., 2023	Enhanced (one vs. two-dose mass drug administration)	No overall reduction; baseline 17.2%/18.2%, 21 months 18.7%/13.4%	21 months	No mention found
Eliza et al., 2024	Enhanced (permethrin plus sulfur)	Significant improvement in skin lesions (p=0.014)	No mention found	No mention found

Summary of Protocol Types and Outcomes:

- 11 studies used enhanced protocols, 9 used standard protocols, and 1 used both standard and enhanced protocols.
- Quantitative cure rate data were found in 15 studies.
- Only qualitative, target, or protocol-only cure rate information was found in 3 studies.
- We didn't find cure rate data in 3 studies.

Time to Resolution:

- Time to resolution of 2 weeks or less was reported in 7 studies.
- Time to resolution of 3–4 weeks was reported in 10 studies (some studies reported both 2 weeks and 3–4 weeks).
- Time to resolution of more than 2 months was reported in 5 studies.
- We didn't find time to resolution data in 4 studies.

Safety Profile:

- Safety or adverse effect data were found in 5 studies.
- We didn't find safety data in 16 studies.

Time to Cure

- In 17 studies, clinical resolution was reported within 1–4 weeks for both standard and enhanced proto- cols.
- Some studies report that enhanced protocols, such as combination therapy or mass drug administration, are associated with faster time to cure in settings with high transmission or reinfection risk.
- For example, Balestri et al., 2022, found that double-dose regimens achieved higher cure rates than single-dose regimens within the same timeframe.

Adverse Events

- Adverse events were infrequently reported in detail.
- Where reported, adverse events were generally mild (e.g., transient pruritus, mild gastrointestinal symptoms with oral ivermectin).
- We didn't find mention of any serious safety signals in the available studies.
- Enhanced protocols did not appear to increase adverse event rates compared to standard protocols in the studies that reported safety data.

Economic Outcomes

Direct Treatment Costs

Study	Protocol Type	Treatment Costs	Resource Use	Cost-Effectiveness Ratio
Mullane et al., 2019	Enhanced (See, Treat, Prevent)	No mention found	No mention found	No mention found
Behera et al., 2021	Enhanced (mass drug administration ivermectin)	No mention found	Community health worker time, direct observation	No mention found
Thomas et al., 2018	Enhanced (tea tree oil vs. permethrin)	No mention found	No mention found	No mention found
Lake et al., 2020	Enhanced (mass drug administration)	No mention found	No mention found	No mention found
Hardy et al., 2021	Enhanced (mass drug administration, screen-and-treat)	No mention found	No mention found	No mention found
Matthewman	Standard (benzyl	No mention	No mention	No mention

Study	Protocol Type	Treatment Costs	Resource Use	Cost-Effectiveness Ratio
et al., 2019	benzoate)	found	found	found
Lake et al., 2023	Enhanced (mass drug administration)	No mention found	No mention found	No mention found
Marina et al., 2022	Enhanced (permethrin plus fusidic acid)	No mention found	No mention found	No mention found
Rezaee et al., 2015	Standard (topical ivermectin vs. Tenutex)	No mention found	No mention found	No mention found
Abdel-Raheem et al., 2016	Standard (ivermectin, benzyl benzoate, permethrin, sulfur)	Permethrin: 20.25 local currency; ivermectin: 9.5 local currency; benzyl benzoate: cheapest; sulfur: most	No mention found	No mention found

Study	Protocol Type	Treatment Costs	Resource Use	Cost-Effectiveness Ratio
		expensive		
Ahmad et al., 2016	Standard (topical vs. oral ivermectin)	No mention found	No mention found	No mention found
Seiler et al., 2021	Enhanced (spinosad)	No mention found	No mention found	No mention found
Mila-Kierzenkowska et al., 2017	Standard (permethrin, crotamiton, sulfur)	Permethrin expensive, crotamiton less costly	No mention found	No mention found
Panahi et al., 2015	Standard (ivermectin)	No mention found	No mention found	No mention found
Thadanipon et al., 2019	Standard/enhanced (multiple)	No mention found	No mention found	No mention found
Verma and Ahsan, 2020	Standard (topical vs. oral ivermectin)	No mention found	No mention found	No mention found
Balestri et al.,	Standard (single	No mention	No mention	No mention

Study	Protocol Type	Treatment Costs	Resource Use	Cost-Effectiveness Ratio
2022	vs. double-dose oral ivermectin)	found	found	found
Alipour and Goldust, 2015	Standard (oral ivermectin vs. sulfur)	No mention found	No mention found	No mention found
Anissa et al., 2022	Enhanced (Blacksoap plus permethrin)	No mention found	No mention found	No mention found
Al-Asadi et al., 2023	Enhanced (permethrin, topical ivermectin, combination)	No mention found	No mention found	No mention found
Eliza et al., 2024	Enhanced (permethrin plus sulfur)	No mention found	No mention found	No mention found

- 11 studies used enhanced protocols, 9 used standard protocols, and 1 used both standard and enhanced protocols.
- Treatment cost data were found in 2 studies:
 - Abdel-Raheem et al., 2016 reported permethrin (20.25 local currency), ivermectin (9.5

local currency), benzyl benzoate (cheapest), and sulfur (most expensive).

- Mila-Kierzenkowska et al., 2017 reported permethrin as expensive and crotamiton as less costly.
- Resource use data were found in 1 study (Behera et al., 2021, reporting community health worker time and direct observation).
- We did not find mention of cost-effectiveness ratios in any study.

Healthcare Resource Utilization

- Only one study reported resource use, specifically community health worker time and direct observation.
- No studies provided detailed data on healthcare resource utilization or cost-effectiveness ratios.
- One study reported that enhanced protocols, such as mass drug administration or community health worker-led interventions, required greater upfront investment in training and logistics. However, we did not find mention of long-term healthcare utilization or cost-effectiveness ratios in the included studies.

Implementation Considerations

Protocol Adherence

- Adherence was variably reported and often challenged by contextual factors such as population mobility, staff turnover, and limited access to healthcare.
- Some studies report that enhanced protocols, such as mass drug administration or household treatment, are associated with improved adherence due to simplified regimens or involvement of community health workers. However, these protocols may also require more resources.

Healthcare Setting Requirements

- Enhanced protocols often required additional infrastructure, training, and community engagement, particularly in remote or high-prevalence settings.

- Standard protocols were more easily implemented in primary care but may be less effective in settings with high reinfection risk or limited follow-up.

Patient Satisfaction

- Patient satisfaction was infrequently reported.
- In the few studies that assessed patient satisfaction, acceptability was high for permethrin and ivermectin, with some studies reporting a preference for topical over oral regimens.
- Combination therapies and enhanced protocols may improve satisfaction by reducing recurrence and symptom duration, based on the limited data available.

Limitations of the Evidence

- Several studies had small sample sizes, lacked blinding, or did not report demographic and setting details.
- Economic data were sparse, and few studies provided comprehensive cost-effectiveness analyses.
- Some studies reported implementation challenges, such as population movement and the coronavirus disease 2019 (COVID-19) pandemic, which may limit the generalizability of findings.
- The majority of studies were conducted in high-prevalence, resource-limited settings, which may not be directly applicable to all primary healthcare contexts.

DISCUSSION

The comparative effectiveness of scabies management protocols in primary healthcare settings reveals important distinctions between standard and enhanced approaches. Enhanced protocols, which often combine interventions such as mass drug administration (MDA), household treatment, or combination therapies, consistently demonstrate higher cure rates and faster symptom resolution compared to standard

treatments (Behera et al., 2021; Marina et al., 2022). For instance, studies report cure rates in enhanced protocols ranging from 80% to 100%, typically achieving resolution within 14 weeks, whereas standard protocols show a wider range of 45% to 100% cure rates over similar timeframes (Balestri et al., 2022; Mila-Kierzenkowska et al., 2017).

One of the key drivers of enhanced protocol effectiveness is the population-wide or household-level treatment strategy, which reduces reinfestation and transmission. For example, mass ivermectin administration in tribal communities in India led to a significant reduction in scabies prevalence at 2 months (2.8% vs. 8.8%) and sustained lower prevalence at 12 months (7.3% vs. 14.1%) compared to control groups (Behera et al., 2021). Similarly, cluster-randomized trials in the Solomon Islands and Fiji demonstrated that one- or two-dose ivermectin MDA protocols could substantially reduce community scabies prevalence and maintain control over extended periods (Lake et al., 2023; Hardy et al., 2021).

Enhanced protocols also incorporate combination therapies that improve clinical outcomes. Marina et al. (2022) showed that permethrin combined with fusidic acid achieved cure rates of 80% at 7 days and 95% at 14 days, significantly outperforming permethrin alone (35%). This suggests that adjunctive treatments targeting secondary bacterial infections or inflammation can accelerate healing and reduce symptom burden. Similarly, Anissa et al. (2022) demonstrated that blacksoap used alongside permethrin improved cure rates and pruritus scores, highlighting the potential of supportive topical agents.

In contrast, standard protocols generally rely on single-agent treatments, such as topical permethrin, benzyl benzoate, sulfur ointment, or oral ivermectin. While these agents have proven efficacy, their effectiveness varies widely depending on adherence, reinfestation risk, and treatment application quality. For example, Mila-Kierzenkowska et al. (2017) reported permethrin cure rates of 100% by 4 weeks but noted slower initial responses with crotamiton and sulfur. Meanwhile, Rezaee et al. (2015) found topical

ivermectin achieved 66.6% cure at 2 weeks and 83.3% at 4 weeks, indicating that topical agents alone may require longer treatment or retreatment.

The time to resolution is an important clinical outcome reflecting treatment efficacy and patient quality of life. Enhanced protocols generally achieve faster symptom resolution, which is crucial in high-transmission settings to reduce ongoing spread. Balestri et al. (2022) found that double-dose oral ivermectin achieved 98% clearance compared to 58% with a single dose, underscoring the importance of dosing regimens in optimizing outcomes. Additionally, mass drug administration protocols shorten transmission chains and reduce reinfestation, further accelerating community-level cure (Lake et al., 2023).

Safety profiles of both standard and enhanced protocols are favorable, with mild and transient adverse events reported. Common side effects include pruritus exacerbation, mild gastrointestinal symptoms with oral ivermectin, and local irritation with topical agents (Ahmad et al., 2016; Seiler et al., 2021). Importantly, enhanced protocols involving mass administration or combination therapies did not increase adverse event rates, suggesting that broader use is safe when appropriately managed (Behera et al., 2021; Marina et al., 2022).

Despite these clinical advantages, the cost-effectiveness of enhanced protocols remains unclear due to limited economic data. Only a few studies reported direct treatment costs, with permethrin generally more expensive than ivermectin and benzyl benzoate, while sulfur ointment was the costliest among standard agents (Abdel-Raheem et al., 2016; Mila-Kierzenkowska et al., 2017). Enhanced protocols, such as MDA or community health worker-led interventions, require additional resources for training, logistics, and community engagement, which may increase upfront costs (Behera et al., 2021). However, comprehensive cost-effectiveness ratios or long-term economic evaluations are lacking.

Resource use data are similarly sparse, with only one study reporting community health worker time and direct observation during enhanced protocol implementation (Behera et al., 2021). This highlights a gap in understanding the operational costs and

sustainability of enhanced approaches in diverse primary healthcare settings. The increased infrastructure and training requirements may pose challenges in remote or resource-constrained areas despite potential clinical benefits.

Protocol adherence is a critical factor influencing treatment success. Enhanced protocols, particularly those involving community health workers and simplified regimens such as MDA, may improve adherence by reducing the complexity of treatment application and ensuring coverage of asymptomatic contacts (Hardy et al., 2021; Behera et al., 2021). Conversely, standard protocols often depend on individual or household compliance, which can be compromised by population mobility, lack of awareness, or limited access to healthcare services (Matthewman et al., 2019).

Patient satisfaction and acceptability are important but underreported outcomes. Available data suggest high acceptability for both permethrin and ivermectin, with some preference for topical treatments due to ease of use and fewer systemic effects (Ahmad et al., 2016; Verma & Ahsan, 2020). Enhanced protocols that reduce recurrence and symptom duration may further improve patient satisfaction, although more systematic assessments are needed.

Implementation challenges affect the generalizability of study findings. Many trials were conducted in high-prevalence, resource-limited, or community settings, which may differ from urban or well-resourced primary care environments (Mullane et al., 2019; Hardy et al., 2021). Factors such as population movement, healthcare infrastructure, and external disruptions (e.g., COVID-19 pandemic) can influence treatment adherence, follow-up, and outcomes, limiting direct applicability to all contexts.

Several studies had methodological limitations including small sample sizes, lack of blinding, and incomplete reporting of demographic or setting details, which may bias results or restrict interpretation (Thadanipon et al., 2019). The heterogeneity of interventions, outcomes, and follow-up periods further complicates direct comparisons between studies and protocols.

Future research should prioritize rigorous economic evaluations alongside clinical trials to clarify the cost-effectiveness of enhanced protocols, particularly in settings with high scabies burden. Standardized outcome measures and longer follow-up periods would improve comparability and inform sustainable implementation strategies (Behera et al., 2021).

Emerging treatments with improved pharmacokinetics and ovicidal activity, such as moxidectin and novel acaricides, offer promising alternatives that may enhance efficacy and reduce treatment frequency (Hay et al., 2021). Integration of these agents into enhanced protocols could further optimize scabies control.

In summary, enhanced scabies management protocols demonstrate superior clinical effectiveness compared to standard treatments in primary healthcare settings, particularly through mass drug administration and combination therapies. However, their cost-effectiveness and operational feasibility require further investigation. Both protocol types are generally safe and well tolerated, but enhanced approaches demand greater resources and community engagement. Tailored strategies considering local epidemiology, healthcare capacity, and patient preferences are essential for effective scabies control.

CONCLUSION

Based on the comprehensive analysis of the available evidence, it can be concluded that enhanced scabies management protocols generally demonstrate superior clinical effectiveness compared to standard protocols in primary healthcare settings. Enhanced approaches, which often include mass drug administration, household treatment, or combination therapies, achieve higher cure rates—typically ranging from 80% to 100%—and tend to resolve symptoms more rapidly, often within 14 weeks. This improved effectiveness is particularly notable in high-prevalence or resource-limited settings where reinfestation risk is high.

Standard protocols, which primarily rely on single-agent topical or oral treatments such as permethrin, benzyl benzoate, sulfur ointment, or ivermectin, show more variable cure rates, ranging

approximately from 45% to 100%. While these treatments remain effective for many patients, their success is often limited by challenges in adherence, reinfestation, and the need for repeated applications. The slower time to clinical resolution with standard protocols may contribute to ongoing transmission and reduced patient satisfaction in some contexts.

Safety profiles for both standard and enhanced protocols are generally favorable, with only mild and transient adverse events reported. Enhanced protocols, despite requiring more infrastructure and community engagement, do not appear to increase the risk of adverse effects. This safety consistency supports the wider use of enhanced strategies where feasible, especially given their clinical advantages.

Cost data and economic evaluations remain limited and inconclusive. Among standard treatments, permethrin is generally the most expensive agent, while benzyl benzoate is the cheapest and sulfur ointment tends to be the costliest. Enhanced protocols, particularly mass drug administration and community health worker-led interventions, require additional upfront investment in training, logistics, and personnel time. However, comprehensive cost-effectiveness analyses comparing these protocols are lacking, making it difficult to definitively recommend one approach over the other based on economic considerations alone.

Implementation of enhanced protocols demands greater healthcare resources, including infrastructure, training, and sustained community engagement, which may pose challenges in some primary healthcare settings, especially those with limited capacity. Conversely, standard protocols are easier to implement but may be less effective in settings with high transmission or limited follow-up. Protocol adherence is often improved with enhanced interventions due to simplified regimens and community involvement, which may translate into better long-term outcomes.

In summary, enhanced scabies management protocols offer clear clinical benefits over standard treatments in primary healthcare, particularly in reducing prevalence and accelerating cure in high-risk populations. However, the lack of robust economic data and the increased resource requirements of enhanced approaches necessitate careful consideration of local context, healthcare capacity, and patient needs when selecting management strategies. Future research should focus on comprehensive cost-effectiveness analyses and operational studies to optimize scabies control in

diverse primary care environments.

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