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SYSTEMATIC REVIEW

Systematic review of the evidence for treatment and management of common skin conditions in resource-limited settings: An update

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Abstract

Introduction: The skin is the largest and most visible organ of the human body. As such, skin infections can have a significant impact on overall health, social wellbeing and self-image. In 2019, we published a systematic review of the treatment, prevention and public health control of skin infections including impetigo, scabies, crusted scabies and tinea in resource-limited settings where skin infections are endemic. This current review serves as an update to assess the evidence for treatment of these conditions as well as atopic dermatitis, molluscum contagiosum and head lice in endemic settings. The data from this systematic review have supported an update to the Australian National Healthy Skin guidelines.

Methods: A systematic review was conducted using two separate searches in MEDLINE, PubMed, Embase, CINAHL, Cochrane and Web of Science. The first search

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was an update of the 2018 systematic review using the same search strategy for the same skin conditions to identify emerging literature from 2018 to 2022. The second search strategy used the same key terms but with the addition of atopic dermatitis, head lice and molluscum contagiosum from 1960 to 2022. Eligible studies included Indigenous peoples and populations in resource-limited settings with a diagnosis of impetigo, scabies, crusted scabies, tinea capitis, atopic dermatitis, molluscum contagiosum or who presented with head lice. Studies conducted in high-income countries were excluded. Articles were screened for inclusion independently by one author with a second group of reviewers independently double screening. Data extraction and an in-depth quality assessment conducted by one author and checked by two others.

Results: Of 1466 original articles identified, 68 studies were included and key findings outlined for impetigo, scabies, crusted scabies, atopic dermatitis, head lice and molluscum contagiosum. Recommendations for each condition based on the available evidence are provided.

Conclusion: The importance of assessing literature relevant to the populations with heavy burden of skin infections is outlined in this systematic review. We have summarised updates to this literature, which may benefit in developing guidelines for skin infection management similar to the National Healthy Skin Guidelines for Australia.

KEYWORDS

atopic dermatitis, crusted scabies, head lice, impetigo, management, molluscum contagiosum, scabies, systematic review, treatment

INTRODUCTION

The skin is the largest organ of the body and is commonly visible, particularly on the arms and legs of children. As such, skin infections can have a significant impact on overall health, wellbeing and self-image. Indigenous peoples' cultures and knowledge have existed globally for tens of thousands of years. These cultures and knowledge inform world-leading comprehensive healthcare models that meet the holistic needs of respective communities. Such models and services are a critical part of healthcare to address challenges that have arisen for Indigenous peoples through the colonisation, genocide and dispossession that has occurred in recent centuries. Indigenous children in colonised nations experience high rates of health disparities linked to historical trauma resulting from displacement and dispossession, as well as ongoing systemic racism [1]. Skin infections and their complications are one such health inequity, with some of the highest global burdens described in remote-living Aboriginal and/or Torres Strait Islander children in Australia [2].

In 2019, May et al. published a systematic review of the treatment, prevention and public health control of skin infections including impetigo, scabies, crusted scabies and tinea in resource-limited settings where skin infections are endemic [3]. This current review serves as an update to assess the evidence for treatment of these conditions as well as atopic dermatitis (AD), molluscum contagiosum (MC) and head lice in endemic settings. Whilst other skin conditions (e.g., leprosy and cutaneous mycoses), often known as Neglected Tropical Dermatoses, affect Indigenous peoples in resource limited settings, we have chosen to focus on highly prevalent skin conditions and those common in Australia.

The data from this systematic review arise from resource-limited settings but the focus of the outcomes is for Indigenous communities in Australia and has supported an update to the Australian National Healthy Skin guidelines [4] published in 2023.

Impetigo, scabies and crusted scabies

Observational studies over two decades in remote northern Australia have found that Aboriginal children living in remote communities of Australia have the highest burden of impetigo worldwide [5]. The median prevalence of impetigo in Aboriginal children living in remote Australia is 45% (interquartile range [IQR], 34%–49%), surpassing Africa (7% [IQR 4%–12%]), Asia (7% [IQR 3%–16%]) and Oceania (30% [IQR 15%–42%]) [5]. Scabies has a similarly high burden, with up to 35% of children affected at any one time [5]. Although rare in urban settings of Australia, crusted scabies is a notifiable disease in remote Aboriginal communities in the Northern Territory (NT) of Australia [6]. The global incidence rates for crusted scabies are yet to be described. Scabies outbreaks with secondary bacterial infection are common when war or famine lead to refugee migration and crowded living conditions [7].

Tinea

The World Health Organization has estimated that 7%–33% of children in resource-limited countries are affected by scalp tinea [8], and 11% are affected by nail tinea [9]. Estimates of the tinea burden in Australia are not well established [10]; however, tinea was recorded in 7% of children prospectively assessed for skin infections on admission to

hospital in Western Australia (WA) [11], and 4.3% of those participants had skin sores [12].

Atopic dermatitis

AD is the most common chronic inflammatory skin condition in children and young people (CYP); however, its prevalence varies across countries, geographic regions and genetically similar populations [13, 14]. The population prevalence of AD in Australia in 2017 was estimated to be 20.3% in 1-year-olds [15] and 16% in 4-year olds in 2013 [16]. A higher AD prevalence is generally observed in urban settings relative to rural populations [13, 17]. Current and severe symptoms of AD were more prevalent in urban-living Indigenous CYP in high-income countries globally than their non-Indigenous peers [18]. This implicates environmental factors (i.e., industrialisation and an urban lifestyle) in the pathogenesis of AD [14].

Head lice

Head lice are a common and costly global public health problem [19], that is notably high in resource-limited settings characterised by poverty and overcrowding. In a study in a rural community in the Solomon Islands, baseline prevalence of active head lice infestation was 25.4% and prevalence of head lice eggs was 42.3% [20]. In another study in rural Honduras, baseline head lice prevalence was 83% [21]. Whilst there are no published studies on the prevalence of head lice in remote Australia, the See, Treat, Prevent (SToP) Trial [22] measured the considerable burden of head lice in remote Kimberley communities of WA. These results are yet to be published. Breaks in the epidermis of the scalp due to severe itching can lead to secondary bacterial skin infections [23], as has been described in remote-living Aboriginal children [24].

Molluscum contagiosum

MC is a common viral infection caused by a poxvirus (molluscum contagiosum virus [MCV]) [25]. It is seen most often in children, AD sufferers and the immunocompromised. While typically asymptomatic, MC lesions can be itchy and infection may induce surrounding eczema. MC papules can also occasionally become secondarily infected with bacteria. Molluscum contagiosum has been included in this review due to the frequency of it being found in children, the risk of secondary bacterial infections, and community consultations which identified this as a common but poorly understood condition.

Consequences of untreated skin conditions

Whilst the incidence of complications from skin infections has declined in children from more affluent populations, people living in resource-poor settings are at substantial risk of infective complications and post-streptococcal sequelae [26]. Left untreated, skin infections can have serious consequences leading to group A streptococcal (GAS) and staphylococcal sepsis [27], bone and joint infections [28], and pneumonia [29], as well as post-infectious sequelae including acute post-streptococcal glomerulonephritis (APSGN) [30] and potentially acute rheumatic fever (ARF) which progresses to rheumatic heart disease (RHD) in some individuals [31]. GAS-related kidney disease and RHD occur in Australian Aboriginal people at among the highest rates in the world [32]. In Australia and New Zealand, *Staphylococcus aureus* sepsis has a mortality rate between 3% and 5% in children aged under 18 years, with higher incidence and poorer outcomes in Indigenous children compared to non-Indigenous children in the same settings [33]. Scabies has been found to be an important predisposing condition for fatal staphylococcal sepsis [34].

METHODS

Design

This systematic review is reported in accordance with the Preferred Reporting items for Systematic Reviews and Meta-Analyses (PRISMA) statement [35]. The review is registered with PROSPERO (International prospective register of systematic reviews) at the National Institute for Health Research and Centre for Reviews and Dissemination at the University of York (registration ID CRD42022343076).

Search strategy and data sources

Two separate searches were conducted in MEDLINE, PubMed, Embase, CINAHL, Cochrane and Web of Science. The first search was an update of the 2018 systematic review [3] using the same search strategy for the same skin conditions to identify emerging literature from 2018 to 2022 (Appendix A). The second search strategy used the same key terms but with the addition of AD, head lice and MC from 1960 to 2022 (Appendix B). Filters in Medline were (1) Humans, and (2) English language. Search terms and filters were tailored to each subsequent database, as required. Reference lists from included studies and relevant systematic reviews and meta-analyses were hand searched for additional eligible studies.

Eligibility criteria

Eligible participant types included Indigenous peoples and populations in resource-limited settings (low, low–middle and middle-income countries and resource-limited populations in Organisation for Economic Cooperation and Development [OECD] countries) [36] with a diagnosis of impetigo, scabies,

crusted scabies, tinea capitis, AD, MC or who presented with head lice (skin conditions which are common in Australia). Studies conducted in high-income countries were excluded. Any experimental or observational study designs were eligible for inclusion. The review included any clinical intervention aimed at reducing skin infections with any type of comparator.

Study selection, data extraction and management

Search results were imported into Endnote X7 software, duplicates removed and then exported into Covidence (Veritas Health Innovation, Melbourne, VIC, Australia). One reviewer (IAD) screened all titles and abstracts for eligibility, with a second group of reviewers (TP, KW, GK) independently double screening. Following this, the full texts of potentially relevant articles were retrieved where available, which were again reviewed by the first author (IAD) and a second group of reviewers (TP, KW, GK) independently. Exclusions were documented only for articles that required full-text to make a formal decision. Inter-reviewer disagreement on included studies was discussed with the scientific advisory group to resolve any discrepancies. Data was extracted by a single reviewer (IAD) using an electronic proforma, with another two reviewers (AB and HT) providing oversight.

Risk of bias assessment

Risk of bias was assessed for all studies by one reviewer (IAD), with another two reviewers (HT and AB) completing a random 10% sample of the studies. Clinical trials were assessed using The Cochrane risk of bias tool [37] comprising assessment of random sequence generation, allocation concealment, blinding of participants, personnel and outcome assessors, incomplete outcome data and other sources of bias that may have affected the results. Observational studies were assessed using the ROBINS-E tool [38]. Any discrepancies between reviewer scores were settled by discussion among reviewers or taken to the Scientific Advisory Group meetings for resolution.

Data synthesis

The data are presented in a narrative synthesis. Meta-analysis was not performed due to the heterogeneity of studies. For reading ease, results are presented in common theme groups in each area of clinical treatment relevant to skin infections in resource-limited settings. As many population-based studies incorporate multiple strategies such as health education, treatment and hygiene practices, it is recommended that all evidence is considered by the reader as a whole.

A comprehensive set of synthesised quantitative findings are presented which forms the basis for development of future guidelines. The Grading of Recommendations, Assessment, Development and Evaluation (GRADE) approach [39] was employed to rate evidence across studies for specific clinical outcomes to link evidence-quality evaluations to recommendations in clinical guidelines (Appendix C).

RESULTS

The updated database search yielded 1411 records, and an additional 55 were found through the hand search. After removal of 75 duplicates and 1163 records through title and abstract screening, we reviewed 228 full text papers and subsequently excluded 160, resulting in 68 studies included in the systematic review (Figure 1).

Characteristics of included studies

The study details and characteristics are summarised in Table 1.

Summary of clinical treatment recommendations for resource-limited settings

In this section studies are grouped according to the skin condition under study and the intervention type.

The quality score for each domain as well as the overall quality rating based on consensus of experts are summarised for experimental studies in Appendix D and likewise for observational studies in Appendix E. Of the 48 experimental trials that were included, 3 (5%) were high-quality RCTs, 28 (58%) were of moderate quality and 17 (35%) were low quality. Two observational studies were rated high quality, four moderate quality and the remaining eight were of low quality.

Results are provided in detail and quality scores for each study according to the GRADE system are provided with these study results. Recommendations from both the original systematic review and any new evidence are reported. The updated evidence summaries from the current review can be found in Appendix F.

Impetigo

Directed antimicrobial therapy

There is high-quality evidence to support the use of oral trimethoprim-sulfamethoxazole (SXT) or intramuscular benzathine penicillin G (BPG) for the treatment of impetigo in resource-limited settings (GRADE 1A) [3]. Oral trimethoprim-sulfamethoxazole has fewer side effects. In an RCT [12], 49 of 160 (31%) recipients of BPG reported side

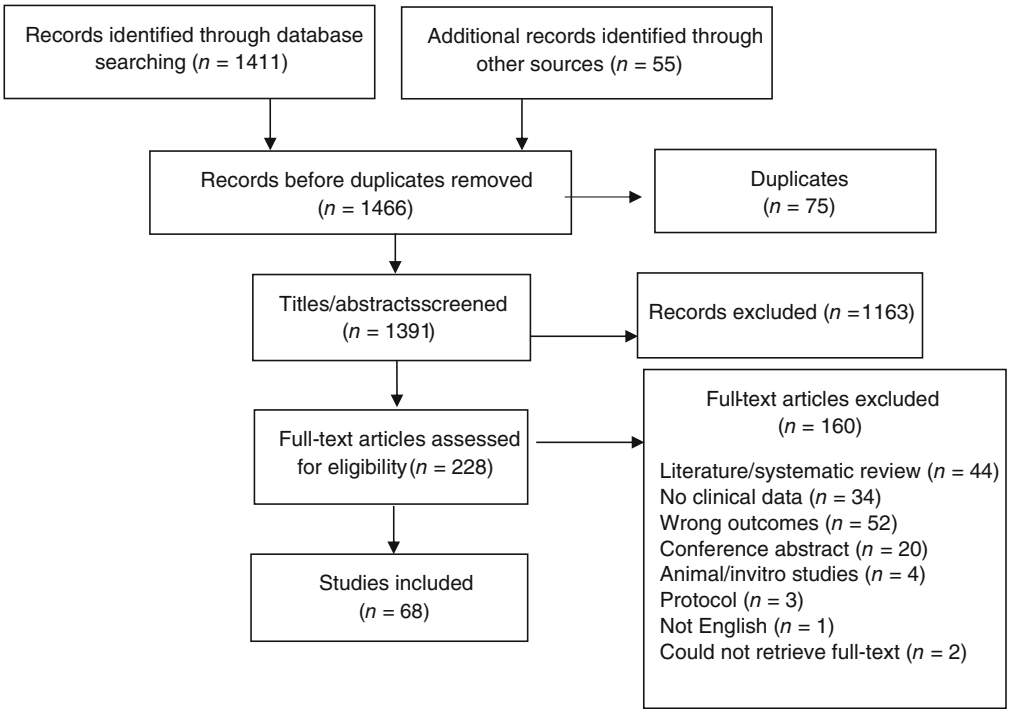

FIGURE 1 PRISMA flow diagram of search results.

effects including injection site abscess ($n = 1$), pain requiring analgesia ($n = 10$) and pain at 48 h (48/160; 30%). In contrast, 5 of 343 (2%) SXT recipients had side effects including inability to tolerate large volumes of syrup, but tolerated tablets ($n = 3$), vomiting (n = 1) and rash (n = 1). There is moderate quality evidence to support the use of oral amoxicillin and oral erythromycin as suitable alternatives in resource limited settings, with amoxicillin having the more favourable safety profile (GRADE 2B) [3]. Oral penicillin G is not recommended for treatment of impetigo in resource-limited settings due to limited low-quality evidence (GRADE 2D) [3]. There is low-quality evidence to support the use of topical fusidic acid 2% or topical mupirocin 2% in resource-limited settings (GRADE 2C) [40].

Hygiene practices

High-quality evidence supports daily hand washing with soap for the treatment and prevention of impetigo in resource-limited settings. There is no added benefit to the use of antibacterial soap over regular soap (GRADE 1A) [3].

Scabies

Directed anti-parasitic therapy

Topical treatment versus topical treatment

There is low to moderate quality evidence to recommend the use of topical permethrin [41–45] (GRADE 2B) in the treatment of scabies. Permethrin is superior to lindane (GRADE 1A) [3], topical crotamiton (GRADE 2C) [41] or tenutex emulsion (disulphiram and benzyl benzoate [BB]) in those >4 years of age (GRADE 2C) [3]. There is moderate quality evidence to recommend the use of topical ivermectin (GRADE 2B) [42, 46]. Topical ivermectin is superior to topical crotamiton in those >2 years of age (GRADE 2C) [3]. Very low-quality shows that topical benzyl benzoate or topical permethrin is safe in pregnant women living in resource-limited settings (GRADE 2C) [3]. As there is no high-quality evidence to support modified applications of topical treatments for scabies over standard treatment regimens in resource-limited settings, the standard application of whole-body treatment remains strongly recommended (GRADE 1D) [3].

Oral versus topical treatment

There is moderate to high-quality evidence supporting the use of oral ivermectin (GRADE 1A) [43–47] or topical permethrin (GRADE 2B) [41–45, 48] for the treatment of scabies.

Oral ivermectin is superior to topical permethrin and standard of care for community-wide use in children >5 years of age and non-pregnant adults in isolated settings with high prevalence of scabies and impetigo (GRADE 1B) [3]. High-quality studies conducted in mainland populations are required to determine the effectiveness of the MDA approach in highly mobile populations.

Oral ivermectin alone

There is high-quality evidence supporting the use of oral ivermectin for the treatment of scabies (GRADE 1A) [3].

TABLE 1 Table of characteristics ($n = 68$).

Study	Country	Study design	Setting	Sample size	Age group	Treatment arms
Impetigo						
Rani, 2019	India	PC	Hospital	100	Adults and children	**Arm 1**: Fusidic acid 2%[1] **Arm 2**: Mupirocin 2%[1]
Scabies						
Dey, 2022	India	RCT	Hospital	120	NR	**Arm 1**: Permethrin 1%[1] + Vitamin B complex (placebo)[1] **Arm 2**: Placebo cream[1] + Ivermectin[2] **Arm 3**: Gamma benzene hexachloride[1] + vitamin B complex (placebo)[2] **Arm 4**: 5% permethrin[1] + ivermectin[2] + placebo Vitamin B complex[2]
Marina, 2022	Indonesia	RCT	Schools: two Islamic boarding schools	40	Children	**Arm 1**: 5% permethrin-2% fusidic acid cream[1] **Arm 2**: 5% permethrin-placebo (glycerol-based cream) [1]
Hardy, 2021	Fiji	RCT (MDA)	Community	3812	Adults and children	**Arm 1**: 1-dose Ivermectin [2] **Arm 2**: 2-dose Ivermectin[2] **Arm 3**: 1-dose Permethrin[1]
Usman, 2021	Pakistan	RCT	Hospital	200	Adults	**Arm 1**: Ivermectin 1%[1] **Arm 2**: Permethrin 5%[1]
Verma, 2021	India	RCT	Hospital	101	Adults	**Arm 1**: Ivermectin 0.5%[1] **Arm 2**: Ivermectin[2]
Kawen, 2020	Iraq	RCT	Hospital (outpatient)	373	Adults and children	**Arm 1**: 1% Ivermectin[2] + 5% permethrin[1] **Arm 2**: 5% Permethrin[1]
Matthewman, 2020	Gabon	RCT	Community	104	Adults and children	**Arm 1**: Benzyl benzoate (Individual Treatment) [1] **Arm 2**: Benzyl benzoate (household Treatment) [1]
Babu, 2019	India	RCT	Hospital	178	Adults and children	**Arm 1**: Permethrin 5%[1] **Arm 2**: Ivermectin[2]
Ibraheem, 2019	Iraq	RCT	Community: 7 camps of internally displaced population	195	Adults	**Arm 1**: Permethrin 10%[1] **Arm 2**: Crotamiton 10%[1] **Arm 3**: Sulphur 10% **Arm 4**: Permethrin 10% + Sulphur 10% **Arm 5**: Crotamiton 10% + Sulphur 10% **Arm 6**: Crotamiton 10% + Permethrin 10% **Arm 7**: Placebo
Scabies and impetigo						
Thean, 2022	Fiji	Before-after (MDA)	Community	1st Rx: 135,744 (97% coverage) 2nd Rx: 121,760 (87% coverage)	Not specified	Ivermectin[2] (or Permethrin 5%[1] for individuals whom ivermectin was contraindicated)
Behera, 2021	India	RCT (MDA)	Community	2526	Adults and children	**Arm 1**: Ivermectin[2] **Arm 2**: Usual care
Marks, 2019	Solomon Islands	RCT (MDA)	Community	1291	Adults and children	**Arm 1**: Ivermectin[2] **Arm 2**: Ivermectin[2] + azithromycin[2]
Romani, 2019	Solomon Islands	Before-after (MDA)	Community	1399	Adults and children	Azithromycin Ivermectin[2] (or Permethrin 5%[1] for individuals whom ivermectin was contraindicated)

TABLE 1 (Continued)

Study	Country	Study design	Setting	Sample size	Age group	Treatment arms
Tinea						
Abdullah, 2022	Egypt	RCT	Hospital	52	Children	**Arm 1**: Cur-PDT **Arm 2**: Curcumin[1] **Arm 3**: Blue light **Arm 4**: Griseofulvin[2]
Kowser, 2022	India	RCT	Hospital	30	Adults	**Arm 1**: Anti-microbial soap[1][cited 20 May 16]. **Arm 2**: Placebo soap
Ramesh, 2022	India	RCT	Hospital (outpatient)	60	Adults	**Arm 1**: Terbinafine[2] + itraconazole[2] **Arm 2**: Terbinafine[2] + Griseofulvin[2]
Dakhale, 2021	India	RCT	Hospital (outpatient)	59	Adults	**Arm 1**: Sertaconazole 2%[1] **Arm 2**: Luliconazole 1%[1]
Fonseka, 2021	Sri Lanka	RCT	Outpatient dermatology clinic	30	Adolescents and adults	**Arm 1**: Modified Whitfield Ointment (5% benzoic acid and 5% salicylic acid)[1] **Arm 2**: Emulsifying ointment[1]
Gideon, 2021	India	RCT	Hospital	100	Adults	**Arm 1**: Terbinafine[1] **Arm 2**: Miconaole[1]
Meghana, 2021	India	RCT	Research institute	60	Adults	**Arm 1**: Terbinafine 1%[1] **Arm 2**: Sertaconazole 2%[1]
Ravichandran, 2021	India	RCT	Hospital (outpatient)	85	Adults	**Arm 1**: Sertaconazole 2%[1] **Arm 2**: Eberconazole 1%[1]
Shenoy, 2021	India	RCT	Hospital (outpatient)	59	Adults	**Arm 1**: Conventional Itraconazole[2] **Arm 2**: Super Bioavailable Itraconazole[2]
Eusebio-Alpapara, 2020	Philippines	Clinical case series	Outreach skin clinic	20	Adults	All *Senna alata* leaf decoction[1]
Singh, 2020a	India	RCT	A tertiary-care healthcare centre	200	Adults and children	**Arm 1**: Fluconazole[2] **Arm 2**: Griseofulvin[2] **Arm 3**: Itraconazole **Arm 4**: Terbinafine
Singh, 2020b	India	RCT	A tertiary healthcare centre	275	Adolescents and adults	**Arm 1**: Terbinafine 250 mg/day[2] **Arm 2**: Itraconazole 200 mg/day[2] **Arm 3**: Terbinafine 250 mg + Itraconazole 200 mg/day **Arm 4**: Terbinafine 500 mg/day **Arm 5**: Itraconazole 400 mg/day
Bhatia, 2019	India	RCT	NR	320	Adults	**Arm 1**: Terbinafine[2] **Arm 2**: Itraconazole[2]
Prabha, 2019	India	RCT	Dermatology outpatient clinic	100	Adolescents and adults	**Arm 1**: 1% luliconazole[1] **Arm 2**: 1% clotrimazole[1]
Das, 2018	India	RCT	Hospital (outpatient)	66	Adults	**Arm 1**: Amorolfine 0.25%[1] **Arm 2**: Sertaconazole 2%[1]
Singh, 2018	India	PC	Hospital	500	Adults and children	Terbinafine oral[2] + Terbinafine topical[1] 1%
Atopic dermatitis						
Novianto, 2022	Indonesia	RCT	Hospital	26	Adults and children	**Arm 1**: Cimetidine[2] **Arm 2**: Placebo
Sivapiromrat, 2021	Thailand	RCT	University	26	Children	**Arm 1**: Shea butter-ceramide cream[1] **Arm 2**: 1% hydrocortisone[1]

(Continues)

TABLE 1 (Continued)

Study	Country	Study design	Setting	Sample size	Age group	Treatment arms
Mansour, 2020	Egypt	RCT	Research institute	86	Children	**Arm 1**: vitamin D3[2] + 1% hydrocortisone[1] **Arm 2**: Placebo[2] + 1% hydrocortisone[1]
Dwiyana, 2019	Indonesia	RCT	Hospital (outpatient) and school	20	Children	**Arm 1**: 20% sunflower seed oil[1] **Arm 2**: Moisturising cream (placebo)[1]
Hung, 2019	China	PC	NR	30	Adults and children	Pure silk clothing
Agrawal, 2018	India	Quasi-experimental	Hospital	60	Adults and children	**Arm 1**: Betamethasone valerate 0.1%[1] **Arm 2**: Narrowband ultraviolet B (NB-UVB) therapy
Ordonez Rubiano, 2018	Colombia	RC	Tertiary care hospital and a phototherapy centre	317 medical records	Adults and children	Previously treated with UVA-1 phototherapy
Sanchez-Armendairiz, 2018	Mexico	RCT	Hospital	58	Adults and children	**Arm 1**: Vitamin D3[2] **Arm 2**: Placebo[2]
Abbasi, 2017	Iran	RCT	Hospital	45	Children	**Arm 1**: Hydrocortisone 1%[1] **Arm 2**: Melfi cream (aqueous extract of *Ficus carica* 8%)[1] **Arm 3**: Placebo
Jaffary, 2015	Iran	RCT	Hospital	70	Adults and children	**Arm 1**: Vitamin E[2] **Arm 2**: Placebo[2]
Evangelista, 2013	Philippines	RCT	Medical centre: Dermatology Outpatient	117	Children	**Arm 1**: Virgin coconut oil[1] **Arm 2**: Mineral oil[1]
Wong, 2013	Malaysia	RCT	Hospital	36	Adults and children	**Arm 1**: Diluted sodium hypochlorite (bleach) bath **Arm 2**: Distilled water bath
El-Khalawany, 2012	Egypt	RCT	Hospital	40	Children	**Arm 1**: Methotrexate[2] **Arm 2**: Cyclosporine[2]
Atakan, 1998	Turkey	PC	NR	22	Adults and children	Sandimmun Neoral[2]
Head lice						
Hamedanian, 2021	Iran	RCT	NR	179	Adults and children	**Arm 1**: Ivermectin lotion[1] **Arm 2**: Permethrin shampoo[1] **Arm 3**: Dimethicone lotion[1]
Kassiri, 2020	Iran	RCT	Primary schools	444	Children	**Arm 1**: Permethrin 1% shampoo[1] **Arm 2**: Lindane 1% shampoo[1] **Arm 3**: Dimeticone 4% lotion[1] **Arm 4**: Placebo shampoo[1]
Coscione, 2018	Solomon Islands	Before-after (MDA)	Community	118	Adults and children	Ivermectin[2]
Soleimani-Ahmadi, 2017	Iran	RCT	Community—six villages in Iran	300	Children	**Arm 1**: 1% permethrin shampoo[1] **Arm 2**: No treatment
Leulmi, 2016	Senegal	RCT	Community—two villages in Senegal	440	Adults and children	**Arm 1**: Ivermectin[2] **Arm 2**: Shampoo (based on D-phenothrin; synthetic pyrethroid)[1]
Ahmad, 2014	Egypt	RCT	Hospital	62	Adults and children	**Arm 1**: Ivermectin[1] **Arm 2**: Ivermectin[2]
Shahraki, 2013	Iran	RCT	Primary schools	1242	Children	**Arm 1**: Permethrin 1% shampoo[1] **Arm 2**: Lindane 1% shampoo[1] **Arm 3**: Placebo shampoo[1]

TABLE 1 (Continued)

Study	Country	Study design	Setting	Sample size	Age group	Treatment arms
Aktürk, 2012	Turkey	PC	Primary school	681	Children	1% permethrin shampoo[1]
Ameen, 2010	Mexico	PC	Community: Two rural Indigenous communities in Mexico	44	Children	Ivermectin[2]
Nofal, 2010	Egypt	RCT	University hospital	80	Children	**Arm 1**: Ivermectin[2] **Arm 2**: 0.5% malathion[1]
Pilger, 2010	Brazil	RCT	Community: A slum in north-eastern Brazil	132	Children	**Arm 1**: Ivermectin[2] **Arm 2**: No treatment
Chouela, 1997	Argentina	PC (MDA)	Kindergarten and primary school	310	Adults and children	A neutral shampoo and 1% permethrin rinsing cream[1]
Molluscum contagiosum						
Khan, 2022	Pakistan	RCT	Hospital	60	Children	**Arm 1**: Adapalene 0.1%[1] **Arm 2**: Trichloroacetic acid 30%[1]
Kumar, 2021	India	Randomised case–control	Outpatient dermatology	40	Adults and children	**Arm 1**: Povidone iodine[1] **Arm 2**: 0.05% tretinoin[1]
Khattab, 2020	Egypt	RCT	Hospital (outpatient)	40	Adults and children	**Arm 1**: Cantharidin[1] **Arm 2**: Tuberculinpurified protein derivatives (PPDs) (injection)
Nguyen Huu, 2019	Vietnam	RCT	NR	70	Children	**Arm 1**: 10% KOH solution[1] **Arm 2**: Salicyclic Acid ointment[1]
Ozturk, 2019	Sudan	RCT	Dermatology Outpatient clinic	101	Children	**Arm 1**: 10% KOH solution[1] **Arm 2**: 16.7% salicylic acid +16.7% lactic acid[1]
Al-Sudany, 2016	Iraq	RCT	Hospital	52	Adults and children	**Arm 1**: 10% KOH solution[1] **Arm 2**: 25% podophyllin solution[1]
Kashif, 2016	Pakistan	RCT	Hospital	60	Children	**Arm 1**: Trichloroacetic acid 35%[1] **Arm 2**: Adapalene 0.1%[1]
Qureshi, 2016	Pakistan	RCT	Hospital	120	Adults and children	**Arm 1**: 10% KOH solution[1] **Arm 2**: Cryotherapy
Chathra, 2015	India	RCT	Hospital	40	Children	**Arm 1**: 10% KOH solution[1] **Arm 2**: 5% imiquimod cream[1]
Handjani, 2014	Iran	RCT	NR	30	Adults and children	**Arm 1**: 10% KOH solution[1] **Arm 2**: Cryotherapy
Muzaffar, 2014	Pakistan	RCT	Hospital	33	Children	**Arm 1**: 10% KOH solution[1] **Arm 2**: 5% KOH solution[1]
Muzaffar, 2011	Pakistan	Case–control	Hospital	31	Children	**Arm 1**: 10% KOH solution[1] **Arm 2**: Cryotherapy

Abbreviations: KOH, potassium hydroxide; MDA, mass drug administration; NR, not reported; PC, prospective cohort; RC, retrospective cohort; RCT, randomised controlled trial.
[1]Topical treatment
[2]Oral treatment

Complementary/alternative therapy

Moderate quality evidence supports the use of cold cream as an adjunct to topical sulphur therapy for classical scabies (GRADE 2B) [3].

Communicable disease control and prevention

Treatment of cases and contacts is recommended in scabies outbreaks (GRADE 2C) [3], however, high-quality studies comparing treatments during outbreaks are required. There is low-quality evidence for treatment of household contacts as well as individual treatment for the community control of scabies (GRADE 2C) [49].

Hygiene practices

Although washing clothing and bed linen, storage of items in plastic bags, exposure to sunlight and household spraying are encouraged [50], high-quality studies assessing the

clinical effectiveness are required before these measures can be strongly recommended as adjuncts in the control of classical scabies in resource-limited settings [3].

Crusted scabies

Directed anti-parasitic therapy

There is evidence of moderate quality to support the use of oral ivermectin with topical keratolytics (e.g., salicyclic acid 5%–10% in cream base) and topical antiparasitic (e.g. permethrin) for crusted scabies (GRADE 1B) [3]. Comparative trials are needed to explore more effective treatments. Patients with crusted scabies require intensive supportive treatment (GRADE 1B) [3]. Coordinated case management in the home may be of benefit (GRADE 2C) [3].

Scabies and impetigo

Directed anti-microbial therapy

There is high-quality evidence to support the use of oral ivermectin for the treatment of scabies and impetigo in children >5 years old and non-pregnant adults (GRADE 1A) [51–54]. There is high-quality evidence to show that co-administration of azithromycin with ivermectin leads to similar decreases in scabies and impetigo as ivermectin alone (GRADE 1A) [53, 54]. Additional azithromycin is not needed for treatment of impetiginized/infected scabies. Topical permethrin with fusidic acid is effective for infected scabies (GRADE 2C) [48].

Water provision

There is low-quality evidence that an adequate supply of water for washing and cleaning will reduce the incidence of impetigo and scabies in resource-limited settings (GRADE 2C) [3].

Tinea

Directed antimicrobial therapy

Tinea of the skin alone (tinea corporis)
Topical therapies. There is low-quality evidence for use of topical terbinafine [55], luliconazole [56, 57], amorolfine [58] or erberconazole [59] for the treatment of tinea of the skin (GRADE 2C). There is moderate quality evidence for sertraconazole [55, 57, 59, 60], butenafine [3], miconazole [3] or clotrimazole [56] over other agents for tinea of the skin alone (GRADE 2C).

Oral therapies. There is low-quality evidence for oral itraconazole [61–65], oral terbinafine [61], oral griseofulvin [64] or fluconazole [3] (GRADE 2C). Itraconazole is superior to terbinafine, griseofulvin and fluconazole (GRADE 2C) [61–64]. Additional studies of antifungal treatments for tinea of the skin conducted in community settings would be beneficial in assessing the effectiveness of treatment at the population level in resource-limited settings.

Tinea of the scalp and hair follicles (tinea capitis)
There is moderate quality evidence for oral griseofulvin, terbinafine and fluconazole having similar efficacy for tinea capitis (GRADE 2B) [3, 66]. There is no evidence to support use of blue light therapy or curcumin for the treatment of tinea capitis (GRADE 2D) [66]. Tinea capitis is difficult to treat, taking several months and mycological cure is challenging.

Tinea of the nail (tinea unguium/onychomycosis)
For onychomycosis, clinical treatment with oral terbinafine is recommended (GRADE 1A) [3]. There is no added benefit to the use of combinations of topical therapy and oral therapy for onychomycosis in resource limited settings (GRADE 1B) [3]. Surgical avulsion prior to treatment of onychomycosis is not recommended (GRADE 2D) [3]. High-quality studies assessing photodynamic therapy (PDT) regimens for onychomycosis are required to determine the utility of this therapy in resource-limited settings.

Complementary/alternative therapy

Further studies are required before community-prepared *Senna (Cassia) alata* (Linn.) Roxb. leaf decoction can be recommended as an alternative treatment for tinea imbricata in resource limited settings, as only low-quality evidence from one study is available (GRADE 2D) [67].

Hygiene practices

Anti-microbial soap may be of benefit in the treatment of tinea corporis (GRADE 2C) [68], but due to low-quality evidence this is recommended in combination with anti-fungal treatment (GRADE 2C) [3]. There is no evidence to support added benefit of triclosan soap over normal soap in resource-limited settings [3].

Head lice (pediculosis capitis)

Directed anti-microbial therapy

There is moderate quality evidence for the use of oral ivermectin for the treatment of head lice (GRADE 1C) [20, 69–73]. There is low-quality evidence to support the use of either topical ivermectin [74], permethrin [74–78], lindane [74, 77], dimeticone [74, 77] or malathion shampoos [73] for the treatment of head lice (GRADE 2C).

Atopic dermatitis (AD)

Pharmacological therapy

Topical therapies
There is low-quality evidence for dilute bleach baths [79] or topical betamethasone balerate 0.1% [80] in the treatment of moderate–severe/refractory AD (GRADE 2C).

Oral therapies
There is low-quality evidence for oral methotrexate [81] or oral cyclosporine [81, 82] in the treatment of moderate–severe/refractory AD (GRADE 2C).

Physical therapies

There is low-quality evidence for the use of phototherapy [80, 83] for the treatment of AD (GRADE 2C).

Complementary/alternative therapy

Mild to moderate AD

There is low-quality evidence for the use of topical virgin coconut oil/mineral oil [84], topical shea butter and ceramide [85], sunflower seed oil [86], or topical *Ficus carica* [87] for mild to moderate AD (GRADE 2C). There is very low-quality evidence for the use of pure silk clothing [88] or oral vitamin E [89] for the treatment of mild to moderate AD (GRADE 2D).

Moderate to severe AD

There is low-quality evidence oral vitamin D [90, 91] in the treatment of moderate–severe/refractory AD (GRADE 2C). There is very low-quality evidence to support the use of cimetidine as adjunctive therapy [92] in treating moderate to severe AD in resource-limited settings (GRADE 2D).

Molluscum Contagiosum

Directed anti-microbial therapy

There are few effective, available treatments for this condition which is usually self-limiting and resolves over months to years. It is important for clinicians to be aware of this condition and to make an accurate diagnosis to avoid costly treatment occurring and to reassure families that it will resolve. MC is infectious so accurate diagnosis and advice on prevention is also a priority. MC can spread to other parts of the body through autoinoculation and bathing, or to siblings through swimming, shared bathwater and shared towels. Therefore, prevention involves avoiding sharing of water or towels with a child with MC [4].

DISCUSSION

This updated systematic review provides a synthesis of the additional literature available for the treatment of skin infections applicable in resource-limited settings. Both the original systematic review and the updated systematic review informed the development of the second edition of the National Healthy Skin Guidelines for skin infections in Indigenous populations [4]. The key differences from the original systematic review and this update are described below.

Firstly, low-quality evidence from one RCT in India supports the use of fusidic acid 2% or topical mupirocin 2% for the treatment of Impetigo in resource-limited settings (GRADE 2C) [40]. This was a trial of low quality due to lack of blinding in participants and outcome assessors, and unclear method of blinding and allocation concealment. This treatment efficacy is consistent with the evidence appraised for treatment of impetigo [93, 94] which arose in high-income, urban, dermatology clinics. This low-quality evidence for topical antibiotics to treat impetigo must be balanced with the risks of progressing antimicrobial resistance (AMR) where the community-wide impetigo burden is heavy [95, 96]. In summarising the strength of the evidence, and the risk of antimicrobial resistance progressing, we recommend not using topical therapy where community prevalence of impetigo is above 10% or the disease for the individual is extensive (>2 sores).

New high-quality evidence from four ivermectin-based mass drug administration (MDA) programmes [51–54] supported the use of oral ivermectin for the treatment of scabies and impetigo in children older than 5 years and non-pregnant adults (GRADE 1A). Although these are high-quality evidence for oral ivermectin for control of scabies at the community level, they are not individually randomised which may have a different impact on the efficacy of ivermectin compared to alternative scabicides. Like MDA for other neglected tropical diseases, MDA for scabies faces several challenges, including the achievement of high community coverage, especially in highly populated urban areas and in highly remote areas, and ensuring cost-effectiveness accessibility of healthcare services and water [52]. While MDA has been shown to be a highly effective public health strategy for control of a high burden of disease in island populations, MDA should be part of a broader comprehensive approach with thorough management of community consent and community-level consultation [97]. Awareness of scabies within communities and health systems, access and supply of effective treatments and factors related to social determinants of health such as housing, and environmental health initiatives around hygiene, sanitation and education, are all critical to ensure control of skin infections on a sustained basis. Until such broader environmental

issues can be addressed, MDA and mass screening is an effective short-term strategy to control skin infections in endemic settings where the burden of scabies in the community is high, and both may be needed together ongoing for outbreaks [98].

There was low to moderate quality evidence to support the use of itraconazole for tinea corporis [61–65], which was not a recommendation supported by the 2019 systematic review. Itraconazole is more expensive than other tinea treatments, may not be widely available, can be challenging to achieve high serum levels with, and may also cause blood test abnormalities [99, 100]. Whilst the evidence to support itraconazole is available, it remains cost prohibitive in most resource-limited settings. We have summarised the evidence for the reader to determine the benefit in their own community based on availability and cost. Antimicrobial soap may be of benefit in the treatment of tinea [68] but due to the low-quality evidence from only one RCT in India, this is recommended in combination with anti-fungal treatment (GRADE 2C) [3]. While the 2019 review found no benefit of anti-fungal soap, there is one new low-quality study from India that supports the use of anti-fungal soap in combination with topical or systemic therapy. The additive cost of this regimen reduces the appeal of this option when topical or systemic therapy is already indicated. There is no evidence that it has benefit without systemic therapy.

A single new complementary/alternative therapy for tinea imbricata that came from the updated systematic review was community-prepared *S. alata* leaf decoction. *Senna (Cassia) alata* (L.) Roxb is a tropical ornamental shrub which grows throughout the low and medium altitude areas of the Philippines [67]. It is well-studied locally for its anti-fungal activity, making it one of the 10 herbal medicines endorsed by the Philippines Department of Health. This plant is not widely available outside of The Philippines, nor is there a commercially available formulation. However, this evidence is included in recognition of the longstanding community knowledge for treatment of skin conditions held by Indigenous populations. Further research to support the use of these remedies alongside modern medications both for prevention and treatment of skin conditions is needed.

In this updated review we found that despite the heavy burden of head lice in resource limited settings, there is limited available evidence. There was low-quality evidence for the use of oral ivermectin (GRADE 1C) [20, 69–73] or topical ivermectin, topical permethrin, lindane, dimethicone or malathion shampoos for the treatment of head lice (GRADE 2C) [73–78, 101]. The widespread availability of oral ivermectin at a low cost makes it attractive as a systemic treatment for head lice in resource limited settings, however higher quality RCTs including the applicability of oral ivermectin MDAs for head lice are required to make a robust recommendation about the use of these treatments for head lice. Data on head lice should be collected alongside impetigo and scabies when MDA is conducted. It may also be effective for this ectoparasite, but higher doses are usually recommended.

Atopic dermatitis has been included in this updated review due to the previously under recognised burden of AD in Indigenous populations and the cross over with bacterial skin infections [18]. We have provided recommendations for treatment however further study is needed to improve the quality of some of these recommendations, and the availability of effective, low cost and locally sourced therapies for AD. The American Academy of Dermatology Association (AAD) updated guidelines for AD recommends the application of moisturisers and topical corticosteroids for AD-affected individuals who have failed to respond to good skin care and regular emollients alone. In patients with moderate to severe AD and clinical signs of secondary bacterial infection, they recommend bleach baths and intranasal mupirocin to reduce the severity of AD [102].

The AAD strongly recommends the use of dupilumab, tralokinumab, abrocitinib, baricitinib and upadacitinib as systemic therapies for severe AD; however, these can only be prescribed on the Pharmaceuticals Benefit Scheme (PBS) by dermatologists in Australia and are likely to be unavailable or prohibitively expensive in resource-limited settings. The guidelines make conditional recommendations for the use of phototherapy, azathioprine, cyclosporine, methotrexate and mycophenolate for the treatment of severe AD although these may not be available in all sites in resource-limited settings [103].

The evidence-based recommendations in this review do not take into account community preferences for treatment regimens or historical experiences and perceptions. For example, topical permethrin has more rapid reduction in symptoms [104, 105] but requires a private space in which to apply the cream to the full body, an assistant to cover hard to reach body surfaces and a functioning shower or bath to wash the cream off the body after 8 hours. Furthermore, carers in a qualitative study set in an Aboriginal community in the Pilbara region of WA spoke about barriers related to the smell, the 'funny' texture, and the time it took for the skin infections to heal when using topical permethrin [106]. Future work is needed to bring these two lenses together to ensure culturally appropriate and targeted treatments as well as representation of community perspectives.

LIMITATIONS

Limitations are that only English language and published studies were included. Although best efforts were made to ensure all relevant studies were captured, some may have been missed. Additional limitations include that there are few authors from low-middle income countries, and without a full representation of Africa, Asia, Oceania and Latin America. However, our inclusion of a broader range of skin conditions where systematic review evidence is not available is a strength of the review.

FUTURE DIRECTIONS

The evidence synthesised in the systematic review have been applied to update the Australian National Healthy Skin

Guidelines [4]. The GRADE evidence ratings have been applied to each recommendation in the review in order to inform the next edition of these guidelines—a resource designed for health care providers to easily recognise, diagnose and treat skin infections with up-to-date evidence-based information accompanied by online resources such as photographs and learning tools. Evidence described in this systematic review often does not take into account the practical considerations for the treatment of skin infections in remote versus urban settings, as well as place-based programmes that have identified local initiatives for skin infection control. In resource-poor settings, or where disease burden surpasses other contexts and population-specific guidance is not available in national guidelines, there may be a need for clinicians to look for different levels of evidence to provide excellence in patient care. In this example from the Australian context, where Aboriginal and Torres Strait Islander peoples have not always been prioritised in clinical guidelines, a resource that empowers clinicians to provide best possible, evidence-based care through generation of knowledge and experience, was needed. This systematic review underpins the accompanying NHSG [4].

Evidence suggests that although the burden of bacterial skin infections and parasitic skin infestations is highest in remote Indigenous communities, there is also a significant burden for Indigenous populations living within urban communities [18]. As such, the recommendations in the guideline have attempted to provide evidence for all endemic situations where individual treatment and community-wide interventions are likely to be of benefit.

CONCLUSION

We have summarised the available evidence for treatment of impetigo, scabies, crusted scabies, tinea, head lice, atopic dermatitis and molluscum contagiosum for clinicians working in resource limited contexts to inform Australian guidelines. All information presented in this systematic review must be considered in the context of affordability, acceptability and applicability when developing guidance for respective populations. The guidance derived from this systematic review to inform skin health care for Australian Aboriginal and Torres Strait Islander people can be found here (National Healthy Skin Guideline; telethonkids.org.au) [4].

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APPENDIX A: MEDLINE search strategy—original SR update: 2018–2022

Search	Query
Concept 1: Low resource	
1	Oceanic ancestry group OR minority groups OR Health Services, Indigenous OR American native continental ancestry group OR developing countries OR poverty OR social class OR educational status OR "developing countr* OR Developing nation* OR poverty OR low income countries OR low income nations OR middle income countries OR middle income nations OR less developed countries OR less developed nations OR third world countries OR third world nations OR socioeconomic inequality OR socioeconomic inequalities OR living standard* OR socioeconomic factors OR low resource setting* OR Aboriginal* OR Aborigines OR Indigenous* OR Inuit OR Inuits OR Maori* OR Native American* OR American Indian* OR First Nation* OR Torres Strait Island* OR Metis OR Amerindian* OR native people*
Concept 2: Skin infections	
2	Impetigo OR skin sores OR school sores OR pyoderma NOT gangrenosum
3	Exp scabies OR Sarcoptes scabiei
4	Exp Tinea OR Onychomycosis OR dermatophyte OR ringworm
5	2 OR 3 OR 4
Concept 3: Treatment and management	
6	"Disease management" OR "Therapeutics" OR "drug therapy" OR "pharmaceutical preparations" OR treatment OR intervention* OR therapy OR medicine OR management OR "Anti-infective Agent*" OR "Anti-bacterial Agent*" OR "Antibiotic" OR "Antibiotic prophylaxis" OR Anti-parasitic Agent*" OR Anti-fungal Agent* OR "herbal medicine" OR "herbalism" OR "complementary therapies" OR herbal OR traditional OR complementary OR healer OR *ngangkari OR boylyada OR chingaruck OR "witch doctor" OR "bush medicine"*
7	1 AND 5 AND 6
8	Filters activated: Publication date from 2018 to 2022, Humans, English

APPENDIX B: MEDLINE search strategy—updated skin conditions: 1960–2022

Search	Query
Concept 1: Low resource	
1	Oceanic ancestry group OR minority groups OR Health Services, Indigenous OR American native continental ancestry group OR developing countries OR poverty OR social class OR educational status OR "developing countr* OR Developing nation* OR poverty OR low income countries OR low income nations OR middle income countries OR middle income nations OR less developed countries OR less developed nations OR third world countries OR third world nations OR socioeconomic inequality OR socioeconomic inequalities OR living standard* OR socioeconomic factors OR low resource setting* OR Aboriginal* OR Aborigines OR Indigenous* OR Inuit OR Inuits OR Maori* OR Native American* OR American Indian* OR First Nation* OR Torres Strait Island* OR Metis OR Amerindian* OR native people*
Concept 2: Skin infections	
2	Lice infestation OR head louse OR head lice OR pediculus*
3	Atopic dermatitis OR exp Eczema
4	Molluscum contagiosum OR molluscum
5	2 OR 3 OR 4
Concept 3: Treatment and management	
6	"Disease management" OR "Therapeutics" OR "drug therapy" OR "pharmaceutical preparations" OR treatment OR intervention* OR therapy OR medicine OR management OR "Anti-infective Agent*" OR "Anti-bacterial Agent*" OR "Antibiotic" OR "Antibiotic prophylaxis" OR Anti-parasitic Agent*" OR Anti-fungal Agent* OR "herbal medicine" OR "herbalism" OR "complementary therapies" OR herbal OR traditional OR complementary OR healer OR *ngangkari OR boylyada OR chingaruck OR "witch doctor" OR "bush medicine"*
7	1 AND 5 AND 6
8	Filters activated: Publication date from 1960 to 2022, Humans, English

APPENDIX C: Grading of recommendations assessment, development and evaluation evidence grades and strength of recommendations [39]

Code	Quality of evidence	Definition
A	High	Further research is very unlikely to change the level of confidence in the estimate of effect, that is • Several high-quality studies with consistent results
B	Moderate	Further research is likely to have an impact in current confidence in the estimate of effect and may change the estimate, that is • One high-quality study • Several studies with some limitations
C	Low	Further research is very likely to have an important impact on the level of confidence in the estimate of effect and would likely change the estimate, that is • One or more studies with severe limitations
D	Very Low	Estimate of effect is very uncertain, that is • No direct research evidence • One of more studies with very severe limitations

Code	Strength of recommendation [107]	Implications when combined with evidence grade
1	Strong	1A: Strong recommendation, applies to most patients without reservation. Clinicians should follow a strong recommendation unless a clear and compelling rationale for an alternative approach is present 1B: Strong recommendation, applies to most patients. Clinicians should follow a strong recommendation unless a clear and compelling rationale for an alternative approach is present 1C: Strong recommendation, applies to most patients. Some of the evidence base supporting the recommendation is, however, of low quality 1D: Strong recommendation, applies to most patients. However, the recommendation is based on expert consensus only[a]
2	Weak	2A: Weak recommendation and best action may differ depending on circumstances or patients or societal values 2B: Weak recommendation and alternative approaches likely to be better for some patients under some circumstances 2C: Very weak recommendation; other alternatives may be equally reasonable 2D: Very weak recommendation based on expert consensus. Further research is necessary[a]

[a] 1D and 2D recommendations are not routinely included by the GRADE approach as these are based on expert consensus, rather than scientific evidence. These additional recommendation grades were created due to lack of available supporting evidence but an identified need to make recommendations to guide clinical and public health management.

APPENDIX D: Risk of bias table using the ROBINS-E tool with overall quality ratings using the GRADE approach for included Observational studies

Study and year	Bias due to confounding	Bias in selection of participants into study	Bias in classification of exposures	Bias due to deviations from intended exposure	Bias due to missing data	Bias in measurement of outcomes	Bias in the selection of the reported results	Overall quality (high, moderate or low quality)
Thean, 2022	+	+	+	+	?	+	+	High (A)
Hamedanian, 2021	?	+	−	+	+	?	?	Low (C)
Kumar, 2021	?	+	+	+	?	?	+	Low (C)
Eusebio-Alpapara, 2020	−	+	+	+	+	+	+	Low (C)
Babu, 2019	?	?	+	−	+	−	+	Low (C)
Hung, 2019	−	+	+	+	+	+	+	Low (C)
Romani, 2019	?	+	+	+	+	+	+	High (A)
Agrawal, 2018	?	+	+	+	+	+	+	Low (C)
Coscoine, 2018	?	+	+	+	+	+	+	Moderate (B)
Singh, 2018	−	+	+	+	+	+	+	Low (C)
Ordonez Rubiano, 2018	−	+	?	?	?	+	−	Low (C)
Soleimani-Ahmadi, 2017	−	−	+	?	+	+	−	Low (C)
Chathra, 2015	+	−	+	+	+	+	+	Moderate (B)
Ahmad, 2014	−	?	−	?	+	?	+	Moderate (B)
Aktürk, 2012	−	−	−	+	−	+	+	Low (C)
Muzaffar, 2011	?	?	+	+	?	−	+	Moderate (B)
Ameen, 2010	−	+	−	+	+	−	+	Low (C)
Atakan, 1998	−	−	−	+	?	+	+	Low (C)
Chouela, 1997	−	+	+	+	−	+	+	Low (C)

APPENDIX E: Risk of bias table using the COCHRANE Risk of Bias Tool with overall quality ratings using the GRADE approach for included RCT's

Study and year	Random sequence generation	Allocation concealment	Blinding of personnel and participants	Blinding of outcome assessors	Incomplete outcome data	Selective outcome reporting	Other sources of bias	Quality rating (high, moderate or low quality)
Abdullah, 2022	?	?	?	?	+	+	+	Low (C)
Dey, 2022	?	?	?	?	?	−	?	Moderate (B)
Khan, 2022	+	?	?	?	−	?	+	Low (C)
Kowser, 2022	+	+	+	+	+	+	+	Low (C)
Marina, 2022	+	?	?	?	+	−	−	Low (C)
Novianto, 2022	+	+	?	?	+	+	+	Low (C)
Ramesh, 2022	+	?	?	?	+	+	+	Moderate (B)
Behera, 2021	?	?	+	+	+	+	+	High (A)
Dakhale, 2021	+	−	−	−	−	−	+	Low (C)
Fonseka, 2021	+	+	+	+	−	−	−	Low (C)
Gideon, 2021	+	?	−	−	+	+	+	Moderate (B)
Hardy, 2021	+	−	−	−	+	+	?	High (A)
Meghana, 2021	+	?	?	?	?	−	?	Moderate (B)
Ravichandran, 2021	?	?	−	−	+	−	−	Moderate (B)
Shenoy, 2021	?	?	−	−	−	+	?	Moderate (B)
Sivapiromrat, 2021	+	?	−	−	+	−	+	Low (C)
Usman, 2021	?	?	?	?	+	−	−	Moderate (B)
Verma, 2021	+	+	−	−	+	+	+	Moderate (B)
Kawen, 2020	?	?	?	+	+	+	?	Low (C)
Kassiri, 2020	?	?	+	+	?	+	+	Moderate (B)
Mansour, 2020	+	+	+	+	+	+	+	Moderate (B)
Matthewman, 2020	+	+	−	−	+	−	+	Moderate (B)
Singh, 2020a	+	+	−	−	+	+	+	Moderate (B)
Singh, 2020b	+	+	−	−	+	+	?	Moderate (B)
Bhatia, 2019	?	?	−	−	+	−	?	Moderate (B)
Dwiyana, 2019	?	?	+	?	+	−	+	Low (C)
Ibraheem, 2019	?	?	?	?	+	−	−	Low (C)
Marks, 2019	?	?	−	−	+	+	+	High (A)
Nguyen Huu, 2019	?	?	?	?	?	?	?	Moderate (B)
Ozturk, 2019	−	?	−	−	+	+	−	Moderate (B)
Prabha, 2019	+	?	?	?	+	+	+	Moderate (B)
Rani, 2019	?	?	?	?	+	+	−	Low (C)
Das, 2018	+	+	+	+	+	+	+	Low (C)
Sanchez-Armendairiz, 2018	+	?	+	+	+	−	?	Moderate (B)
Al-Sudany, 2016	?	?	?	?	+	+	?	Moderate (B)
Kashif, 2016	?	?	?	?	?	+	?	Moderate (B)
Leulmi, 2016	?	?	−	−	+	+	+	Moderate (B)
Qureshi, 2016	+	?	?	?	−	−	?	Moderate (B)
Abbasi, 2017	+	+	+	+	+	+	+	Moderate (B)
Jaffary, 2015	+	?	?	?	+	−	+	Low (C)
Handjani, 2014	?	?	+	+	+	?	?	Moderate (B)
Muzaffar, 2014	?	?	?	?	+	+	?	Moderate (B)

Study and year	Random sequence generation	Allocation concealment	Blinding of personnel and participants	Blinding of outcome assessors	Incomplete outcome data	Selective outcome reporting	Other sources of bias	Quality rating (high, moderate or low quality)
Evangelista, 2013	+	+	+	+	+	+	+	Low (C)
Shahraki, 2013	?	?	?	?	−	−	−	Low (C)
Wong, 2013	?	?	+	?	−	+	+	Moderate (B)
El-Khalawany, 2012	+	?	?	?	+	+	?	Low (C)
Nofal, 2010	?	?	?	−	−	+	+	Moderate (B)
Pilger, 2010	−	?	−	−	+	+	−	Moderate (B)

Key

+	Low risk of bias
−	High risk of bias
?	Unclear risk of bias

APPENDIX F: Updated evidence summaries

Skin condition	Updated author evidence summary
Impetigo	
Directed antimicrobial therapy	
Topical versus topical	
Fusidic acid 2% versus mupirocin	Low-quality evidence from an RCT in India assessed the efficacy of topical fusidic acid 2% and topical mupirocin 2% for the treatment of impetigo [40]. At the end of the 1st week, efficacy was 92% in the fusidic acid group and 96% in patients receiving mupirocin 2% ($p > 0.05$)
Mass drug administration	No studies assessed MDA for impetigo alone. Impetigo was a secondary outcome in scabies MDAs reported in the systematic review
Complimentary/alternative therapies	No studies assessed complimentary therapies for impetigo
Communicable disease control	No studies assessed disease control activities to prevent transmission of impetigo
Hygiene practices	No new studies assessed hygiene practices to treat or prevent impetigo
Scabies	
Directed anti-parasitic therapy	
Topical versus topical	
Permethrin versus crotamiton and topical sulphur	An RCT of 195 participants in community camps in Iraq compared the efficacy of topical permethrin, crotamiton, and topical sulphur [41]. The highest cure rate was 93.3% in the permethrin 10% + sulphur 10% group
Permethrin versus ivermectin	Moderate-quality evidence from an RCT of 200 patients in a hospital in Pakistan, compared the efficacy of topical permethrin 5% and topical ivermectin 1% in the treatment of scabies. There was no statistically significant difference in clinical cure between the two groups ($p = 0.074$) [42]
Permethrin and fusidic acid versus permethrin and placebo	Low-quality evidence from West Java gave cure rates of 95% in the permethrin and fusidic acid group compared to the control group of permethrin and placebo (35%; $p \leq 0.001$) [48]
Oral versus topical treatment	
Topical permethrin versus oral ivermectin	Comparison of topical permethrin with oral ivermectin in a low-quality RCT found that the combined effect of both lines of treatment showed significant reduction in the time of treatment and higher complete clearance rate of lesion with full recovery rate without considerable side effect [44]. Another low-quality study from India found permethrin to be more efficient than ivermectin in improving the clinical grade of scabies [43]. At the end of 4 and 6 weeks, however, this difference was not significant ($p > 0.05$)

(Continues)

Skin condition	Updated author evidence summary
Topical permethrin versus oral ivermectin versus lindane	Moderate-quality evidence from a study in India comparing topical permethrin, topical lindane and oral ivermectin [45]. The group with topical permethrin AND oral ivermectin had the best improvement in lesions; however, the groups were not significantly different
Oral ivermectin alone	High-quality evidence from one study in Fiji assessed the population effects of ivermectin MDA on scabies prevalence [47] Participants were randomised to two-dose ivermectin-based MDA (IVM-2), one-dose ivermectin-based MDA (IVM-1) or screen and treat with topical permethrin 5% for individuals with scabies and their household contacts. The study found no significant difference between the MDA agents
	Moderate quality evidence from India showed significant improvement in scabies severity in both a single dose oral ivermectin (200 μg/kg body weight) versus two doses of topical ivermectin, 1 week apart [46]
Complementary therapy	No new studies assessed the effect of complimentary therapies for scabies
Communicable disease control and prevention	In an RCT in Gabon, Africa, the effectiveness of individual versus household benzyl benzoate treatment for scabies was compared. The authors concluded that treating close contacts of persons affected by scabies had approximately twice the odds of being cured of scabies, however this was not statistically significant ($p = 0.17$) [49]
Hygiene practices	No new studies assessed the effect of hygiene practices or environmental interventions for scabies
Crusted scabies	
Anti-parasitic therapy	There were no new studies that assessed therapies for crusted scabies only
Scabies and impetigo	
Directed anti-microbial therapy	
Oral treatment only	
Oral ivermectin	High-quality evidence from an ivermectin cluster RCT in India showed a significant reduction in the prevalence of scabies, but not impetigo, in the ivermectin group versus usual care groups [51]
	Thean et al [52] conducted a population-based before-after study of MDA for scabies and impetigo from 2018 to 2020 in Fiji. The study population was offered a first dose of ivermectin, diethylcarbamazine and albendazole as recommended for lymphatic filariasis mass drug administration, followed by a second dose of ivermectin after 7–14 days. The incidence of hospitalisations with skin and soft tissue infections was 17% lower after the intervention compared to baseline ($p = 0.002$). Incidence of primary healthcare presentations with scabies and skin infections was 21% lower. Crude community prevalence of scabies declined from 14.2% to 7.7%
Ivermectin and azithromycin	High-quality evidence from an ivermectin versus ivermectin co-administered with azithromycin MDA in six communities in the Solomon islands showed a reduction in scabies and impetigo prevalence from baseline to 12 months after MDA [53]. At baseline, scabies and impetigo prevalence were 11.8% and 10.1% in the ivermectin-only arm and 9.2% and 12.1% in the combined treatment arm. At 12 months the prevalence of scabies and impetigo had fallen to 1.0% (95% CI 0.3%–2.6%) and 2.5% (95% CI 1.4%–4.5%), respectively, in the ivermectin-only treatment arm and to 0.7% (95% CI 0.2%–1.8%) and 3.3% (95% CI 2.1%–5.1%), respectively, in the combined treatment arms. There was no significant difference between the two groups from baseline to 12 months in either group
	A second single-arm, before-after community intervention in the Solomon Islands assessed the efficacy of MDA of ivermectin for scabies and impetigo, with coadministration of azithromycin for trachoma [54]. The regimen for the trachoma-based MDA is not reported here. At baseline, 18.7% had scabies and 24.8% had impetigo. At 12 months after MDA, 2.3% had scabies (relative reduction 88%, 95% CI 76.5%–99.3%) and 6.4% had impetigo (relative reduction 74%, 63.4%–84.7%)
Water provision	There were no new studies that assessed water provision in scabies and impetigo
Tinea of the skin (tinea corporis, tinea pedis, tinea cruris, tinea manuum, tinea faciei, etc)	
Topical treatment	
Terbinafine versus sertraconazole	Low-quality evidence from an Indian RCT assessing the effect of topical terbaniafine 1% twice daily and 2% sertraconazole once daily for 4 weeks [55] showed an overall reduction of 98.3% in terbinafine and 99.4% in sertaconazole ($p = 0.9$)
Sertraconazole versus luliconazole	Low-quality evidence of topical sertaconazole –%) and luliconazole (1%) cream for the treatment of tinea corporis and tinea cruris showed significant changes in clinical changes (pruritus, erythema, vesicle, and desquamation ($p < 0.0001$) in both luliconazole and sertaconazole groups. There was a significant reduction in mean total composite score

Skin condition	Updated author evidence summary
	(pruritus, erythema, vesicle, and desquamation) after the end of treatment in the sertaconazole group ($p = 0.0002$) compared to the luliconazole group. Both the groups showed equal negative mycological assessment [57]
Sertraconazole versus erberconazole	Ravichandran et al conducted an RCT on 85 adults in a tertiary care teaching hospital in India to assess the effectiveness of topical eberconazole 1% versus sertaconazole 2% cream applied twice daily for 4 weeks [59]. The resolution of pruritus (90.5%), erythema (83.3%) and scaling (85.7%) was in higher proportion of study participants of sertaconazole group compared to eberconazole group. Intergroup comparison with respect to pruritus and scaling showed significant difference with sertaconazole having better reduction in pruritus and scaling scores ($p < 0.001$)
Sertraconazole versus amorolfine	Das et al conducted an RCT of amorolfine 0.25% cream and sertaconazole 2% cream in a dermatology outpatient hospital department in India [60]. Both sertaconazole and amorolfine significantly reduced symptoms in both groups ($p < 0.001$). However, improvement in symptoms (pruritus, burning sensation, erythema, scaling and crusting) was significantly greater in the sertaconazole group at every follow-up visit
Luliconazcole versus clotrimazole	Prabha et al conducted a randomised comparative study in India to assess the efficacy of topical luliconazole versus topical clotrimazole in tinea corporis and tinea cruris [56]. At the end of 1st week, the mycological cure was 78% in luliconazole and 12% in clotrimazole ($p < 0.05$) and complete clearance was achieved in 11 patients (22%) in luliconazole group. By the end, 98% got cured in luliconazole group and 80% in the clotrimazole group ($p < 0.05$)
Modified Whitfield ointment (5% benzoic acid and 5% salicylic acid) versus emulsifying ointment	One RCT assessed treatment for difficult-to-treat forms of dermatophytosis, with two or more skin lesions, in 30 adults patients in an outpatient dermatology clinic in Sri Lanka [108]. Lesions were randomised to receive modified Whitfield ointment (MWO-5% benzoic acid and 5% salicylic acid) or emulsifying ointment (EO). At 2 weeks, there was a statistically significant improvement in MWO arm in the clinical assessment of disease severity and the patients' perception. There was a 7.59% reduction in the surface area of lesions in MWO arm and a 5.83% increase in the surface area of lesions in the EO arm at 2 weeks. The difference between the two arms in surface area changes was not statistically significant ($p = 0.107$)
Oral treatment only	
Oral terbinafine versus oral itraconazole	Bhatia et al conducted a randomised comparative study of 320 participants in India to assess the efficacy of a daily dose of oral terbinafine 500 mg versus oral itraconazole 200 mg for 4 weeks [61]. Mycological cure was achieved in 147 (91.8%) in the itraconazole group and 119 (74.3%) in the terbinafine group at the end of 4 weeks. There was a significant improvement in percentage change in pruritus, scaling, and erythema in both the groups from 0 to 4 weeks ($p < 0.01$). On comparing groups, the percentage change was significantly different in scaling from 0 to 2 weeks (5.4 vs. −4.8) and 2–4 weeks (16.7 vs. 29.6) between the terbinafine group and the itraconazole group, respectively A parallel RCT in India [63] demonstrated significantly higher cure rates in the Itraconazole containing groups compared to the terbinafine only groups at both 4 and 8 weeks
Itrazonazole versus super bioavailable itraconazole	Shenoy et al conducted an RCT of oral itraconazole 100 mg twice daily or super bioavailable itraconazole 50 mg twice a day in 500 adults in India [65]. At week 4, 33.33% in the itraconazole group and 65.38% in the super bioavailable itraconazole group achieved complete cure ($p < 0.05$), where as in mycologically cleared patients, no statistically significant difference was found ($p = 0.14$)
Oral terbinafine + itraconazole versus oral terbinafine + griseofulvin	Ramesh et al examined the efficacy of oral terbinafine 250 mg with itraconazole 200 mg or oral griseofulvin 250 mg in 60 adult participants [64]. Clinical cure rates were higher in itraconazole containing group at 4 and 8 weeks than the group containing griseofulvin ($P < 0.001$).
Fluzonazole versus griseofulvin versus itraconazole versus terbinafine	An Indian RCT [62] showed that at 8 weeks, the cure rates were as follows: fluconazole (42%), griseofulvin (14%), itraconazole (66%) and terbinafine (28%) ($p < 0.001$). Itraconazole was superior to fluconazole, griseofulvin and terbinafine ($p \leq 0.048$)
Oral versus topical treatment	
Oral Terbinafine versus topical terbinafine	An earlier prospective cohort study by Singh et al in 2018 assessed the effectiveness of oral terbinafine 5 mg/kg/day in addition to topical terbinafine 1% applied twice daily for 4 weeks in 500 participants [109]. At 4 weeks follow- up 30.6% achieved clinical and microscopic cure. The p value for these results were not provided

(Continues)

Skin condition	Updated author evidence summary
Tinea of the skin and hair follicles (tinea capitis)	
Griseofulvin versus Cur-PTD versus blue light therapy versus curcumin	One RCT of 52 children compared Cur-PDT group (photodynamic therapy), oral griseofulvin group (12.5 mg per kg body weight per day for 6–12 weeks), curcumin group (NSV-Cur gel (1.25 mg/g) once daily for 6 weeks, without light exposure) and blue light group (repeated every two weeks for a maximum of 6 sessions) for the treatment of tinea capitis [66]. The phototherapy group showed complete clearance in 46% of children and 100% in the griseofulvin group ($p = 0.0001$). No effects were observed in curcumin or light groups
Tinea of the nail (tinea unguium/onychomycosis)	
Directed antimicrobial treatment	There were no new studies that assessed directed antimicrobial treatment for tinea unguium/onychomycosis
Mass drug administration	No studies assessed the effect of antifungal MDAs on the prevalence of tinea infections
Complimentary/alternative therapy	Low-quality evidence of the efficacy of community-prepared *S. alata* leaf decoction for the treatment of tinea imbricata showed that after 4 weeks of treatment, 95% had decreased pruritus scores with a mean reduction of 4.05 (mean VAS before treatment: 7.75, after treatment: 3.7) [67]
Communicable disease prevention and control	No studies assessed the effect of communicable disease control practices on tinea on which to base relevant recommendations for resource-limited settings
Hygiene practices	From India, low-quality evidence found erythema, pruritis, desquamation, and total symptom score were significantly reduced by treatment with antimicrobial soap but not by treatment with placebo soap [68]
Atopic dermatitis (AD)	
Directed anti-microbial therapy	
Topical therapies	
Dilute bleach baths	One Malaysian RCT assessed the efficacy and safety of diluted sodium hypochlorite (bleach) baths as an adjunctive treatment in patients aged 2–30 years old with moderate to severe AD [79]. The control group bathes in distilled water. At 2 months, there was a significant difference between the treatment and placebo groups ($p = 0.02$). Patients in the treatment group showed a significant reduction in the Eczema Area and Severity Index (EASI) scores at both 1 and 2 months ($p < 0.001$)
Betamethasone balerate 0.1%	An Indian quasi-experimental study compared the efficacy of narrowband ultraviolet B (NB-UVB) therapy versus topical betamethasone valerate 0.1% in patients aged 5–60 years old with AD [80]. Four percent of participants in the NB-UVB group showed >50% reduction in SCORAD, whereas 84% patients in group in the betamethasone group showed >50% reduction in SCORAD. This difference was not statistically significant ($p = 0.554$)
Oral therapies	
Methotrexate versus cyclosporine	An Egyptian study of 40 children diagnosed with severe AD at an outpatient dermatology clinic assessed the efficacy of methotrexate (7.5 mg/week) and cyclosporine (2.5 mg/kg/day) [81]. The severity SCORAD score was used to indicate efficacy of the treatment. In the methotrexate group, the mean SCORAD score at the beginning of the study was 57.90 ± 3.21, which was reduced to 29.35 ± 6.32 with a mean absolute reduction of 26.25 ± 7.03 at the end of the treatment period. In the cyclosporine group, the mean SCORAD score was 56.54 ± 4.82 at the start of treatment and 31.35 ± 8.89 at the end of 12 weeks of treatment. The mean absolute reduction was 25.02 ± 8.21. There was no statistically significant difference in the reduction of SCORAD score between both groups ($p \pm 0.93$)
Sandimmun neoral (cyclosporine)	A prospective cohort study conducted in Turkey, investigated the efficacy of Sandimmun Neoral in AD [82]. The study included 22 patients aged 13–70 years with severe atopic dermatitis and was conducted in 3 parts: After 2 weeks of screening, Sandimmun Neoral was commenced at a dose of 3 mg/kg/day and continued until remission *or* for a maximum of 8 weeks, after which the dose was reduced by half and continued for another 2 weeks and then discontinued. After the treatment period, patients were followed up first for 8 weeks and then until relapse or for a maximum of 24 weeks. There was no control group. At the end of the treatment phase, significant reductions were noted in all of the parameters of disease activity; the Extent of Disease Severity (EDS), intensity of disease and Disease Severity Score (DSS) decreased at the end of treatment by 85, 88, and 79%, respectively. The pruritus score was reduced by 85% and the sleep loss score by 96% at the end of the treatment ($p < 0.001$)

Skin condition	Updated author evidence summary
Physical therapies	
Phototherapy	Ordonez Rubiano et al. [83] revealed that patients exposed to UVA-1 phototherapy showed a decrease in the SCORAD (30.1 points)—total cumulative dose-dependent ($p < 0.0001$)—regardless of multiple variables studied
	An Indian quasi-experimental study compared the efficacy of narrowband ultraviolet B (NB-UVB) therapy versus topical betamethasone valerate 0.1% in patients aged 5–60 years old with AD [80]. Four percent of participants in the NB-UVB group showed >50% reduction in SCORAD, whereas 84% patients in group in the betamethasone group showed >50% reduction in SCORAD. This difference was not statistically significant ($p = 0.554$)
Complimentary/alternative therapy	
Virgin coconut oil versus mineral oil	An RCT on the effects of topical virgin coconut oil (VCO) and mineral oil, on SCORAD index values, transepidermal water loss (TEWL), and skin capacitance for the treatment of AD was conducted [84]. The post-treatment reduction in the mean SCORAD value in the VCO group was 68.23%, which was significantly higher ($p < 0.001$) than that in the mineral oil group (38.13%)
Hydrocortisone versus shea butter-ceramide cream	An RCT from Thailand assessing the efficacy of shea butter and ceramide versus 1% hydrocortisone in mild to moderate childhood AD [85] found a significant improvement in both the SCORAD and POEM in both groups after 8 weeks of treatment. There was no statistical difference between the two groups
Sunflower seed oil versus moisturiser cream	Dwiyana et al conducted an RCT in a hospital outpatient clinic and a primary school in Indonesia [86] assessing the effect of 20% sunflower seed oil (SSO) in decreasing the transepidermal water loss (TEWL) and scoring of atopic dermatitis (SCORAD) index for mild AD. In the first week, the control group had TEWL score decrement by 36.62% while the experimental group by 28.89% ($p = 0.88$). In the fourth week, the TEWL decrements of the experimental and control group were by 56.94% and 52.50%, respectively ($p = 0.20$), and this was followed by an improvement of SCORAD index in both treatment groups
Edible dried fig fruit (*F. carica*)	One Iranian study investigated the effects of aqueous extract of edible dried fig fruit (*F. carica*) 8% (Melfi cream) on the severity of AD compared with Hydrocortisone 1.0% or placebo (base cream) [87]. Results show that Melfi cream and hydrocortisone 1.0% cream effectively reduced the SCORAD index and severity of symptoms (intensity and pruritus) ($p < 0.001$) and the placebo cream failed to ameliorate the symptoms. Moreover, the pairwise comparison results showed that the Melfi cream provided significantly better outcomes in comparison with the base cream ($p < 0.001$).
Pure silk clothing	Hung et al evaluated the effects of wearing pure silk clothing for the whole day as an alternative therapy for AD [88]. Significant differences in severity of AD were found at 0–8 weeks and from weeks 2 to 8 ($p < 0.001$), at 0–4 weeks ($p < 0.01$), and at weeks 2–4 and 4–8 ($p < 0.05$)
Vitamin E	A low-quality RCT in Iran assessed the efficacy of vitamin E (400 IU/day) versus placebo for the treatment of AD [89]. Itching, extent of lesions, and SCORAD index improvement was significantly higher in vitamin E treated group compared to placebo (−1.5 vs. 0.218 in itching, −10.85 vs. −3.54 in extent of lesion, and − 11.12 vs. −3.89 in SCORAD index, respectively, $p < 0.05$). The highest reduction in total score of SCORAD index was observed in the placebo group. In the group receiving vitamin E, the total average differences in all measured variables were negative, which shows favourable response to vitamin E therapy
Vitamin D	One Egyptian RCT had children randomised to receive either vitamin D3 1600 IU/day or placebo, plus baseline therapy of topical 1% hydrocortisone cream twice daily for 12 weeks [90]. The vitamin D3 group achieved a significantly higher level of 25 hydroxy vitamin D compared to control group at week 12 ($p < 0.001$). The mean EASI score was significantly lower in the vitamin D group compared to placebo ($p = 0.035$)
	Sanchez-Armendariz et al conducted an RCT in Mexico including 58 patients with AD to evaluate the clinical change in the SCORAD severity score in patients who received either vitamin D3 5000 IU/day or placebo capsules [91]. At the end of the intervention, the treated group achieved higher levels of 25(OH)D ($p < 0.001$)
Cimetidine	Novianto et al conducted an RCT in a hospital setting in Indonesia with 26 participants aged 12–60 to assess the effectiveness of cimetidine versus placebo as an adjuvant to standard treatment in acute extrinsic AD [92]. Significant differences were observed in SCORAD changes at every time point week between each group

(Continues)

Skin condition	Updated author evidence summary
Head lice	
Directed antimicrobial therapy	
Topical treatment/shampoo	
Permethrin shampoos	Low-quality evidence is provided from three studies in Iran [78], Turkey [75] and Argentina [76], all showing an improvement in head lice after treatment (vs. no treatment) with 1% permethrin shampoo
Permethrin versus lindane shampoo	Shahraki et al conducted an RCT assessing the efficacy of permethrin 1% and lindane 1% for head lice in 1242 primary school girls in Iran [101] Although no P values were provided, the authors state that all girls in placebo group remained infested at the end of the 10 days and recovery with permethrin shampoo was 54.29% and with lindane shampoo was 50.96%
Permethrin versus lindane versus dimeticone shampoo	An Iranian RCT [77] found significant differences among the treated groups of cases on days 2 ($P < 0.001$), 8 ($p < 0.001$) and 15 ($p < 0.001$) post-application. On the other hand, permethrin outcome was not significantly different from that of dimeticone on day 2 after post-application ($p = 0.42$), which means the similar success of these two pediculicides. The results showed a significant P value ($p = 0.003$) for dimeticone treatment compared with application of lindane on day 2 post-application. The result of chi-squared test at primary endpoint indicated significant p value which prove meaningful difference between permethrin and lindane ($p < 0.001$). The statistical analyses showed no meaningful difference between permethrin and lindane ($p = 0.55$), also permethrin and dimeticone ($p = 0.16$), as well as lindane and dimeticone ($p = 0.43$) on day 8 post-treatment. Furthermore, the statistical analysis indicated no significant difference between permethrin and lindane ($P = 0.4$), also permethrin and dimeticone ($p = 0.21$), as well as lindane and dimeticone ($p = 0.39$) at the third endpoint on day 15 post-treatment
Topical ivermectin versus permethrin versus dimethicone	A low-quality Iranian RCT [74] of permethrin shampoo, 4% dimethicone lotion or 0.05% ivermectin lotion showed that 79.5% of those who received permethrin, 83% of people treated with Dimethicone lotion and 90.6% of those with ivermectin had no head lice. There was no significant difference among these three groups
Oral versus topical	
Oral ivermectin versus topical malathion	Nofal (2010) [73] conducted an RCT in Egypt to compare the efficacy of a single dose of oral ivermectin 200 μg /kg with topical malathion. After a single dose, complete cure was achieved in 77.5% and 87.5% of ivermectin and malathion groups, respectively. After the second dose for non-responders, the cure rate increased to 92.5% in the ivermectin group and 95% in the malathion group
Oral ivermectin versus topical ivermectin	A moderate-quality Egyptian study assessing topical application of 1% ivermectin versus a single dose of 200 μg/kg oral ivermectin [72] showed eradication rates and improvement of pruritus which were significantly higher among patients who received topical than oral ivermectin. When a second treatment was given to non-responders, the cure rates of infestation was 100% patients treated with topical and oral ivermectin, with no significant difference between the two groups
Oral ivermectin versus head lice shampoo (placebo)	Leulmi et al. [71] conducted a study in two villages of Sine-Saloum, Senegal: Dielmo (ivermectin group) and Ndiop (shampoo group). In the ivermectin group, patients received two doses of oral ivermectin (400 μg/kg body weight) 7 days apart. At baseline, 34.8% of participants in the ivermectin group were had head lice versus 60.7% in the shampoo group. At day 15 post-treatment, the efficacy of the treatment against head lice reached 77.4% in the ivermectin group and 32.3% in the shampoo group
Oral treatment only	
Oral ivermectin	Leulmi et al [71] conducted a study in two villages of Sine-Saloum, Senegal: Dielmo (ivermectin group) and Ndiop (shampoo group). In the ivermectin group, patients received two doses of oral ivermectin (400 μg/kg body weight) 7 days apart. At baseline, 34.8% of participants in the ivermectin group were had head lice versus 60.7% in the shampoo group. At Day 15 post-treatment, the efficacy of the treatment against head lice reached 77.4% in the ivermectin group and 32.3% in the shampoo group Ameen et al conducted a prospective cohort study evaluating the efficacy and safety of oral ivermectin for head lice in an indigenous community in Mexico [69]. Participants were treated with a single dose of oral ivermectin 3 mg at 200 μg/kg. At the second visit, 1 week after treatment with a single dose of ivermectin, adult lice had been eradicated in all the children. Head lice were still present in 40 (90.1%) children, although there was a reduction in lice density and most of these were non-viable

Skin condition	Updated author evidence summary
	Pilger et al conducted an RCT to assess the effectiveness of household-wide treatment with ivermectin for preventing the transmission of head lice in children and teenagers in a slum in north-eastern Brazil [70]. Households of participating children were randomised into the 200 ug/kg oral ivermectin group or control (no treatment). Children in the intervention group remained free from infestation with head lice significantly longer than children in the control group
	Coscoine et al. [20] conducted an ivermectin MDA to establish baseline prevalence of head lice infestation in a rural community in the Solomon Islands and to assess whether MDA using ivermectin, at the lower dose of 200 mg/kg (the same regimen that has already shown to be effective for scabies treatment) would be an effective method to lower community prevalence of head lice. At 2 weeks after MDA, the prevalence of active infestation had declined significantly (25.6% vs. 2.5%, $p < 0.001$). At 3 months, the prevalence of active head lice infestation remained significantly lower than at baseline (25.6% vs. 7.5%, $p < 0.001$)
Complimentary/alternative therapy	There were no studies that assessed complementary/alternative therapy for head lice
Molluscum contagiosum	
Trichloroacetic acid versus adapalene cream	A Pakistani RCT of 60 participants with MC assessed the efficacy of Trichloroacetic acid (TCA) 30% to the centre of the lesion versus adapalene cream 0.1% twice daily for 3 weeks [110]. At 6 weeks follow up, the lesions disappeared in 25 (83.3%) participants in TCA group and in 20 (66.7%) patients in the adapalene group. Recurrence of lesions was observed in 5 (16.7%) patients of the TCA group and in 10 (33.3%) participants of the adapalene group. The authors concluded that TCA was found effective in 25 (83.3%) patients, while Adapalene was found effective in 20 (66.7%) patients, although these results were not significant ($p = 0.136$)
	An RCT of 60 children in Pakistan studied the efficacy and safety of weekly 35% trichloroacetic acid (TCA) versus a daily dose of adapalene 0.1% for 3 weeks for the treatment of MC [111]. Participants were followed-up at weekly intervals for 6 weeks. At 6 weeks follow-up, in the TCA group, the lesions disappeared in 25 (83.3%) patients and in 20 (66.7%) patients in the adapalene group. Recurrence of lesions was observed in 5 (16.7%) patients in the TCA group and in 10 (33.3%) patients in the adapalene group. Overall efficacy of TCA was 83.3% and that of adapalene was 66.7% ($p = 0.136$)
Povidone iodine versus tretinoin	A randomised case–control study by Kumar et al assessed the efficacy and safety of povidone iodine with dimethyl sulfoxide versus 0.05% tretinoin in the treatment of MC [112]. There was no statistically significant difference between the two treatment groups
Potassium hydroxide (KOH) 10% solution versus KOH 5%	A Pakastani study comparing two different concentrations of KOH solution (5% and 10%) [113] showed that none of the patients showed complete clearance in the 5% KOH group however, partial clearance was seen in 25%. In the 10% KOH group, complete clearance of lesions was seen in 41.2% patients whereas 58.8% had partial remission ($p < 0.05$)
KOH 10% solution versus salicylic acid	Nguyen Huu et al compared the efficacy of 10% KOH solution versus 10% salicylic pomade in the treatment of MC [114]. The clearance of all lesions after 2, 4, 6, 8 weeks of treatment in both groups were 7.7%; 23.1%; 53.8%; 79.5% and 0%; 3.2%, 9.7% 22.6%, respectively ($p < 0.05$)
	An RCT in Sudan, Africa compared the efficacy and safety of 10% KOH with 16.7% salicylic acid (SAL) and lactic acid (LAC) [115] showing a mean duration time of disease of 8.63 ± 2.17 months(1–14 months) in the KOH group and 7.96 ± 4.48 months (1–11 months) in the SAL + LAC group. After 60 days of treatment, the rates of complete resolution in 54 patients treated with KOH 10% solution and 47 patients treated with 16.7% SAL + LAC combination solution were 87.0% and 85.1% ($p > 0.05$), respectively
KOH solution versus 25% podophyllin solution	Al-Sudany conducted a comparative RCT in 52 participants in a hospital setting in Iraq to compare the effectiveness of topical 10% KOH solution and 25% podophyllin solution as home-based treatments for MC [111]. At the end of the study, 16/25 participants (64%) in the KOH group showed complete clearance of lesions (181 [82.3%] lesions out of 220), while cases in the podophyllin group showed total clearance of lesions in 14 (70%) out of 20 patients with 143 (78.1%) lesions out of 183. The results of both groups were comparable and there was no significant difference between them ($p > 0.67$)
KOH solution versus 5% imiquimod	Comparing the efficacy of 10% KOH versus 5% imiquimod in one study [116] showed that after 12 weeks, 17/20 (80%) in the 10% KOH group showed complete disappearance and only 50% in the imiquimod group. The comparison between the number of lesions at baseline and the number of lesions at week 12 was found to be statistically significant with $p = 0.000$ in the imiquimod group patients. This reduction in the number of lesions at the

(Continues)

Skin condition	Updated author evidence summary
	end of 12 weeks was statistically significant $p = 0.000$ in the KOH group. Overall, a better response was shown by patients who received KOH as compared to those who received imiquimod, and the difference was statistically significant
Topical cantharidin versus tuberculin-purified protein derivatives (PPDs)	A moderate quality RCT conducted in Egypt assessed the effectiveness and security of intralesional immunotherapy in the therapy of MC with tuberculin PPD versus topical cantharidin [117]. Complete clearance of lesions was detected in 90.0% of patients in the cantharidin group; the partial response was detected in10.0% of the patients. However, in the PPD group, 85% of the patients showed a complete response and 15% showed a partial response, with no significant difference in the clinical response between the two groups
10% KOH Solution versus cryotherapy	There were three RCTs that compared the efficacy of 10% KOH solution with cryotherapy [118–120] all showing an improvement of MC lesions in both groups (not significant between groups)

Abbreviations: AD, atopic dermatitis; CI, confidence intervals; EASI, Eczema Area and Severity Index; KOH, potassium hydroxide; MC, molluscum contagiosum; MDA, mass drug administration; RCT, randomised controlled trial; SCORAD, scoring of atopic dermatitis.