

Guidelines for the treatment of tungiasis



PAHO



Pan American
Health
Organization



World Health
Organization
Americas Region

Guidelines for the treatment of tungiasis

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Preface

This technical guide emerged in response to the urgent need for an evidence-based approach to managing and preventing tungiasis, a neglected tropical disease caused by the sand flea *Tunga penetrans*. This disease is prevalent in South America, the Caribbean, and sub-Saharan Africa and causes severe inflammation, pain, itching, and disability, as well as cognitive impairment in children and social stigma.

Developed by a multidisciplinary group of experts from the Pan American Health Organization and the World Health Organization, in collaboration with many experts such as clinicians, methodologists, and stakeholders, this document provides clear and practical recommendations grounded in a rigorous analysis of the available scientific evidence.

Designed for a wide audience, including patients, caregivers, clinicians, and other stakeholders, these guidelines serve as a valuable resource to guide clinical decision-making, promote effective interventions that reduce the burden of this disease, and support policymakers in developing local or national strategies aimed at alleviating the impact of tungiasis among children and adults.

The implementation of these guidelines depends on the collective commitment of stakeholders, including local authorities, healthcare professionals, and members of affected communities, and they serve as a reminder that even the most neglected diseases deserve attention, with the goal of building a more equitable and healthier world.

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Director

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These guidelines were developed under the leadership and coordination of PAHO's Neglected, Tropical, and Vector-Borne Diseases Unit and the Department of Communicable Disease Prevention, Control, and Elimination, with support from WHO's Department of Control of Neglected Tropical Diseases.

PAHO/WHO extend their gratitude to the many experts and professionals who dedicated their time, knowledge, and expertise to the development of these guidelines.

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PAHO/WHO acknowledge the dedication and collaboration of all contributors who ensured the successful completion of these guidelines.

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Conflicts of interest

Hermann Feldmeier declared a financial conflict of interest with the manufacturer of low-viscosity dimeticone, resulting in his recusal from the recommendations concerning its use. Likewise, Lynne Elson, as the lead trial author, declared an intellectual conflict of interest with neem oil and recused herself from participating in the related recommendations. The remaining members of the Guideline Development Group, as well as all members of the Evidence Synthesis Team, declared no conflicts of interest.

Abbreviations and acronyms

CI	confidence interval
EtD	Evidence to Decision
GDG	guideline development group
GRADE	Grading of Recommendations Assessment, Development and Evaluation
OR	odds ratio
PAHO	Pan American Health Organization
RCT	randomized controlled trial
RR	relative risk
WHO	World Health Organization

Executive summary

Background

Tungiasis is a neglected tropical skin disease caused by the sand flea *Tunga penetrans* that is prevalent in South America, the Caribbean, and sub-Saharan Africa. The female flea burrows into the skin, causing severe inflammation, pain, itching, and disability, as well as cognitive impairment in children and social stigma. Prevalence rates vary widely, from less than 1% in some Kenyan schools to over 50% in remote Ethiopian and Ugandan communities. The primary transmission site is unsealed earthen floors, where the flea's life cycle continues after eggs are laid by the female embedded in the skin. Risk factors include poverty, poor hygiene, and lack of sealed flooring.

Recommendations

Severe tungiasis

Recommendation 1

In individuals with severe tungiasis, the World Health Organization (WHO) recommends the use of low-viscosity dimeticone as the preferred treatment (strong recommendation, based on moderate certainty of evidence about the effects).

Remarks

- The low-viscosity dimeticone formula offers a method for killing embedded sand fleas, although its availability may be limited in endemic areas. Therefore, it would be beneficial to encourage support at national and local levels to make low-viscosity dimeticone accessible to communities in need.
- Tungiasis lesions are almost constantly superinfected with Gram-positive and/or Gram-negative bacteria. Healthcare practitioners should consider adding topical antibiotic treatment and anti-tetanus immunization, according to local guidelines and policies.
- Along with treatment, educational and community-focused prevention efforts may help reduce the risk of reinfection.

Recommendation 2

In individuals with severe tungiasis, WHO advises **against** the use of mechanical extraction of embedded sand fleas (conditional recommendation, based on very low certainty of evidence about the effects).

Mild tungiasis

Recommendation 3

In individuals with mild tungiasis, WHO suggests the use of low-viscosity dimeticone (conditional recommendation, based on moderate certainty of evidence about the effects) or mechanical extraction (conditional recommendation, based on very low certainty of evidence about the effects). When both options are available, WHO suggests the use of low-viscosity dimeticone over mechanical extraction (conditional recommendation, based on very low certainty of evidence about the effects).

Remarks

- The low-viscosity dimeticone formulation offers a relatively straightforward method for treating tungiasis, although availability may be limited in endemic areas. Therefore, it could be beneficial to encourage support at national and local levels to make these treatments more accessible to communities in need.
- Treatment of mild tungiasis with a low-viscosity dimeticone formulation may be preferred when access to health care is limited, or when treating individuals, especially children, for whom a higher value is placed on avoiding a surgical procedure.
- Mechanical extraction of embedded sand fleas should be carried out only by trained medical staff. This procedure requires the use of appropriate and sterile surgical instruments and local anesthesia, and should be performed under aseptic conditions to prevent superinfection of lesions.
- It is important to advise against self-treatment using inappropriate tools such as safety pins, thorns, sharpened pieces of wood, and sewing needles. Such practices are associated with a high risk of secondary bacterial infection and may traumatize children.
- Mechanical extraction may be the preferred treatment for mild tungiasis in settings with prompt access to health care, especially when treating individuals for whom a relatively low value is placed on avoiding a surgical procedure.

Recommendation 4

In individuals with tungiasis (any severity), WHO suggests the use of coconut oil (*Cocos nucifera*) in combination with neem oil (*Azadirachta indica*) when other treatments are not available (conditional recommendation, based on very low certainty of evidence about the effects).

Remarks

- *Azadirachta indica*, commonly known as the neem tree, is indigenous to the Indian subcontinent and was introduced into various regions in Africa. This plant is not typically found in Latin American countries.

Recommendation 5

In individuals with tungiasis (any severity), WHO suggests the use of topical ivermectin when other treatments are not available (conditional recommendation, based on very low certainty of evidence about the effects).

Recommendation 6

In individuals with tungiasis (any severity), WHO advises **against** the use of potassium permanganate (conditional recommendation, based on very low certainty of evidence about the effects).

Remarks

- The application of potassium permanganate results in a distinctive dark or purple discolouration of the skin, potentially exacerbating social stigma and diminishing its acceptability.
- Potassium permanganate is an oxidizing agent and is used as a disinfectant for topical treatment of suppurating lesions caused by fungal or bacterial infections. It can burn the skin if not carefully prepared to a 0.01% dilution.

Recommendation 7

In individuals with tungiasis (any severity), WHO recommends **against** the use of hydrogen peroxide (strong recommendation, based on very low certainty of evidence about the effects).

Remarks

- Hydrogen peroxide is an oxidizing and bleaching agent used as a disinfectant for surgical instruments and hospital, laboratory, and household surfaces.
- Its use in individuals with tungiasis has no known benefit and poses a significant risk of harm.

Summary of the methods

The Pan American Health Organization's (PAHO's) Neglected, Tropical, and Vector-Borne Diseases Unit formed a guideline development group (GDG) comprising clinical experts and a methods team, guided by a steering committee with PAHO stakeholders. The GDG identified nine key clinical questions related to tungiasis management through a prioritization process involving a survey and online discussions.

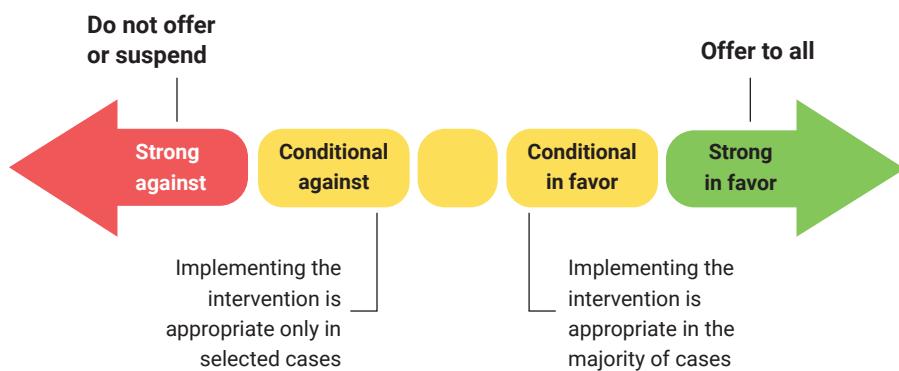
The methods team conducted systematic evidence searches on intervention effects, patient values, resource use, equity, acceptability, and treatment feasibility. Evidence was summarized in Evidence to Decision tables, and the recommendations were developed following the Grading of Recommendations Assessment, Development and Evaluation approach.

The GDG held online meetings in October and November 2023 to discuss the evidence and reach consensus on recommendations, which were based on the Evidence to Decision tables. The direction and strength of the recommendations were determined by consensus or, in rare cases, by voting. All group members declared any potential conflicts of interest, and experts with conflicts recused themselves from relevant discussions. The methodologists had no conflicts of interest.

How to use this guideline

Each recommendation included in this guideline provides a clear and actionable statement about what is being recommended and with what strength. Conditional recommendations emphasize the importance of clinicians and patients weighing individual preferences and the specific context of the decision-making process to ensure proper implementation. In contrast, strong recommendations highlight situations in which one of the alternatives is clearly superior to the other (Figure 1). Additionally, most recommendations are accompanied by remarks intended to assist providers in implementing them within their specific setting.

FIGURE 1. Interpretation of conditional and strong recommendations



Background

1.1. Description of the health problem

Tungiasis is a neglected tropical skin disease caused by the sand flea *Tunga penetrans*. The female flea burrows into the skin, inducing extreme inflammation and causing pain and itching, sleep disturbance, poor concentration, and significant disability (1). The disease is also associated with considerable stigma (1, 2), and children with tungiasis have lower exam scores and are more likely to have impaired cognitive function relative to their uninfected peers (1). Tungiasis is prevalent in South America, the Caribbean, and sub-Saharan Africa, with occurrence rates varying by region and setting. For instance, in Kenya the national prevalence is about 1.4% among children aged 8–14 years, but within schools in different parts of the country the prevalence ranges from less than 1% to 22% (3). However, in some remote rural communities the prevalence can be above 50%; in southwestern Ethiopia in 2016 it was above 50% among children aged 5–14 years (4, 5), and in northeastern Uganda in 2021 the prevalence was 62.8% among adults and children (6).

The main transmission site is the unsealed floor of sleeping rooms, where the off-host stages develop (7). The adult female flea, approximately 1 mm in size, burrows into the host's skin, typically targeting areas in contact with the ground, such as the feet. Only the tip of the flea's abdomen remains exposed for respiration, excretion, and egg-laying. Inside the skin, the flea feeds on blood and grows 2000-fold in size as the eggs develop, causing a small, raised circular lesion on the skin. Over 7 days, the flea swells to about 1 cm in diameter as it matures. A free-living male copulates with the fully developed, embedded

female. The female releases eggs through its exposed posterior end, which fall to the ground, where they hatch into larvae, continuing the life cycle off the host. Poverty, living in a house with an unsealed earthen floor, and infrequent bathing and use of soap are linked to a higher risk of infection (3, 8).

1.2. Definitions of mild and severe tungiasis used in these guidelines

The products and methods considered in these guidelines are used to treat individuals with tungiasis by killing female sand fleas embedded in the skin. Clinical studies show that the greater the number of viable fleas that a patient has embedded in the skin, the higher the level of clinical morbidity (8). Therefore, the following definitions are based on the number of viable fleas embedded in the skin, and not on symptoms, signs, complications, and sequelae.

In terms of treatment, the definition of severity is driven mainly by the feasibility of mechanical extraction, which requires trained personnel, appropriate sterile surgical instruments, local anesthesia, adequate hygiene standards, and appropriate health infrastructure for aftercare.

In this context, two possible definitions for the severity of tungiasis are proposed:

- A. Mild tungiasis is defined as having 1–5 viable embedded sand fleas, and severe tungiasis as having more than 5 viable fleas.
OR
- B. Mild tungiasis is defined as having 1–10 viable fleas, and severe tungiasis as having more than 10 viable fleas.

Whether definition A or B is used is left to the healthcare provider, who should consider the following factors:

- 1.** Age of the patient: for children, definition A should be used to reduce the experience of pain associated with mechanical extraction;
- 2.** Lesion location (e.g., if there are multiple locations requiring multiple punctures to anesthetize the area around embedded fleas or if lesions are located in an area where an injection would be very painful);
- 3.** Hygienic and sanitary conditions at the healthcare setting;
- 4.** Number of individuals to be treated at the same time in the area;
- 5.** Sociocultural acceptance and norms (e.g., knowledge of the parasite, common practice regarding treatment in the community, access to the health system, economic situation).

Chapter 2

Objective of the guidelines

The primary objective of these guidelines is to offer evidence-informed advice on the management of tungiasis. They are designed for a wide audience, including patients, caregivers, clinicians, and other stakeholders, providing them with actionable recommendations. These guidelines are intended to support policymakers in developing local or national strategies aimed at alleviating the impact of tungiasis among children and adults.

Chapter 3

Methods

The Pan American Health Organization's (PAHO's) Neglected, Tropical, and Vector-Borne Diseases Unit established a guideline development group (GDG) comprised of a panel of clinical experts and a methods team. This group operated under the guidance of a steering committee, which included key stakeholders from PAHO.

The GDG identified key questions relevant to the management of tungiasis. Through a prioritization process that included a survey of panelists and an online discussion, the group selected nine essential clinical questions.

The methods team conducted a systematic search of relevant evidence about the effects of the interventions, patients' values, resource use, equity considerations, and acceptability and feasibility of the treatment alternatives. When possible, the evidence was meta-analyzed using the Mantel-Haenszel method with a random effects model. Effect estimates were presented using relative risks and absolute risk differences and their corresponding 95% confidence intervals (CIs). When the available data were not suitable for meta-analysis, a narrative summary was developed. Two methodologists assessed the risk of bias of the trials included using validated tools such as Cochrane Risk of Bias 2.0 and ROBINS-I (9, 10). The methodologists also assessed inconsistency, indirectness, publication bias, and imprecision following the Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach (11, 12).

The evidence identified was critically appraised and summarized in Evidence to Decision (EtD) tables following the Guidelines International Network–McMaster Guideline Development Checklist (13).

The GDG discussed the evidence in online meetings during October and November 2023 (25 October and 1, 8, and 15 November). In these meetings, the GDG agreed on recommendations following the standard GRADE EtD framework (12). For each recommendation, panelists made judgments for each domain of the EtD table, which included evaluating the desirable and undesirable consequences of each intervention, the certainty of the evidence, the variability and uncertainty in values, and the resources required for implementation, as well as the intervention's acceptability, feasibility, and potential impact on health equity. Subsequently, the panelists integrated these individual judgments to determine the direction and strength of each recommendation (14). In the majority of cases, these decisions were reached through consensus; however, in rare instances voting took place. The direction of the recommendation was decided by simple majority, whereas an 80% majority was required to issue a strong recommendation.

All the members of the GDG submitted a declaration of competing interest. Neither of the methodologists had any conflicts of interest. Clinical experts with a conflict of interest were asked to recuse themselves from the discussion of the recommendations in which they had an intellectual or financial conflict of interest.

Chapter 4

Recommendations

4.1. Severe tungiasis

Severe tungiasis typically occurs in rural and impoverished communities, where affected children and adults face significant barriers to accessing health care.

Recommendation 1

In individuals with severe tungiasis, WHO recommends the use of low-viscosity dimeticone as the preferred treatment (strong recommendation, based on moderate certainty of evidence about the effects).

Remarks

- The low-viscosity dimeticone formula offers a method for killing embedded sand fleas, although its availability may be limited in endemic areas. Therefore, it would be beneficial to encourage support at national and local levels to make low-viscosity dimeticone accessible to communities in need.
- Tungiasis lesions are almost constantly superinfected with Gram-positive and/or Gram-negative bacteria. Healthcare practitioners should consider adding topical antibiotic treatment and anti-tetanus immunization, according to local guidelines and policies.

- Along with treatment, educational and community-focused prevention efforts may help reduce the risk of reinfection.

Summary of findings

Only one trial evaluating the use of low-viscosity dimeticone compared with potassium permanganate in individuals with severe tungiasis was identified (15). The study showed that low-viscosity dimeticone results in 357 fewer viable embedded sand fleas per 1000 individuals (95% CI from 454 fewer to 188 fewer), with a relative risk of 0.41 (95% CI 0.25 to 0.69). No adverse events were reported in this trial. The certainty of evidence was rated as moderate, given the large effect of the intervention.

Evidence to Decision

The GDG judged that the balance between desirable and undesirable effects clearly favors the intervention: the use of low-viscosity dimeticone probably results in a large net benefit.

While the low-viscosity dimeticone formulation is generally affordable, its restricted availability in certain endemic regions may be a barrier to its use. A PAHO strategy aims to increase its accessibility and affordability in communities across Latin America. Similar efforts could facilitate the implementation of this recommendation and help bridge existing equity gaps. Low-viscosity dimeticone is expected to be highly acceptable by both patients and caregivers.

Recommendation justification

The use of low-viscosity dimeticone will probably result in a large net benefit for individuals with severe tungiasis. This treatment is generally affordable and highly acceptable to both patients and caregivers.

Recommendation 2

In individuals with severe tungiasis, WHO advises **against** the use of mechanical extraction (conditional recommendation, based on very low certainty of evidence about the effects).

Summary of findings

No studies evaluating the use of mechanical extraction in individuals with severe tungiasis were identified.

Evidence to Decision

The effectiveness of mechanical extraction for severe tungiasis may vary depending on the level of the medical professional's expertise, the resources available, and the number of embedded sand fleas present in clusters. There may be a considerable risk of rupturing the embedded fleas during extraction, releasing flea proteins and endosymbiotic bacteria that could exacerbate inflammation. There may also be a significant risk of bacterial superinfection and sepsis associated with mechanical extraction

when done without proper antiseptic measures or adequate surgical instruments, or when done by lay people (2, 16, 17).

The resource requirements for mechanical extraction vary; however, moderate costs are expected in most healthcare settings. The intervention's feasibility and acceptability are unclear due to lack of data; however, mechanical extraction of embedded sand fleas may be traumatizing for children.

Recommendation justification

In settings where severe tungiasis is prevalent, particularly in impoverished communities within endemic regions, mechanical extraction can result in net harm, especially due to the risk of secondary complications such as infection. Clinically, it is well established that the risk of infection increases when the skin's barrier function is disrupted. In cases with extensive skin lesions, the likelihood of complications is significantly higher, particularly among patients in communities with limited access to basic sanitation. Furthermore, in many rural areas, mechanical extraction is often performed without adequate antiseptic measures, substantially elevating the risk of net harm associated with this intervention.

4.2. Mild tungiasis

Mild tungiasis, which is characterized by few lesions, commonly occurs in rural and impoverished communities where the disease is endemic. However, it can also be seen in travelers returning to high-income settings from endemic regions.

Recommendation 3

In individuals with mild tungiasis, WHO suggests the use of low-viscosity dimeticone (conditional recommendation, based on moderate certainty of evidence about the effects) or mechanical extraction (conditional recommendation, based on very low certainty of evidence about the effects). When both options are available, WHO suggests the use of low-viscosity dimeticone over mechanical extraction (conditional recommendation, based on very low certainty of evidence about the effects).

Remarks

- The low-viscosity dimeticone formulation offers a relatively straightforward method for treating tungiasis, although availability may be limited in endemic areas. Therefore, it could be beneficial to encourage support at national and local levels to make these treatments more accessible to communities in need.
- Treatment of mild tungiasis with a low-viscosity dimeticone formulation may be preferred when access to health care is limited, or when treating individuals, especially children, for whom a higher value is placed on avoiding a surgical procedure.

- Mechanical extraction of tungiasis lesions should be carried out only by trained medical staff. This procedure requires the use of appropriate and sterile surgical instruments and local anesthesia, and should be performed under aseptic conditions to prevent superinfection of lesions.
- It is important to advise against self-treatment using inappropriate tools such as safety pins, thorns, sharpened pieces of wood, and sewing needles. Such practices are associated with a high risk of secondary bacterial infection and may traumatize children.
- Mechanical extraction may be the preferred treatment for mild tungiasis in settings with prompt access to health care, especially when treating individuals for whom a relatively low value is placed on avoiding a surgical procedure.

Summary of findings

No trials evaluating the use of low-viscosity dimeticone in individuals with mild tungiasis were identified. However, the evidence from a trial evaluating the effects of low-viscosity dimeticone versus potassium permanganate in individuals with severe tungiasis was considered relevant and direct enough to inform this recommendation. This trial showed that low-viscosity dimeticone results in 357 fewer viable embedded sand fleas per 1000 individuals than potassium permanganate (95% CI from 454 fewer to 188 fewer), with a relative risk of 0.41 (95% CI 0.25 to 0.69). No adverse events were reported in the trial (15). However, in contrast with severe cases, mild tungiasis may be characterized by few lesions and limited impact on the feet. Therefore, the anticipated benefit was considered moderate.

Data regarding the effect of mechanical extraction in individuals with one or few lesions are limited to case series and case reports. A systematic review of the literature identified 83 case reports of tungiasis in travelers returning to their home countries in the Global North (18). The most common treatment was aseptic surgical extraction with topical application of an antibiotic. No important complications were noted in any of the reports examined. Further case reports identified after the publication of the systematic review also described successful treatment of returning travelers with aseptic surgical extraction (total cases: $n = 95$) (19–22).

Evidence to Decision

The GDG determined that, under suitable conditions, the efficacy of mechanical extraction may be comparable to that of low-viscosity dimeticone. However, low-viscosity dimeticone is likely simpler to apply and may require fewer resources. While both methods are generally acceptable and feasible, practical barriers could limit their widespread implementation.

Although low-viscosity dimeticone is typically inexpensive, its limited availability in some endemic areas poses a barrier to its use. To address this, PAHO has initiated efforts to improve its accessibility and affordability across Latin America.

Mechanical extraction, while safe and effective in high-standard clinical settings, may have variable outcomes depending on the expertise and resources available. Although the risk of superinfection and sepsis is lower than in cases of severe tungiasis, it remains a concern. Resource requirements for mechanical extraction can vary but are expected to be moderate in most scenarios. However, due to insufficient data, the feasibility and acceptability of this intervention remain uncertain.

Recommendation justification

Mild tungiasis, characterized by few lesions and limited impact on the feet, may benefit from treatment with low-viscosity dimeticone, which likely offers a moderate net benefit. This treatment is generally affordable and highly acceptable to both patients and caregivers.

Mechanical extraction is also a viable option for treating a small number of lesions, provided it is performed by trained clinicians under proper medical care, with adequate antiseptic measures and using appropriate surgical instruments.

For individuals with mild tungiasis, the effectiveness of mechanical extraction and low-viscosity dimeticone is likely comparable. However, due to its simplicity and greater affordability, low-viscosity dimeticone may be the preferred option for most patients.

Recommendation 4

In individuals with tungiasis (any severity), WHO suggests the use of coconut oil (*Cocos nucifera*) in combination with neem oil (*Azadirachta indica*) when other treatments are not available (conditional recommendation, based on very low certainty of evidence about the effects).

Remarks

- *Azadirachta indica*, commonly known as the neem tree, is indigenous to the Indian subcontinent and was introduced into various regions in Africa. This plant is not typically found in Latin American countries.

Summary of findings

One randomized trial was identified (23). The trial found that coconut oil (*Cocos nucifera*) in combination with neem oil from *Azadirachta indica*, in comparison with potassium permanganate, in individuals with tungiasis may result in 108 fewer viable embedded sand fleas per 1000 individuals (95% CI from 243 fewer to 86 more). The certainty of the evidence was rated as very low due to serious risk of bias (attrition bias: 19 out of 119 fleas lost to follow-up) and very serious imprecision (the CI around the absolute effect included benefit, no effect, and harm).

Evidence to Decision

The GDG judged that the balance between desirable and undesirable effects probably favors the intervention: the use of coconut oil in combination with neem oil may result in a small net benefit. Neem trees are endemic in the Indian subcontinent and various regions in Africa; however, neem oil may not be available in other settings. The use of coconut oil in combination with neem oil is likely to be acceptable and feasible where the neem tree is endemic.

Recommendation justification

In settings where other treatments are unavailable (such as low-viscosity dimeticone for severe and mild tungiasis, and sterile mechanical extraction for mild tungiasis), neem oil may provide a small benefit compared with no treatment.

Recommendation 5

In individuals with tungiasis (any severity), WHO suggests the use of topical ivermectin when other treatments are not available (conditional recommendation, based on very low certainty of evidence about the effects).

Summary of findings

Only one study using a lotion with 0.8% w/v ivermectin, applied once a day for two days, was identified (24). The use of topical ivermectin in comparison with no ivermectin in individuals with tungiasis may result in 167 fewer viable embedded sand fleas per 1000 individuals (95% CI from 227 fewer to 35 fewer). The certainty of the evidence was rated as very low due to serious risk of bias (attrition bias: 17 out of 125 participants originally randomized were not included in the analysis) and very serious imprecision (although the CI and *p* value are significant, the number of participants in the comparison of ivermectin versus placebo was very small).

Evidence to Decision

The GDG judged that the balance between desirable and undesirable effects probably favors the intervention: the use of topical ivermectin may result in a small net benefit. Topical ivermectin is relatively inexpensive and easy to use; however, its nonavailability may be a barrier in endemic communities.

Recommendation justification

In settings where other treatments are unavailable (such as low-viscosity dimeticone for severe and mild tungiasis, and mechanical extraction for mild tungiasis), topical ivermectin may provide a small benefit compared with no treatment.

Recommendation 6

In individuals with tungiasis (any severity), WHO advises **against** the use of potassium permanganate (conditional recommendation, based on very low certainty of evidence about the effects).

Remarks

- The application of potassium permanganate results in a distinctive dark or purple discoloration of the skin and nails, potentially exacerbating social stigma and diminishing its acceptability.
- Potassium permanganate is an oxidizing agent and is used as a disinfectant for topical treatment of suppurating lesions caused by fungal or bacterial infections. It is more cumbersome to use than the other tungiasis products, as it involves preparing five liters of a 0.01% (100 mg/liter) solution in a basin. The affected feet are immersed in the solution for 15 minutes followed by air drying and application of petroleum jelly.
- It can burn the skin if not carefully prepared to a 0.01% dilution.

Summary of findings

No trials evaluating potassium permanganate versus no active treatment were identified. However, two trials showed that potassium permanganate was inferior to other treatment alternatives (15, 23). One trial showed that low-viscosity dimeticone, compared with potassium permanganate, may result in 357 fewer viable embedded sand fleas per 1000 individuals (95% CI from 454 fewer to 188 fewer) (15). The other trial found that use of coconut oil (*Cocos nucifera*) in combination with neem oil from *Azadirachta indica* compared with potassium permanganate may result in 108 fewer viable embedded sand fleas per 1000 individuals (95% CI from 243 fewer to 86 more) (23).

Evidence to Decision

The GDG judged that the use of potassium permanganate, compared with other alternatives, may result in a net harm. Additionally, although the intervention may have a relatively small cost when used at community level, it may be unaffordable and cumbersome for individual patients. Importantly, its application results in a distinctive dark or purple discoloration of the skin, potentially exacerbating social stigma and diminishing its acceptability among patients, especially children.

Recommendation justification

The use of potassium permanganate, compared with other alternatives, may be associated with net harm in individuals with tungiasis. Additionally, it may exacerbate social stigma.

Recommendation 7

In individuals with tungiasis (any severity), WHO recommends **against** the use of hydrogen peroxide (strong recommendation, based on very low certainty of evidence about the effects).

Remarks

- Hydrogen peroxide is an oxidizing and bleaching agent used as a disinfectant for surgical instruments and hospital, laboratory, and household surfaces.
- Its use in individuals with tungiasis has no known benefit and poses a significant risk of harm.

Summary of findings

No trials evaluating the use of hydrogen peroxide in individuals with tungiasis were identified. However, hydrogen peroxide is a chemical with known adverse effects – it can cause irritation to skin and eyes, and in high concentrations it can cause burns or blisters on the skin (25, 26). Inhalation of hydrogen peroxide vapors or accidental ingestion may cause symptoms such as a cough, abdominal pain, or nausea (27, 28). Finally, it poses a fire hazard due to its strong oxidizing properties.

Evidence to Decision

There is no established benefit of using hydrogen peroxide in individuals with tungiasis. Potential harms were considered moderate, as hydrogen peroxide may be toxic, especially at high concentrations.

Recommendation justification

Strong recommendations typically require high or moderate certainty of evidence; however, in this instance, while the benefits of hydrogen peroxide remain uncertain, there is a clear understanding of its potential harms. This combination of uncertain benefits and certain harms justifies a strong recommendation within the GRADE framework.

Chapter 5

Practical advice

Severe tungiasis predominantly affects rural and impoverished communities, where children and adults often face significant barriers to healthcare access. In these environments, using low-viscosity dimeticone offers a simple, scalable treatment option that requires minimal investment, making it the preferred choice (strong recommendation in favor). Mechanical extraction, on the other hand, does not appear to be a suitable treatment option for severe tungiasis in endemic communities (conditional recommendation against), given the limited access to health care, the high risk of infection from the disruption to the skin's protective barrier, and the generally poor sanitation conditions.

It is important to emphasize that, in addition to treating tungiasis, preventing reinfection is essential in endemic communities. Achieving this requires breaking the cycle of transmission through education and improving the living conditions of those affected.

Mild tungiasis, characterized by few lesions, can also be effectively treated with low-viscosity dimeticone. However, some individuals may prefer mechanical extraction. This procedure requires access to health care, as it must be performed by trained clinicians under aseptic conditions with appropriate surgical materials. For returning travelers, mechanical extraction may be the preferred option in their home country. However, for individuals living in endemic areas, the choice of treatment may depend on their access to health care and their personal preference.

Recognizing the current limited access to the most effective treatments, these guidelines also offer alternatives that may provide some benefit compared with no treatment. These alternatives include neem oil, a natural product, and topical ivermectin. These treatments can be used as interim solutions while efforts are made to make more effective treatments available.

Finally, these guidelines discourage the use of potassium permanganate and hydrogen peroxide. Potassium permanganate is less effective than other alternatives, may cause discomfort, and can exacerbate social stigma. Hydrogen peroxide, while a disinfectant, has no known benefits for individuals with tungiasis and may pose significant safety risks and potential harms. Box 1 provides practical advice on how to use low-viscosity dimeticone and neem oil effectively.

BOX 1. Practical advice

Practical advice on how to use low-viscosity dimeticone:

- The treatment for tungiasis utilizes a specific two-component low-viscosity dimeticone oil. This formulation consists of 50% dimeticone with a viscosity of 100 centistokes and 40% dimeticone with a viscosity of less than 10 centistokes. As of the time of writing, there is only one commercially available product that meets these specifications.
- Before a patient is treated the affected areas should be clean and dry.
- A drop of the dimeticone oil formula is placed on the top of the exposed abdominal tip of the embedded female sand flea protruding above the skin. A common approach is to apply three to four drops, within a time interval of 10 minutes, on each embedded sand flea. If there are many lesions or lesion clusters, an alternative approach is to cover or immerse the skin of the whole foot with the dimeticone.
- Treatment may be repeated after two days if there is no significant improvement in pain and/or itching.
- Low-viscosity dimeticone is flammable, therefore it should be stored away from any source of heat. Any treated person should avoid fires or other sources of ignition for two hours, particularly if an extensive area of skin has been treated.

BOX 1. Practical advice (continued)

Practical advice on how to use the coconut oil (*Cocos nucifera*) and neem oil (*Azadirachta indica*) combination:

- Before a patient is treated the affected areas should be clean and dry.
- A single drop of each oil is typically placed on the exposed abdominal tip of each flea. If there are many lesions, the oils can be spread over the area with a gloved hand.
- A common approach is to apply the oils once a day for three days.
- The product used in the trial was a mixture of 20% neem oil and 80% coconut oil. Production should follow good manufacturing practices.

Chapter 6

Discussion

Despite being a relatively common disease in rural and impoverished communities of Latin America and sub-Saharan Africa, tungiasis remains largely neglected. This is evident in the absence of international guidelines, lack of research, and significant barriers to implementing effective treatments in affected communities.

These are the first evidence-based guidelines published for the treatment of tungiasis. They represent a collaborative effort between PAHO and WHO to synthesize the current evidence and provide actionable recommendations that can be implemented in various settings.

6.1. Ethical considerations

The assessment of the evidence raises several ethical considerations, including those pertaining to equity. Indeed, persons affected by tungiasis tend to belong to the most disadvantaged population groups. Tungiasis is endemic in indigenous communities that are minorities already suffering from extreme poverty and limited access to healthcare services due to geographical barriers, which are often aggravated by language and cultural barriers (17, 29–40). Suffering from tungiasis is indeed associated with poverty, and it further exacerbates disadvantages; for example, tungiasis can lead to disability, which is more challenging in rural environments. These compounding inequities stress the moral urgency of offering therapeutic interventions to persons affected by tungiasis.

Moreover, the recommendations above are informed by an ethical judgment in response to the limited availability of low-viscosity dimeticone. While the evidence shows that it is beneficial for severe and mild tungiasis, it is ethically imperative to prioritize its use for treating persons suffering from severe tungiasis when access to the product is limited. This recommendation is responsive to current scenarios, yet efforts must be made to ensure access for all affected communities, as well as to ensure access to medically provided mechanical extraction when appropriate.

Lastly, it is also ethically imperative to conduct research to meet this historically neglected health need.

6.2. Knowledge gaps

Despite tungiasis being a relatively common disease in endemic communities, research remains limited. Most of the literature comprises case series and case reports, with few clinical trials conducted. Treatment options are also limited, with only a few interventions currently available. There is a pressing need for more comprehensive research to better characterize the population at risk, develop a wider range of therapeutic alternatives, and create community-level interventions aimed at interrupting the cycle of transmission and reinfection. Addressing these research gaps could lead to more effective control and prevention strategies, ultimately reducing the burden of tungiasis in affected areas.

6.3. Future challenges

The most pressing challenge in managing tungiasis is the implementation of effective interventions, such as low-viscosity dimeticone, in communities heavily impacted by the disease. While low-viscosity dimeticone is readily available in developed countries, it is generally scarce in regions where tungiasis is endemic.

Economic constraints play a significant role in the unavailability of effective treatments. Many of the affected populations live in poverty, limiting their ability to afford even basic health care. Additionally, government and nongovernmental organizations often have limited resources to address these needs comprehensively. Logistic challenges also limit the distribution of treatments. Poor infrastructure, such as inadequate roads and transportation networks, makes it difficult to reach remote communities. This results in delays and increased costs in delivering medical supplies.

Addressing these challenges requires a coordinated effort at multiple levels. International aid, local government initiatives, and the involvement of nongovernmental organizations are important in improving healthcare infrastructure, training healthcare workers, and ensuring the consistent supply of effective treatments. Innovative solutions, such as community-based health programs and mobile clinics, could help bridge the gap in healthcare access. Furthermore, public health campaigns that raise awareness about tungiasis and its treatment can empower communities to seek and demand better healthcare services.

Ultimately, overcoming these barriers is essential for improving the management of tungiasis and reducing its impact on vulnerable populations.

6.4. Dissemination, implementation, and updating of the guidelines

The recommendations in these guidelines will be published in English, Spanish, and Portuguese to increase accessibility for practitioners in endemic communities. Developing tungiasis guidelines is part of a broader effort to raise awareness and ensure the appropriate treatment of diseases that, despite affecting large populations globally, often receive inadequate attention. As part of these efforts, PAHO has established a strategic fund to make low-viscosity dimeticone available in endemic areas in Latin America. Similar initiatives may be undertaken to support affected individuals in Africa. The recommendations will be updated as new evidence emerges. Currently, a randomized trial investigating the use of low-viscosity dimeticone for severe tungiasis is under way, with results expected in approximately two years.

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Annexes

Annex 1. Summary of Evidence to Decision tables

Question 1: Should low-viscosity dimeticone vs. no dimeticone be used for individuals with severe tungiasis (several lesions)?

Patient or population: individuals with severe tungiasis (several lesions)

Setting: outpatients

Intervention: low-viscosity dimeticone

Comparison: no dimeticone

Certainty assessment						No. of patients	Effect	Certainty	Importance
No. of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Low-viscosity dimeticone	Relative risk (95% CI)	Absolute (95% CI)
1	Non-randomized studies	Not serious	Not serious	Not serious	Not serious	Strong association*	19/86 (22.1%)	RR 0.41 (0.25 to 0.69)	357 fewer per 1000 (from 454 fewer to 188 fewer)

* The certainty of evidence was upgraded by one level due to the large relative effect observed. It is unlikely that confounding variables alone could account for this significant effect.
CI, confidence interval; RR, risk ratio.

ASSESSMENT

Desirable effects

How substantial are the desirable anticipated effects?

JUDGMENT

- Trivial
 - Small
 - Moderate
 - Large
-
- Varies
 - Don't know

RESEARCH EVIDENCE

Outcomes	No. of participants (studies) Follow-up	Certainty of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects* (95% CI)	Risk with no dimeticone	Risk difference with dimeticone
Efficacy of treatment assessed with: viability of embedded sand fleas Follow-up: median 7 days	157 (1 non-randomized study)	⊕⊕⊕○ Moderate*	RR 0.41 (0.25 to 0.69)	606 per 1000	357 fewer per 1000 (454 fewer to 188 fewer)	Study population

Undesirable effects

How substantial are the undesirable anticipated effects?

JUDGMENT

- Trivial
 - Small
 - Moderate
 - Large
-
- Varies
 - Don't know

RESEARCH EVIDENCE

ADDITIONAL CONSIDERATIONS
An ongoing randomized controlled trial in Kenya is targeting a sample size of 920 lesions. ¹ Preliminary findings involving 56 children, published after the date of the search, are consistent with a substantial benefit from low-viscosity dimeticone. ²

Certainty of evidence What is the overall certainty of the evidence of effects?		RESEARCH EVIDENCE		ADDITIONAL CONSIDERATIONS	
JUDGMENT		Outcomes	Importance	Certainty of the evidence (GRADE)	
<input type="radio"/> Very low <input type="radio"/> Low <input checked="" type="radio"/> Moderate <input type="radio"/> High		Efficacy of treatment assessed with: viability of embedded sand fleas Follow-up: median 7 days	CRITICAL	⊕⊕⊕○ Moderate ¹	
Values	Is there important uncertainty about or variability in how much people value the main outcomes?	RESEARCH EVIDENCE	JUDGMENT	ADDITIONAL CONSIDERATIONS	
		No evidence was found. However, most individuals probably will place a higher value on treatment response than on the potential adverse events of treatment.	<input type="radio"/> Important uncertainty or variability <input type="radio"/> Possibly important uncertainty or variability <input checked="" type="radio"/> Probably no important uncertainty or variability <input type="radio"/> No important uncertainty or variability		
Balance of effects	Does the balance between desirable and undesirable effects favor the intervention or the comparison?	RESEARCH EVIDENCE	JUDGMENT	ADDITIONAL CONSIDERATIONS	
			<input type="radio"/> Favors the comparison <input type="radio"/> Probably favors the comparison <input type="radio"/> Does not favor either the intervention or the comparison <input type="radio"/> Probably favors the intervention <input checked="" type="radio"/> Favors the intervention	<input type="radio"/> Varies <input type="radio"/> Don't know	

Resources required		
How large are the resource requirements (costs)?		
JUDGMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<ul style="list-style-type: none"> <input type="radio"/> Large costs <input type="radio"/> Moderate costs <input checked="" type="radio"/> Negligible costs and savings <input type="radio"/> Moderate savings <input type="radio"/> Large savings <hr/> <ul style="list-style-type: none"> <input type="radio"/> Varies <input type="radio"/> Don't know 	Through a PAHO strategic fund, some countries offer a product of dimeticone (100 centistokes 92%, drop applicator, 100 mL bottle) at a price of USD 15 per bottle.	
Cost-effectiveness		
Does the cost-effectiveness of the intervention favor the intervention or the comparison?		
JUDGMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<ul style="list-style-type: none"> <input type="radio"/> Favors the comparison <input type="radio"/> Probably favors the comparison <input type="radio"/> Does not favor either the intervention or the comparison <input type="radio"/> Probably favors the intervention <input type="radio"/> Favors the intervention <hr/> <ul style="list-style-type: none"> <input type="radio"/> Varies <input checked="" type="radio"/> No included studies 	No economic evaluation was found.	

Equity		
What would be the impact on health equity?		
JUDGMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<input type="radio"/> Reduced <input type="radio"/> Probably reduced <input type="radio"/> Probably no impact <input type="radio"/> Probably increased <input checked="" type="radio"/> Increased <hr/> <input type="radio"/> Varies <input type="radio"/> Don't know	<p>A systematic search of the literature showed the following:</p> <p>Tungiasis is endemic in low-income communities in tropical and subtropical countries.</p> <p>Disadvantaged populations may include:</p> <ul style="list-style-type: none"> Those living in precarious housing conditions, especially homes with earthen floors; Rural communities; Older persons; Children; Native communities. 	
Acceptability		
Is the intervention acceptable to key stakeholders?		ADDITIONAL CONSIDERATIONS
JUDGMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<input type="radio"/> No <input type="radio"/> Probably no <input type="radio"/> Probably yes <input checked="" type="radio"/> Yes <hr/> <input type="radio"/> Varies <input type="radio"/> Don't know	<p>Dimeticone treatment was acceptable. All the participants of the trial completed follow-up.</p> <p>When study participants were asked about their satisfaction, 37/47 (78%) preferred dimeticone over potassium permanganate.</p>	

Feasibility		Is the intervention feasible to implement?			
JUDGMENT		RESEARCH EVIDENCE		ADDITIONAL CONSIDERATIONS	
<input type="radio"/> No <input type="radio"/> Probably no <input checked="" type="radio"/> Probably yes <input type="radio"/> Yes		<p>A systematic search of the literature showed the following:</p> <p>Barriers to implementing effective treatment may include:</p> <ul style="list-style-type: none"> Social stigma; Lack of knowledge about prevention and control activities; Lack of knowledge about the zoonotic nature of tungiasis and insufficient animal control; Self-treatment of lesions; Normalization of tungiasis, as it may not be considered a health problem. <p>Additionally, dimeticone products are not registered nor available in several endemic countries.</p> <p>They are mostly available to international travelers from developed countries.</p>			

- * The certainty of evidence was upgraded by one level due to the large relative effect observed. It is unlikely that confounding variables alone could account for this significant effect.
- 1 Suzuki K, Kamiya Y, Smith C, Kaneko S, Ongaya A, Amukoye E. Protocol for a randomized control trial for tungiasis treatment in Homa Bay County, Kenya: dimeticone versus sodium carbonate. Methods Protoc. 2023;6:12. Available from: <https://doi.org/10.3390/mps6010012>.
- 2 Suzuki K, Kamiya Y, Smith C, Kaneko S, Okomo G, Ongaya A, et al. A pilot study of dimeticone oils versus sodium carbonate treatment for tungiasis: a randomized cohort trial in Homa Bay County, Kenya. PLoS Negl Trop Dis. 2024;18(7):e0012341. Available from: <https://doi.org/10.1371/journal.pntd.0012341>.
- CI, confidence interval; GRADE, Grading of Recommendations Assessment, Development and Evaluation; PAHO: Pan American Health Organization; RR, risk ratio.

SUMMARY OF JUDGMENTS

	JUDGMENT					
DESIRABLE EFFECTS	Trivial	Small	Moderate	Large	Varies	Don't know
UNDESIRABLE EFFECTS	Trivial	Small	Moderate	Large	Varies	Don't know
CERTAINTY OF EVIDENCE	Very low	Low	Moderate	High		No included studies
VALUES	Important uncertainty or variability	Possibly important uncertainty or variability	Probably no important uncertainty or variability	No important uncertainty or variability		

		JUDGMENT						
		Favors the intervention			Varies			Don't know
BALANCE OF EFFECTS		Favors the comparison	Probably favors the comparison	Does not favor either the intervention or the comparison	Probably favors the intervention	Large savings	Varies	Don't know
RESOURCES REQUIRED		Moderate costs	Negligible costs and savings	Moderate savings	Large savings	Varies	Varies	Don't know
COST-EFFECTIVENESS		Favors the comparison	Probably favors the comparison	Does not favor either the intervention or the comparison	Probably favors the intervention	Favors the intervention	Varies	No included studies
EQUITY		Reduced	Probably reduced	Probably no impact	Probably increased	Increased	Varies	Don't know
ACCEPTABILITY		No	Probably no	Probably yes	Yes		Varies	Don't know
FEASIBILITY		No	Probably no	Probably yes	Yes		Varies	Don't know

TYPE OF RECOMMENDATION

		Conditional recommendation against the intervention	Conditional recommendation for either the intervention or the comparison	Conditional recommendation for the intervention	Strong recommendation for the intervention
<input type="radio"/>	<input type="radio"/>		<input type="radio"/>	<input type="radio"/>	<input checked="" type="radio"/>

Question 2: Should mechanical extraction vs. no extraction be used in individuals with severe tungiasis (several lesions)?

Patient or population: individuals with severe tungiasis (several lesions)

Setting: outpatients

Intervention: mechanical extraction

Comparison: no extraction

No. of studies	Study design	Certainty assessment				Impact	Certainty	Importance
		Risk of bias	Inconsistency	Indirectness	Imprecision			
3	Non-randomized studies	Not serious	Not serious	Very serious*	Not serious	None	⊕○○ Very low*	CRITICAL

* Data available from descriptive studies only. The effect of the intervention was not directly measured.

ASSESSMENT

Desirable effects

How substantial are the desirable anticipated effects?

JUDGMENT

- Trivial
- Small
- Moderate
- Large

- Varies
- Don't know

RESEARCH EVIDENCE

Outcomes

Description of findings

There is no trial assessing the effect of mechanical extraction in individuals with severe tungiasis. Severe tungiasis is seen more often in individuals living in endemic areas. In these communities, observational studies suggest the following ($n = 1855$): (a) mechanical extraction is being used as the main method of self-treatment; (b) the most common instruments used are safety pins, thorns, and sewing needles; (c) instruments are frequently shared among family members; (d) only a minority of individuals use antiseptics before or after the extraction; and (e) superinfections are common.

ADDITIONAL CONSIDERATIONS

The desirable effects may vary with the level of expertise and resources available. Typically, in the context of severe tungiasis, additional measures are required (antibiotics, tetanus vaccine).

Undesirable effects

How substantial are the undesirable anticipated effects?

JUDGMENT

- Trivial
- Small
- Moderate
- Large

- Varies
- Don't know

RESEARCH EVIDENCE

Outcomes

Description of findings

The risk of superinfections was not directly measured in the studies identified. However, indirect evidence suggests that the risk of superinfection and sepsis is increased by mechanical extractions conducted without the proper antiseptic measures and by those without the appropriate training and tools.

ADDITIONAL CONSIDERATIONS

The risk of complications in severe cases is higher than in mild cases.

Certainty of evidence

What is the overall certainty of the evidence of effects?

JUDGMENT

- Very low
- Low
- Moderate
- High

- No included studies

RESEARCH EVIDENCE

Outcomes

Description of findings

ADDITIONAL CONSIDERATIONS

	Importance	Certainty of the evidence (GRADE)
	CRITICAL	⊕○○○ Very low*

Values Is there important uncertainty about or variability in how much people value the main outcomes?	JUDGMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<ul style="list-style-type: none"> <input type="radio"/> Important uncertainty or variability <input checked="" type="radio"/> Possibly important uncertainty or variability <input type="radio"/> Probably no important uncertainty or variability <input type="radio"/> No important uncertainty or variability 		No evidence was found. Individuals will probably place a high value on treatment success and on avoiding serious complications like sepsis.	
Balance of effects Does the balance between desirable and undesirable effects favor the intervention or the comparison?	JUDGMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<ul style="list-style-type: none"> <input type="radio"/> Favors the comparison <input checked="" type="radio"/> Probably favors the comparison <input type="radio"/> Does not favor either the intervention or the comparison <input type="radio"/> Probably favors the intervention <input type="radio"/> Favors the intervention <hr/> <ul style="list-style-type: none"> <input type="radio"/> Varies <input type="radio"/> Don't know 			
Resources required How large are the resource requirements (costs)?	JUDGMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<ul style="list-style-type: none"> <input type="radio"/> Large costs <input checked="" type="radio"/> Moderate costs <input type="radio"/> Negligible costs and savings <input type="radio"/> Moderate savings <input type="radio"/> Large savings <hr/> <ul style="list-style-type: none"> <input type="radio"/> Varies <input type="radio"/> Don't know 		No data were found. Resource requirements are likely variable.	

Cost-effectiveness		Does the cost-effectiveness of the intervention favor the intervention or the comparison?	
JUDGMENT	RESEARCH EVIDENCE	JUDGMENT	RESEARCH EVIDENCE
JUDGMENT	RESEARCH EVIDENCE	JUDGMENT	RESEARCH EVIDENCE
<input type="radio"/> Favors the comparison <input type="radio"/> Probably favors the comparison <input type="radio"/> Does not favor either the intervention or the comparison <input type="radio"/> Probably favors the intervention <input type="radio"/> Favors the intervention <input type="radio"/> Varies <input checked="" type="radio"/> No included studies	No economic evaluation was found.	<input type="radio"/> Reduced <input type="radio"/> Probably reduced <input type="radio"/> Probably no impact <input type="radio"/> Probably increased <input type="radio"/> Increased <input type="radio"/> Varies <input checked="" type="radio"/> Don't know	<p>A systematic search of the literature showed the following:</p> <p>Tungiasis is endemic in low-income communities in tropical and subtropical countries.</p> <p>Disadvantaged populations may include:</p> <ul style="list-style-type: none"> Those living in precarious housing conditions, especially homes with earthen floors; Rural communities; Older persons; Children; Native communities.
Acceptability Is the intervention acceptable to key stakeholders?	RESEARCH EVIDENCE <input type="radio"/> No <input checked="" type="radio"/> Probably no <input type="radio"/> Probably yes <input type="radio"/> Yes <input type="radio"/> Varies <input checked="" type="radio"/> Don't know	RESEARCH EVIDENCE <input type="radio"/> No <input checked="" type="radio"/> Probably no <input type="radio"/> Probably yes <input type="radio"/> Yes <input type="radio"/> Varies <input checked="" type="radio"/> Don't know	RESEARCH EVIDENCE <input type="radio"/> No <input checked="" type="radio"/> Probably no <input type="radio"/> Probably yes <input type="radio"/> Yes <input type="radio"/> Varies <input checked="" type="radio"/> Don't know

Feasibility Is the intervention feasible to implement?		RESEARCH EVIDENCE		ADDITIONAL CONSIDERATIONS	
JUDGMENT		JUDGMENT		JUDGMENT	
<input type="radio"/> No <input type="radio"/> Probably no <input type="radio"/> Probably yes <input type="radio"/> Yes <hr/> <input checked="" type="radio"/> Varies <input type="radio"/> Don't know	<p>A systematic search of the literature showed the following:</p> <p>Barriers to implementing effective treatment may include:</p> <ul style="list-style-type: none"> Social stigma; Lack of knowledge about prevention and control activities; Lack of knowledge about the zoonotic nature of tungiasis and insufficient animal control; Self-treatment of lesions; Normalization of tungiasis, as it may not be considered a health problem. 	Lack of access to health care may be an important barrier.			

* Data available from descriptive studies only. The effect of the intervention was not directly measured.
 GRADE, Grading of Recommendations Assessment, Development and Evaluation.

SUMMARY OF JUDGMENTS

DESIRABLE EFFECTS		Trivial	Small	Moderate	Large	Varies	Don't know
UNDESIRABLE EFFECTS		Trivial	Small	Moderate	Large	Varies	Don't know
CERTAINTY OF EVIDENCE		Very low	Low	Moderate	High	Varies	No included studies
VALUES		Possibly important uncertainty or variability	Probably no important uncertainty or variability	No important uncertainty or variability	Varies	Varies	Don't know
BALANCE OF EFFECTS		Probably favors the comparison	Does not favor either the intervention or the comparison	Probably favors the intervention	Favors the intervention	Varies	Don't know

	JUDGMENT				
RESOURCES REQUIRED	Large costs	Moderate costs	Negligible costs and savings	Moderate savings	Large savings
COST-EFFECTIVENESS	Favors the comparison	Probably favors the comparison	Does not favor either the intervention or the comparison	Probably favors the intervention	Favors the intervention
EQUITY	Reduced	Probably reduced	Probably no impact	Probably increased	Increased
ACCEPTABILITY	No	Probably no	Probably yes	Yes	Varies
FEASIBILITY	No	Probably no	Probably yes	Yes	Varies

TYPE OF RECOMMENDATION

Strong recommendation against the intervention	Conditional recommendation against the intervention	Conditional recommendation for either the intervention or the comparison	Conditional recommendation for the intervention	Strong recommendation for the intervention
○	●	○	○	○

Question 3: Should low-viscosity dimeticon vs. no dimeticon be used in individuals with mild tungiasis (one or few lesions)?

Patient or population: individuals with mild tungiasis (one or few lesions)

Setting: outpatients

Intervention: low-viscosity dimeticon

Comparison: no dimeticon

Certainty assessment						No. of patients	Effect	Certainty	Importance
No. of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Low-viscosity dimeticon	Relative (95% CI)	Absolute (95% CI)
1*	Non-randomized studies	Not serious	Not serious	Not serious	Not serious	Strong association*	19/86 (22.1%)	RR 0.41 (0.25 to 0.69)	357 fewer per 1000 (from 454 fewer to 188 fewer)

* The certainty of evidence was upgraded by one level due to the large relative effect observed. It is unlikely that confounding variables alone could account for this significant effect.
CI, confidence interval; RR, risk ratio.

ASSESSMENT

JUDGMENT

RESEARCH EVIDENCE

Desirable effects

How substantial are the desirable anticipated effects?

JUDGMENT

ADDITIONAL CONSIDERATIONS

Outcomes	No. of participants (studies) Follow-up	Certainty of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects* (95% CI)
			RR 0.41 (0.25 to 0.69)	Risk difference with low-viscosity dimeticon
Efficacy of treatment assessed with: viability of embedded sand fleas Follow-up: median 7 days	157 (1 non-randomized study)*	⊕⊕⊕○ Moderate*	RR 0.41 (0.25 to 0.69)	Study population 357 fewer per 1000 (454 fewer to 188 fewer)

Undesirable effects		How substantial are the undesirable anticipated effects?								
JUDGMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS								
<ul style="list-style-type: none"> ● Trivial <input type="radio"/> Small <input type="radio"/> Moderate <input type="radio"/> Large <hr/> <ul style="list-style-type: none"> <input type="radio"/> Varies <input type="radio"/> Don't know 	Adverse events were not reported in the trial. However, adverse events of topical dimeticone are likely mild and transient (e.g., rash, itching).									
Certainty of evidence	What is the overall certainty of the evidence of effects?			ADDITIONAL CONSIDERATIONS						
JUDGMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS								
<ul style="list-style-type: none"> <input type="radio"/> Very low <input type="radio"/> Low ● Moderate <input type="radio"/> High <hr/> <ul style="list-style-type: none"> <input type="radio"/> No included studies 	<table border="1" style="width: 100%; border-collapse: collapse;"> <thead> <tr> <th>Outcomes</th> <th>Importance</th> <th>Certainty of the evidence (GRADE)</th> </tr> </thead> <tbody> <tr> <td>Efficacy of treatment assessed with: viability of embedded sand fleas Follow-up: median 7 days</td> <td>CRITICAL</td> <td> Moderate*</td> </tr> </tbody> </table>	Outcomes	Importance	Certainty of the evidence (GRADE)	Efficacy of treatment assessed with: viability of embedded sand fleas Follow-up: median 7 days	CRITICAL	Moderate*			
Outcomes	Importance	Certainty of the evidence (GRADE)								
Efficacy of treatment assessed with: viability of embedded sand fleas Follow-up: median 7 days	CRITICAL	Moderate*								
Values	Is there important uncertainty about or variability in how much people value the main outcomes?			ADDITIONAL CONSIDERATIONS						
JUDGMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS								
	No evidence was found. However, most individuals probably will place a higher value on treatment response than on the potential adverse events of treatment.									
	<ul style="list-style-type: none"> <input type="radio"/> Important uncertainty or variability <input type="radio"/> Possibly important uncertainty or variability <input type="radio"/> Probably no important uncertainty or variability ● No important uncertainty or variability 									

Balance of effects Does the balance between desirable and undesirable effects favor the intervention or the comparison?		JUDGMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
		<ul style="list-style-type: none"> <input type="radio"/> Favors the comparison <input type="radio"/> Probably favors the comparison <input type="radio"/> Does not favor either the intervention or the comparison <input checked="" type="radio"/> Probably favors the intervention <input type="radio"/> Favors the intervention <hr/> <ul style="list-style-type: none"> <input type="radio"/> Varies <input type="radio"/> Don't know 		
		Resources required How large are the resource requirements (costs)?	JUDGMENT	RESEARCH EVIDENCE
			<ul style="list-style-type: none"> <input type="radio"/> Large costs <input type="radio"/> Moderate costs <input checked="" type="radio"/> Negligible costs and savings <input type="radio"/> Moderate savings <input type="radio"/> Large savings <hr/> <ul style="list-style-type: none"> <input type="radio"/> Varies <input type="radio"/> Don't know 	<p>Through a PAHO strategic fund, some countries offer a product of dimeticone (100 centistokes 92%, drop applicator, 100 mL bottle) at a price of USD 15 per bottle.</p>

Cost-effectiveness		Does the cost-effectiveness of the intervention favor the intervention or the comparison?	
JUDGMENT	RESEARCH EVIDENCE	JUDGMENT	RESEARCH EVIDENCE
JUDGMENT	RESEARCH EVIDENCE	JUDGMENT	RESEARCH EVIDENCE
<input type="radio"/> Favors the comparison <input type="radio"/> Probably favors the comparison <input type="radio"/> Does not favor either the intervention or the comparison <input type="radio"/> Probably favors the intervention <input type="radio"/> Favors the intervention <input type="radio"/> Varies <input checked="" type="radio"/> No included studies	No economic evaluation was found.	A systematic search of the literature showed the following: Tungiasis is endemic in low-income communities in tropical and subtropical countries. Disadvantaged populations may include: Those living in precarious housing conditions, especially homes with earthen floors; Rural communities; Older persons; Children; Native communities.	Acceptability Is the intervention acceptable to key stakeholders?
<input type="radio"/> Reduced <input type="radio"/> Probably reduced <input type="radio"/> Probably no impact <input type="radio"/> Probably increased <input checked="" type="radio"/> Increased <input type="radio"/> Varies <input type="radio"/> Don't know		JUDGMENT Is the intervention acceptable to key stakeholders?	Acceptability Is the intervention acceptable to key stakeholders?
<input type="radio"/> No <input type="radio"/> Probably no <input type="radio"/> Probably yes <input checked="" type="radio"/> Yes <input type="radio"/> Varies <input type="radio"/> Don't know		JUDGMENT Is the intervention acceptable to key stakeholders?	Acceptability Is the intervention acceptable to key stakeholders?

Feasibility		Is the intervention feasible to implement?											
JUDGMENT		RESEARCH EVIDENCE			ADDITIONAL CONSIDERATIONS								
<input type="radio"/> No													
<input type="radio"/> Probably no													
<input type="radio"/> Probably yes													
<input checked="" type="radio"/> Yes													
<input type="radio"/> Varies													
<input type="radio"/> Don't know													
Barriers to implementing effective treatment may include:													
Social stigma;													
Lack of knowledge about prevention and control activities;													
Lack of knowledge about the zoonotic nature of tungiasis and insufficient animal control;													
Self-treatment of lesions;													
Normalization of tungiasis, as it may not be considered a health problem.													
Additionally, dimeticone products are not registered nor available in several endemic countries.													
They are mostly available to international travelers from developed countries.													
* The certainty of evidence was upgraded by one level due to the large relative effect observed. It is unlikely that confounding variables alone could account for this significant effect. CI, confidence interval; GRADE, Grading of Recommendations Assessment, Development and Evaluation; RR, risk ratio.													
SUMMARY OF JUDGMENTS													
DESIRABLE EFFECTS		Trivial	Small	Moderate	Large	Varies	Don't know						
UNDESIRABLE EFFECTS		Trivial	Small	Moderate	Large	Varies	Don't know						
CERTAINTY OF EVIDENCE		Very low	Low	Moderate	High		No included studies						
VALUES		Important uncertainty or variability	Possibly important uncertainty or variability	Probably no important uncertainty or variability	No important uncertainty or variability								
BALANCE OF EFFECTS		Favors the comparison	Probably favors the comparison	Does not favor either the intervention or the comparison	Probably favors the intervention	Favors the intervention	Varies						
							Don't know						

		JUDGMENT				
RESOURCES REQUIRED	Large costs	Moderate costs	Negligible costs and savings	Moderate savings	Large savings	Varies
COST-EFFECTIVENESS	Favors the comparison	Probably favors the comparison	Does not favor either the intervention or the comparison	Probably favors the intervention	Favors the intervention	Varies
EQUITY	Reduced	Probably reduced	Probably no impact	Probably increased	Increased	Varies
ACCEPTABILITY	No	Probably no	Probably yes	Yes	Varies	Don't know
FEASIBILITY	No	Probably no	Probably yes	Yes	Varies	Don't know

TYPE OF RECOMMENDATION

		Strong recommendation against the intervention	Conditional recommendation against the intervention	Conditional recommendation for either the intervention or the comparison	Conditional recommendation for the intervention	Strong recommendation for the intervention
○	○	○	○	●	○	○

Question 4: Should mechanical extraction vs. no extraction be used in individuals with mild tungiasis (one or few lesions)?

Patient or population: individuals with mild tungiasis (one or few lesions)

Setting: outpatients

Intervention: mechanical extraction

Comparison: no extraction

No. of studies	Study design	Certainty assessment				Other considerations	Impact		Certainty	Importance		
		Risk of bias	Inconsistency	Indirectness	Imprecision							
3	Non-randomized studies	Not serious	Not serious	Very serious*	Not serious	None	<p>There is no trial assessing the effect of mechanical extraction in individuals with mild tungiasis. Mild tungiasis is sometimes seen in individuals living in endemic areas.</p> <p>In these communities, observational studies suggest the following ($n = 1855$):</p> <ul style="list-style-type: none"> (a) mechanical extraction is being used as the main method of self-treatment; (b) the most common instruments used are safety pins, thorns, and sewing needles; (c) instruments are frequently shared among family members; (d) only a minority of individuals use antiseptics before or after the extraction; and (e) superinfections are common. However, mild tungiasis may also be seen in returning travelers. A systematic review of the literature identified 83 case reports of tungiasis in returning travelers. <p>The most common treatment was aseptic surgical extraction and topical antibiotics.</p> <p>No important complications were reported in any of the reports examined. Further case reports identified after the publication of the systematic review also described successful treatment of returning travelers with aseptic surgical extraction (total cases: $n = 95$).</p>				⊕○○○ Very low*	CRITICAL

* Data available from descriptive studies only. The effect of the intervention was not directly measured.

ASSESSMENT

Desirable effects

How substantial are the desirable anticipated effects?

JUDGMENT		RESEARCH EVIDENCE		ADDITIONAL CONSIDERATIONS
<input type="radio"/> Trivial <input type="radio"/> Small <input type="radio"/> Moderate <input type="radio"/> Large <input checked="" type="radio"/> Varies <input type="radio"/> Don't know	Outcomes Description of findings	Impact There is no trial assessing the effect of mechanical extraction in individuals with mild tungiasis. Mild tungiasis is sometimes seen in individuals living in endemic areas. In these communities, observational studies suggest the following ($n = 1855$): (a) mechanical extraction is being used as the main method of self-treatment; (b) the most common instruments used are safety pins, thorns, and sewing needles; (c) instruments are frequently shared among family members; (d) only a minority of individuals use antiseptics before or after the extraction; and (e) superinfections are common. However, mild tungiasis may also be seen in returning travelers. A systematic review of the literature identified 83 case reports of tungiasis in returning travelers. The most common treatment was aseptic surgical extraction and topical antibiotics. No important complications were reported in any of the reports examined. Further case reports identified after the publication of the systematic review also described successful treatment of returning travelers with aseptic surgical extraction (total cases: $n = 95$).		The desirable effects may vary with the level of expertise and resources available.
Undesirable effects How substantial are the undesirable anticipated effects?	JUDGMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS	<ul style="list-style-type: none"> <input type="radio"/> Trivial <input type="radio"/> Small <input type="radio"/> Moderate <input type="radio"/> Large <input checked="" type="radio"/> Varies <input type="radio"/> Don't know

Certainty of evidence										
What is the overall certainty of the evidence of effects?										
JUDGMENT	RESEARCH EVIDENCE			ADDITIONAL CONSIDERATIONS						
<ul style="list-style-type: none"> ● Very low <input type="radio"/> Low <input type="radio"/> Moderate <input type="radio"/> High <p><input type="radio"/> No included studies</p>	<table border="1" style="width: 100%; border-collapse: collapse;"> <thead> <tr> <th style="text-align: center;">Outcomes</th> <th style="text-align: center;">Importance</th> <th style="text-align: center;">Certainty of the evidence (GRADE)</th> </tr> </thead> <tbody> <tr> <td>Description of findings</td> <td style="text-align: center;">CRITICAL</td> <td style="text-align: center;">$\oplus\circ\circ$ Very low*</td> </tr> </tbody> </table>	Outcomes	Importance	Certainty of the evidence (GRADE)	Description of findings	CRITICAL	$\oplus\circ\circ$ Very low*	<p>Values</p> <p>Is there important uncertainty about or variability in how much people value the main outcomes?</p>	<p>RESEARCH EVIDENCE</p>	<p>ADDITIONAL CONSIDERATIONS</p>
Outcomes	Importance	Certainty of the evidence (GRADE)								
Description of findings	CRITICAL	$\oplus\circ\circ$ Very low*								
<p>JUDGMENT</p> <ul style="list-style-type: none"> <input type="radio"/> Important uncertainty or variability ● Possibly important uncertainty or variability <input type="radio"/> Probably no important uncertainty or variability <input type="radio"/> No important uncertainty or variability 	<p>No evidence was found. Individuals probably will place a high value on treatment success and on avoiding serious complications like sepsis.</p>	<p>Balance of effects</p> <p>Does the balance between desirable and undesirable effects favor the intervention or the comparison?</p>	<p>RESEARCH EVIDENCE</p>	<p>ADDITIONAL CONSIDERATIONS</p>						
<p>JUDGMENT</p> <ul style="list-style-type: none"> <input type="radio"/> Favors the comparison <input type="radio"/> Probably favors the comparison <input type="radio"/> Does not favor either the intervention or the comparison ● Probably favors the intervention <input type="radio"/> Favors the intervention <p><input type="radio"/> Varies</p> <p><input type="radio"/> Don't know</p>										

Resources required		How large are the resource requirements (costs)?	
JUDGMENT	RESEARCH EVIDENCE	JUDGMENT	RESEARCH EVIDENCE
JUDGMENT	RESEARCH EVIDENCE	JUDGMENT	RESEARCH EVIDENCE
<p><input type="radio"/> Large costs</p> <p><input type="radio"/> Moderate costs</p> <p><input type="radio"/> Negligible costs and savings</p> <p><input type="radio"/> Moderate savings</p> <p><input type="radio"/> Large savings</p> <p><input checked="" type="radio"/> Varies</p> <p><input type="radio"/> Don't know</p>	No data were found. Resource requirements are likely variable.		
Cost-effectiveness	Does the cost-effectiveness of the intervention favor the intervention or the comparison?	JUDGMENT	RESEARCH EVIDENCE
Equity	What would be the impact on health equity?	JUDGMENT	RESEARCH EVIDENCE

Acceptability Is the intervention acceptable to key stakeholders?		JUDGMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<input type="radio"/> No			No evidence was identified. However, indirect evidence suggests that mechanical extraction is likely acceptable.	
<input type="radio"/> Probably no				
<input checked="" type="radio"/> Probably yes				
<input type="radio"/> Yes				
<input type="radio"/> Varies				
<input type="radio"/> Don't know				
Feasibility Is the intervention feasible to implement?		JUDGMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<input type="radio"/> No			A systematic search of the literature showed the following:	
<input type="radio"/> Probably no				
<input checked="" type="radio"/> Probably yes			Barriers to implementing effective treatment may include:	
<input type="radio"/> Yes			Social stigma;	
<input type="radio"/> Varies			Lack of knowledge about prevention and control activities;	
<input type="radio"/> Don't know			Lack of knowledge about the zoonotic nature of tungiasis and insufficient animal control;	
			Self-treatment of lesions;	
			Normalization of tungiasis, as it may not be considered a health problem.	

* Data available from descriptive studies only. The effect of the intervention was not directly measured
GRADE, Grading of Recommendations Assessment, Development and Evaluation.

SUMMARY OF JUDGMENTS

		JUDGMENT					
		Small	Moderate	Large	Varies	Varies	Dont know
DESIRABLE EFFECTS	Trivial	Small	Moderate	Large	Varies	Varies	Dont know
UNDESIRABLE EFFECTS	Trivial	Small	Moderate	Large	Varies	Varies	Dont know
CERTAINTY OF EVIDENCE	Very low	Low	Moderate	High			No included studies
VALUES	Important uncertainty or variability	Possibly important uncertainty or variability	Probably no important uncertainty or variability	No important uncertainty or variability			
BALANCE OF EFFECTS	Favors the comparison	Probably favors the comparison	Does not favor either the intervention or the comparison	Probably favors the intervention	Favors the intervention	Varies	Dont know
RESOURCES REQUIRED	Large costs	Moderate costs	Negligible costs and savings	Moderate savings	Large savings	Varies	Dont know
COST-EFFECTIVENESS	Favors the comparison	Probably favors the comparison	Does not favor either the intervention or the comparison	Probably favors the intervention	Favors the intervention	Varies	No included studies
EQUITY	Reduced	Probably reduced	Probably no impact	Probably increased	Increased	Varies	Dont know
ACCEPTABILITY	No	Probably no	Probably yes	Yes		Varies	Dont know
FEASIBILITY	No	Probably no	Probably yes	Yes		Varies	Dont know

TYPE OF RECOMMENDATION

Strong recommendation against the intervention	Conditional recommendation against the intervention	Conditional recommendation for either the intervention or the comparison	Conditional recommendation for the intervention	Strong recommendation for the intervention
<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input checked="" type="radio"/>	<input type="radio"/>

Question 5: Should low-viscosity dimeticone vs. mechanical extraction be used in individuals with mild tungiasis (one or few lesions)?

Patient or population: individuals with mild tungiasis (one or few lesions)

Setting: outpatients

Intervention: low-viscosity dimeticone

Comparison: mechanical extraction

No. of studies	Study design	Certainty assessment				Effect	Absolute (95% CI)	Mechanical extraction	Low-viscosity dimeticone	No. of patients	Certainty	Importance
		Risk of bias	Inconsistency	Indirectness	Imprecision							
1	Non-randomized studies	Not serious	Not serious	Serious ¹	Not serious	None	19/86 (22.1%)	43/71 (60.6%)	RR 0.41 357 fewer per 1000 (from 454 fewer to 188 fewer)	⊕○○○ Very low ¹	CRITICAL	
4	Non-randomized studies	Not serious	Not serious	Very serious ²	Not serious	None			Mild tungiasis is sometimes seen in individuals living in endemic areas. In these communities, observational studies suggest the following ($n = 1855$): (a) mechanical extraction is being used as the main method of self-treatment; (b) the most common instruments used are safety pins, thorns, and sewing needles; (c) instruments are frequently shared among family members; (d) only a minority of individuals use antiseptics before or after the extraction; and (e) superinfections are common. However, mild tungiasis may also be seen in returning travelers. A systematic review of the literature identified 83 case reports of tungiasis in returning travelers. The most common treatment was aseptic surgical extraction and topical antibiotics. No important complications were reported in any of the reports examined. Further case reports identified after the publication of the systematic review also described successful treatment of returning travelers with aseptic surgical extraction (total cases: $n = 95$).	⊕○○○ Very low ²	CRITICAL	

¹ Data come from a study conducted in severe cases. The effect may not be the same in individuals with one or few lesions.

² Data available from descriptive studies only. The effect of the intervention was not directly measured.
CI, confidence interval; RR, risk ratio.

ASSESSMENT

Desirable effects
How substantial are the desirable anticipated effects?

JUDGMENT	RESEARCH EVIDENCE				ADDITIONAL CONSIDERATIONS	
	Outcomes	With mechanical extraction	With dimeticone	Difference	Relative effect (95% CI)	
<input type="radio"/> Trivial <input type="radio"/> Small <input type="radio"/> Moderate <input type="radio"/> Large <input checked="" type="radio"/> Varies <input type="radio"/> Don't know	Efficacy of treatment with dimeticone assessed with: viability of embedded sand fleas Follow-up: median 7 days	606 per 1000	248 per 1000 (151 to 418)	357 fewer per 1000 (454 fewer to 188 fewer)	RR 0.41 (0.25 to 0.69)	
	Findings of descriptive studies on mechanical extraction					Mild tungiasis is sometimes seen in individuals living in endemic areas. In these communities, observational studies suggest the following ($n = 1855$): (a) mechanical extraction is being used as the main method of self-treatment; (b) the most common instruments used are safety pins, thorns, and sewing needles; (c) instruments are frequently shared among family members; (d) only a minority of individuals use antiseptics before or after the extraction; and (e) superinfections are common. However, mild tungiasis may also be seen in returning travelers. A systematic review of the literature identified 83 case reports of tungiasis in returning travelers. The most common treatment was aseptic surgical extraction and topical antibiotics. No important complications were reported in any of the reports examined. Further case reports identified after the publication of the systematic review also described successful treatment of returning travelers with aseptic surgical extraction (total cases: $n = 95$).

Undesirable effects		How substantial are the undesirable anticipated effects?			
JUDGMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS			
<input type="radio"/> Trivial <input type="radio"/> Small <input type="radio"/> Moderate <input type="radio"/> Large <input checked="" type="radio"/> Varies <input type="radio"/> Don't know	<p>Adverse events of topical dimeticone are likely mild and transient (e.g., rash, itching).</p> <p>The risk of superinfections with mechanical extraction was not directly measured in the studies identified.</p> <p>However, indirect evidence suggests:</p> <ul style="list-style-type: none"> Surgical extraction professionally conducted by trained clinicians is likely safe. The risk of superinfection and sepsis is increased in mechanical extractions conducted without the proper antiseptic measures and the appropriate training and tools. 	<p>Mechanical extraction is considered safe when performed by trained healthcare professionals in appropriate settings, particularly for individuals living with basic sanitary conditions. However, if not conducted under proper conditions, there is a significant risk of superinfection.</p> <p>Low-viscosity dimeticone has been demonstrated to be safe across various settings.</p>			
Certainty of evidence	What is the overall certainty of the evidence of effects?				ADDITIONAL CONSIDERATIONS
JUDGMENT	RESEARCH EVIDENCE	Outcomes	Importance	Certainty of the evidence (GRADE)	
<input checked="" type="radio"/> Very low <input type="radio"/> Low <input type="radio"/> Moderate <input type="radio"/> High <input type="radio"/> No included studies	<p>Efficacy of treatment with dimeticone assessed with: viability of embedded sand fleas</p> <p>Follow-up: median 7 days</p> <p>Findings of descriptive studies on mechanical extraction</p>	<p>CRITICAL</p>	<p>⊕○○○ Very low¹</p>	<p>⊕○○○ Very low²</p>	

Values Is there important uncertainty about or variability in how much people value the main outcomes?	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<p><input type="radio"/> Important uncertainty or variability</p> <p><input checked="" type="radio"/> Possibly important uncertainty or variability</p> <p><input type="radio"/> Probably no important uncertainty or variability</p> <p><input type="radio"/> No important uncertainty or variability</p>	<p>No evidence was found. Individuals probably will place a high value on treatment success and on avoiding serious complications like sepsis.</p>	
JUDGMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<p><input type="radio"/> Favors the comparison</p> <p><input type="radio"/> Probably favors the comparison</p> <p><input type="radio"/> Does not favor either the intervention or the comparison</p> <p><input type="radio"/> Probably favors the intervention</p> <p><input type="radio"/> Favors the intervention</p>	<p>Does the balance between desirable and undesirable effects favor the intervention or the comparison?</p>	
JUDGMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<p><input type="radio"/> Varies</p> <p><input type="radio"/> Don't know</p>		
Resources required	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
How large are the resource requirements (costs)?		<p>Cost of mechanical extraction may be high in rural areas.</p>
JUDGMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<p><input type="radio"/> Large costs</p> <p><input type="radio"/> Moderate costs</p> <p><input type="radio"/> Negligible costs and savings</p> <p><input type="radio"/> Moderate savings</p> <p><input type="radio"/> Large savings</p>	<p>Cost of dimeticone (50 mL) is approximately USD 10–40.</p> <p>Through a PAHO strategic fund, some countries offer a product of dimeticone (100 centistokes 92%, drop applicator, 100 mL bottle) at a price of USD 15 per bottle.</p>	<p>Cost of mechanical extraction is likely variable.</p>
JUDGMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<p><input type="radio"/> Varies</p> <p><input type="radio"/> Don't know</p>		

Cost-effectiveness		Does the cost-effectiveness of the intervention favor the intervention or the comparison?	
JUDGMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS	
<input type="radio"/> Favors the comparison <input type="radio"/> Probably favors the comparison <input type="radio"/> Does not favor either the intervention or the comparison <input type="radio"/> Probably favors the intervention <input type="radio"/> Favors the intervention <input type="radio"/> Varies <input checked="" type="radio"/> No included studies	No economic evaluation was found.		
Equity	What would be the impact on health equity?	<p>RESEARCH EVIDENCE</p> <p>A systematic search of the literature showed the following:</p> <p>Tungiasis is endemic in low-income communities in tropical and subtropical countries.</p> <p>Disadvantaged populations may include:</p> <ul style="list-style-type: none"> Those living in precarious housing conditions, especially homes with earthen floors; Rural communities; Older persons; Children; Native communities. 	<p>ADDITIONAL CONSIDERATIONS</p> <p>Rural communities often face significant barriers to accessing mechanical extraction under proper conditions, including limited availability of trained healthcare professionals, inadequate medical facilities, and lack of basic sanitary infrastructure. These challenges can exacerbate health disparities and increase the risk of complications from improper treatment.</p> <p>The use of low-viscosity clindamycin, which can be safely applied in various settings and requires less specialized infrastructure, has the potential to enhance health equity.</p>

Acceptability Is the intervention acceptable to key stakeholders?		RESEARCH EVIDENCE		ADDITIONAL CONSIDERATIONS	
JUDGMENT					
<input type="radio"/> No		Dimeticone treatment was acceptable in the study identified. All the participants of the trial completed follow-up. When study participants were asked about their satisfaction, 37/47 (78%) preferred dimeticone over potassium permanganate.		Individuals, particularly children, may prefer topical treatment over mechanical extraction.	
<input checked="" type="radio"/> Yes		Indirect evidence suggests that mechanical extraction is likely acceptable.			
<input type="radio"/> Varies					
<input type="radio"/> Don't know					
Feasibility Is the intervention feasible to implement?		RESEARCH EVIDENCE		ADDITIONAL CONSIDERATIONS	
<input type="radio"/> No		A systematic search of the literature showed the following:		Dimeticone may not be readily available in many endemic areas, limiting its use as a treatment option for affected populations.	
<input type="radio"/> Probably no		Barriers to implementing effective treatment may include:		However, when low-viscosity dimeticone is made available, it proves to be a highly feasible treatment. The ease of application, safety across diverse settings, and minimal need for specialized equipment make it a practical solution for managing conditions in resource-limited environments.	
<input checked="" type="radio"/> Probably yes		Social stigma;			
<input type="radio"/> Yes		Lack of knowledge about prevention and control activities;			
		Self-treatment of lesions;			
		Normalization of tungiasis, as it may not be considered a health problem.			
<input type="radio"/> Varies		Additionally, dimeticone products are not registered nor available in several endemic countries.			
<input type="radio"/> Don't know		They are mostly available to international travelers from developed countries.			

¹ Data come from a study conducted in severe cases. The effect may not be the same in individuals with one or few lesions.

² Data available from descriptive studies only. The effect of the intervention was not directly measured.

CI, confidence interval; GRADE, Grading of Recommendations Assessment, Development and Evaluation; PAHO, Pan American Health Organization.

SUMMARY OF JUDGMENTS

	JUDGMENT				
DESIRABLE EFFECTS	Trivial	Small	Moderate	Large	Varies
UNDESIRABLE EFFECTS	Trivial	Small	Moderate	Large	Varies
CERTAINTY OF EVIDENCE	Very low	Low	Moderate	High	No included studies
VALUES	Important uncertainty or variability	Possibly important uncertainty or variability	Probably no important uncertainty or variability	No important uncertainty or variability	
BALANCE OF EFFECTS	Favors the comparison	Probably favors the comparison	Does not favor either the intervention or the comparison	Probably favors the intervention	Varies
RESOURCES REQUIRED	Large costs	Moderate costs	Negligible costs and savings	Moderate savings	Varies
COST-EFFECTIVENESS	Favors the comparison	Probably favors the comparison	Does not favor either the intervention or the comparison	Probably favors the intervention	Varies
EQUITY	Reduced	Probably reduced	Probably no impact	Probably increased	Increased
ACCEPTABILITY	No	Probably no	Probably yes	Yes	Varies
FEASIBILITY	No	Probably no	Probably yes	Yes	Varies

TYPE OF RECOMMENDATION

Strong recommendation against the intervention	Conditional recommendation against the intervention	Conditional recommendation for either the intervention or the comparison	Conditional recommendation for the intervention	Strong recommendation for the intervention
○	○	○	●	○

Question 6: Should coconut oil (*Cocos nucifera*) plus neem oil (*Azadirachta indica*) vs. no oils be used in individuals with tungiasis (any severity)?

Patient or population: individuals with tungiasis (any severity)

Setting: outpatients

Intervention: coconut oil (*Cocos nucifera*) plus neem oil (*Azadirachta indica*)

Comparison: no oils

No. of studies	Study design	Certainty assessment				Other considerations	Coconut oil (<i>Cocos nucifera</i>) plus neem oil (<i>Azadirachta indica</i>)	No. of patients	Effect	Certainty	Importance	
		Risk of bias	Inconsistency	Indirectness	Imprecision							
1	Randomized trials	Serious ¹	Not serious	Not serious	Very serious ²	None	17/55 (30.9%)	18/45 (40.0%)	OR 0.62 (0.28 to 1.42)	108 fewer per 1000 (from 243 fewer to 86 more)	⊕○○ Very low ¹²	CRITICAL

¹ Attrition bias cannot be ruled out: 19/119 (16%) of the fleas selected for observation were lost to follow-up.

² The confidence interval around the absolute effect includes benefit, no effect and harm. It likely crosses at least two decision thresholds.
CI, confidence interval; OR, odds ratio.

ASSESSMENT

Desirable effects

How substantial are the desirable anticipated effects?

JUDGMENT	RESEARCH EVIDENCE				ADDITIONAL CONSIDERATIONS	
	Outcomes	No. of participants (studies) Follow-up	Certainty of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects* (95% CI)	Risk difference with coconut oil (<i>Cocos nucifera</i>) plus neem oil (<i>Azadirachta indica</i>)
<input type="radio"/> Trivial <input checked="" type="radio"/> Small <input type="radio"/> Moderate <input type="radio"/> Large <input type="radio"/> Varies <input type="radio"/> Don't know	Efficacy of treatment assessed with: viability of embedded sand fleas Follow-up: median 7 days	100 (1 RCT)	⊕○○○ Very low ^{1,2}	OR 0.62 (0.28 to 1.42)	400 per 1000	108 fewer per 1000 (243 fewer to 86 more) Study population
Undesirable effects						
JUDGMENT	RESEARCH EVIDENCE				ADDITIONAL CONSIDERATIONS	
<input checked="" type="radio"/> Trivial <input type="radio"/> Small <input type="radio"/> Moderate <input type="radio"/> Large <input type="radio"/> Varies <input type="radio"/> Don't know	No adverse events were observed in the trial. However, adverse events of topical coconut oil (<i>Cocos nucifera</i>) plus neem oil (<i>Azadirachta indica</i>) are likely mild and transient (e.g., rash, itching, pain).				There may be variability in product quality and potential harms due to factors such as inadequate quality control, possible contamination, and expiration of products.	

Certainty of evidence		RESEARCH EVIDENCE				ADDITIONAL CONSIDERATIONS	
JUDGMENT		Outcomes	Importance	Certainty of the evidence (GRADE)			
<ul style="list-style-type: none"> ● Very low <input type="radio"/> Low <input type="radio"/> Moderate <input type="radio"/> High 		Efficacy of treatment assessed with: viability of embedded sand fleas Follow-up: median 7 days	CRITICAL	⊕○○○ Very low ^{1,2}			
Values	Is there important uncertainty about or variability in how much people value the main outcomes?						
JUDGMENT		RESEARCH EVIDENCE		ADDITIONAL CONSIDERATIONS			
<ul style="list-style-type: none"> <input type="radio"/> Important uncertainty or variability <input type="radio"/> Possibly important uncertainty or variability <input type="radio"/> Probably no important uncertainty or variability ● No important uncertainty or variability 		No evidence was found. However, most individuals probably will place a higher value on treatment response than on the potential adverse events of treatment.					
Balance of effects	Does the balance between desirable and undesirable effects favor the intervention or the comparison?						
JUDGMENT		RESEARCH EVIDENCE		ADDITIONAL CONSIDERATIONS			
<ul style="list-style-type: none"> <input type="radio"/> Favors the comparison <input type="radio"/> Probably favors the comparison <input type="radio"/> Does not favor either the intervention or the comparison ● Probably favors the intervention <input type="radio"/> Favors the intervention 							
		<ul style="list-style-type: none"> <input type="radio"/> Varies <input type="radio"/> Don't know 					

Resources required How large are the resource requirements (costs)?	JUDGMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<ul style="list-style-type: none"> <input type="radio"/> Large costs <input type="radio"/> Moderate costs <input checked="" type="radio"/> Negligible costs and savings <input type="radio"/> Moderate savings <input type="radio"/> Large savings <hr/> <ul style="list-style-type: none"> <input type="radio"/> Varies <input type="radio"/> Don't know 		Data from the included trial: an average case requires two times 1 mL for a full treatment regimen, costing KES 10 (USD 0.10) per patient or a maximum of KES 15 (USD 0.15) should three applications be required.	
		Cost-effectiveness Does the cost-effectiveness of the intervention favor the intervention or the comparison?	
	JUDGMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
	<ul style="list-style-type: none"> <input type="radio"/> Favors the comparison <input type="radio"/> Probably favors the comparison <input type="radio"/> Does not favor either the intervention or the comparison <input type="radio"/> Probably favors the intervention <input type="radio"/> Favors the intervention <hr/> <ul style="list-style-type: none"> <input type="radio"/> Varies <input checked="" type="radio"/> No included studies 	No economic evaluation was found.	
		Equity What would be the impact on health equity?	
	JUDGMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
	<ul style="list-style-type: none"> <input type="radio"/> Reduced <input type="radio"/> Probably reduced <input type="radio"/> Probably no impact <input type="radio"/> Probably increased <input checked="" type="radio"/> Increased <hr/> <ul style="list-style-type: none"> <input type="radio"/> Varies <input type="radio"/> Don't know 	<p>A systematic search of the literature showed the following:</p> <p>Tungiasis is endemic in low-income communities in tropical and subtropical countries.</p> <p>Disadvantaged populations may include:</p> <p>Those living in precarious housing conditions, especially homes with earthen floors;</p> <p>Rural communities;</p> <p>Older persons;</p> <p>Children;</p> <p>Native communities.</p>	

Acceptability Is the intervention acceptable to key stakeholders?		RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
JUDGMENT			
<input type="radio"/> No		Although pain and itching were a frequent complaint, the intervention generally decreased such symptoms.	
<input type="radio"/> Probably no			
<input checked="" type="radio"/> Probably yes			
<input type="radio"/> Yes			
<hr/>			
<input type="radio"/> Varies			
<input type="radio"/> Don't know			
Feasibility Is the intervention feasible to implement?	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS	
JUDGMENT			
<input type="radio"/> No	A systematic search of the literature showed the following:	<i>Azadirachta indica</i> , commonly known as the neem tree, is indigenous to the Indian subcontinent and various regions in Africa. This plant is not typically found in Latin American countries.	
<input type="radio"/> Probably no			
<input type="radio"/> Probably yes	Barriers to implementing effective treatment may include:		
<input type="radio"/> Yes	Social stigma;		
<hr/>	Lack of knowledge about prevention and control activities;		
<input checked="" type="radio"/> Varies	Lack of knowledge about the zoonotic nature of tungiasis and insufficient animal control;		
<input type="radio"/> Don't know	Self-treatment of lesions;		
	Normalization of tungiasis, as it may not be considered a health problem.		

* The risk in the intervention group (and its 95% CI) is based on the assumed risk in the comparison group and the relative effect of the intervention (and its 95% CI).

¹ Attrition bias cannot be ruled out: 19/119 (16%) of the fleas selected for observation were lost to follow-up.

² The confidence interval around the absolute effect includes benefit, no effect and harm. It likely crosses at least two decision thresholds.

CI, confidence interval; GRADE, Grading of Recommendations Assessment, Development and Evaluation; OR, odds ratio; RCT, randomized controlled trial.

SUMMARY OF JUDGMENTS

	JUDGMENT					
DESIRABLE EFFECTS	Trivial	Small	Moderate	Large	Varies	Don't know
UNDESIRABLE EFFECTS	Trivial	Small	Moderate	Large	Varies	Don't know
CERTAINTY OF EVIDENCE	Very low	Low	Moderate	High		No included studies
VALUES	Important uncertainty or variability	Possibly important uncertainty or variability	Probably no important uncertainty or variability	No important uncertainty or variability		
BALANCE OF EFFECTS	Favors the comparison	Probably favors the comparison	Does not favor either the intervention or the comparison	Probably favors the intervention	Favors the intervention	Varies
RESOURCES REQUIRED	Large costs	Moderate costs	Negligible costs and savings	Moderate savings	Large savings	Varies
COST-EFFECTIVENESS	Favors the comparison	Probably favors the comparison	Does not favor either the intervention or the comparison	Probably favors the intervention	Favors the intervention	Varies
EQUITY	Reduced	Probably reduced	Probably no impact	Probably increased	Increased	Varies
ACCEPTABILITY	No	Probably no	Probably yes	Yes	Varies	Don't know
FEASIBILITY	No	Probably no	Probably yes	Yes	Varies	Don't know

TYPE OF RECOMMENDATION

Strong recommendation against the intervention	Conditional recommendation against the intervention	Conditional recommendation for either the intervention or the comparison	Conditional recommendation for the intervention	Strong recommendation for the intervention
○	○	○	●	○

Question 7: Should topical ivermectin vs. no ivermectin be used in individuals with tungiasis (any severity)?

Patient or population: individuals with tungiasis (any severity)

Setting: outpatients

Intervention: topical ivermectin

Comparison: no ivermectin

No. of studies	Study design	Certainty assessment				Other considerations	Topical ivermectin	No. of patients	Effect	Certainty	Importance
		Risk of bias	Inconsistency	Indirectness	Imprecision						
1	Randomized trials	Serious ¹	Not serious	Not serious	Very serious ²	None	4/33 (12.1%)	7/26 (26.9%)	OR 0.31 167 fewer per 1000 (from 227 fewer to 35 fewer)	⊕○○ Very low ^{1,2}	CRITICAL

¹ Attrition bias cannot be ruled out: 17/125 (14%) participants originally randomized were not included in the analysis. Data regarding specific group allocation was not provided.

² Random error cannot be ruled out. Although the confidence interval and the *p* value are significant, the number of participants in the comparison ivermectin versus placebo is very small.
CI, confidence interval; OR, odds ratio.

ASSESSMENT

Desirable effects

How substantial are the desirable anticipated effects?

JUDGMENT

RESEARCH EVIDENCE

ADDITIONAL CONSIDERATIONS

Outcomes	No. of participants (studies) Follow-up	Certainty of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects* (95% CI)	
				Risk with no ivermectin	Risk difference with topical ivermectin
Efficacy of treatment assessed with: viability of embedded sand fleas Follow-up: median 7 days	(1 RCT)	⊕○○ Very low ^{1,2}	OR 0.31 (0.12 to 0.83)	269 per 1000	167 fewer per 1000 (227 fewer to 35 fewer)

Undesirable effects		How substantial are the undesirable anticipated effects?									
JUDGMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS									
<ul style="list-style-type: none"> ● Trivial <input type="radio"/> Small <input type="radio"/> Moderate <input type="radio"/> Large <hr/> <ul style="list-style-type: none"> <input type="radio"/> Varies <input type="radio"/> Don't know 	No adverse events were observed in the trial.										
Certainty of evidence	What is the overall certainty of the evidence of effects?				ADDITIONAL CONSIDERATIONS						
JUDGMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS									
<ul style="list-style-type: none"> ● Very low <input type="radio"/> Low <input type="radio"/> Moderate <input type="radio"/> High <hr/> <ul style="list-style-type: none"> <input type="radio"/> No included studies 	<table border="1" style="width: 100%; border-collapse: collapse;"> <thead> <tr> <th style="text-align: center;">Outcomes</th> <th style="text-align: center;">Importance</th> <th style="text-align: center;">Certainty of the evidence (GRADE)</th> </tr> </thead> <tbody> <tr> <td>Efficacy of treatment assessed with: viability of embedded sand fleas Follow-up: median 7 days</td><td style="text-align: center;">CRITICAL</td><td style="text-align: center;">⊕○○○ Very low^{1,2}</td></tr> </tbody> </table>	Outcomes	Importance	Certainty of the evidence (GRADE)	Efficacy of treatment assessed with: viability of embedded sand fleas Follow-up: median 7 days	CRITICAL	⊕○○○ Very low ^{1,2}				
Outcomes	Importance	Certainty of the evidence (GRADE)									
Efficacy of treatment assessed with: viability of embedded sand fleas Follow-up: median 7 days	CRITICAL	⊕○○○ Very low ^{1,2}									
Values	Is there important uncertainty about or variability in how much people value the main outcomes?				ADDITIONAL CONSIDERATIONS						
JUDGMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS									
		<ul style="list-style-type: none"> <input type="radio"/> Important uncertainty or variability <input type="radio"/> Possibly important uncertainty or variability <input type="radio"/> Probably no important uncertainty or variability ● No important uncertainty or variability 									

Balance of effects Does the balance between desirable and undesirable effects favor the intervention or the comparison?		JUDGMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
		<input type="radio"/> Favors the comparison <input type="radio"/> Probably favors the comparison <input type="radio"/> Does not favor either the intervention or the comparison <input checked="" type="radio"/> Probably favors the intervention <input type="radio"/> Favors the intervention <input type="radio"/> Varies <input type="radio"/> Don't know		
Resources required How large are the resource requirements (costs)?		JUDGMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
		<input type="radio"/> Large costs <input type="radio"/> Moderate costs <input type="radio"/> Negligible costs and savings <input type="radio"/> Moderate savings <input type="radio"/> Large savings <input checked="" type="radio"/> Varies <input type="radio"/> Don't know	Retail prices of ivermectin lotion 1% at 117 g range between USD 15 and 30.	

Cost-effectiveness Does the cost-effectiveness of the intervention favor the intervention or the comparison?		JUDGMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
		<ul style="list-style-type: none"> <input type="radio"/> Favors the comparison <input type="radio"/> Probably favors the comparison <input type="radio"/> Does not favor either the intervention or the comparison <input type="radio"/> Probably favors the intervention <input type="radio"/> Favors the intervention <hr/> <ul style="list-style-type: none"> <input type="radio"/> Varies <input checked="" type="radio"/> No included studies 	No economic evaluation was found.	
		Equity What would be the impact on health equity?	JUDGMENT	<p>A systematic search of the literature showed the following:</p> <ul style="list-style-type: none"> Tungiasis is endemic in low-income communities in tropical and subtropical countries. <p>Disadvantaged populations may include:</p> <ul style="list-style-type: none"> Those living in precarious housing conditions, especially homes with earthen floors; Rural communities; Older persons; Children; Native communities.

Acceptability		Is the intervention acceptable to key stakeholders?	
JUDGMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS	
<input type="radio"/> No <input type="radio"/> Probably no <input checked="" type="radio"/> Probably yes <input type="radio"/> Yes <hr/> <input type="radio"/> Varies <input type="radio"/> Don't know	No evidence was found.		
Feasibility	Is the intervention feasible to implement?	ADDITIONAL CONSIDERATIONS	
<input type="radio"/> No <input type="radio"/> Probably no <input checked="" type="radio"/> Probably yes <input type="radio"/> Yes <hr/> <input type="radio"/> Varies <input type="radio"/> Don't know	<p>A systematic search of the literature showed the following:</p> <p>Barriers to implementing effective treatment may include:</p> <ul style="list-style-type: none"> Social stigma; Lack of knowledge about prevention and control activities; Lack of knowledge about the zoonotic nature of tungiasis and insufficient animal control; Self-treatment of lesions; Normalization of tungiasis, as it may not be considered a health problem. 		

* The risk in the intervention group (and its 95% CI) is based on the assumed risk in the comparison group and the relative effect of the intervention (and its 95% CI).

¹ Attrition bias cannot be ruled out: 17/125 (14%) participants originally randomized were not included in the analysis. Data regarding specific group allocation were not provided.

² Random error cannot be ruled out: Although the confidence interval and the *p* value are significant, the number of participants in the comparison ivermectin versus placebo is very small. CI, confidence interval; GRADE, Grading of Recommendations Assessment, Development and Evaluation; OR, odds ratio; RCT, randomized controlled trial.

SUMMARY OF JUDGMENTS

JUDGMENT						
DESIRABLE EFFECTS	Trivial	Small	Moderate	Large	Varies	Dont know
UNDESIRABLE EFFECTS	Trivial	Small	Moderate	Large	Varies	Dont know
CERTAINTY OF EVIDENCE	Very low	Low	Moderate	High		No included studies
VALUES	Important uncertainty or variability	Possibly important uncertainty or variability	Probably no important uncertainty or variability	No important uncertainty or variability		
BALANCE OF EFFECTS	Favors the comparison	Probably favors the comparison	Does not favor either the intervention or the comparison	Probably favors the intervention	Favors the intervention	Dont know
RESOURCES REQUIRED	Large costs	Moderate costs	Negligible costs and savings	Moderate savings	Varies	Dont know
COST-EFFECTIVENESS	Favors the comparison	Probably favors the comparison	Does not favor either the intervention or the comparison	Probably favors the intervention	Favors the intervention	No included studies
EQUITY	Reduced	Probably reduced	Probably no impact	Increased	Varies	Dont know
ACCEPTABILITY	No	Probably no	Probably yes	Yes	Varies	Dont know
FEASIBILITY	No	Probably no	Probably yes	Yes	Varies	Dont know

TYPE OF RECOMMENDATION

Strong recommendation against the intervention	Conditional recommendation against the intervention	Conditional recommendation for either the intervention or the comparison	Conditional recommendation for the intervention	Strong recommendation for the intervention
○	○	○	●	○

Question 8: Should potassium permanganate vs. no potassium permanganate be used in individuals with tungiasis (any severity)?

Patient or population: individuals with tungiasis (any severity)

Setting: outpatients

Intervention: potassium permanganate

Comparison: no potassium permanganate

No. of studies	Study design	Certainty assessment				Other considerations	No. of patients Potassium permanganate	Relative (95% CI)	Effect	Absolute (95% CI)	Certainty	Importance
		Risk of bias	Inconsistency	Indirectness	Imprecision							
1	Non-randomized studies	Very serious ^{1,2}	Not serious	Not serious	Not serious	Strong association	43/71 (60.6%)	19/86 (22.1%)	RR 2.74 (1.77 to 4.24)	384 more per 1000 (from 170 more to 716 more)	⊕○○○ Very low ^{1,2}	Critical
1	Randomized trials	Serious ³	Not serious	Not serious	Very serious ⁴	None	18/45 (40.0%)	17/55 (30.9%)	OR 1.60 (0.70 to 3.57)	108 more per 1000 (from 71 fewer to 306 more)	⊕○○○ Very low ^{3,4}	Critical

¹ The risk of bias was assessed using ROBINS-I and certainty of evidence was rated down two levels due to residual confounding.

² Participants and study personnel were not blinded; however, certainty of evidence was not penalized further. It was judged unlikely that the lack of blinding may have affected the prognosis of participants or the measurement of the outcome.

³ Attrition bias cannot be ruled out: 19/119 (16%) of the fleas selected for observation were lost to follow-up.

⁴ The confidence interval around the absolute effect includes benefit, no effect and harm. It likely crosses at least two decision thresholds. CI, confidence interval; OR, odds ratio; RR, risk ratio.

ASSESSMENT

Desirable effects
How substantial are the desirable anticipated effects?

JUDGMENT

- Trivial
- Small
- Moderate
- Large

- Varies
- Don't know

RESEARCH EVIDENCE

Potassium permanganate is probably less effective than other interventions

JUDGMENT	RESEARCH EVIDENCE					ADDITIONAL CONSIDERATIONS
	Outcomes	No. of participants (studies) Follow-up	Certainty of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects* (95% CI)	
	Efficacy of treatment versus dimeticone assessed with: viability of embedded sand fleas Follow-up: median 7 days	157 (1 observational study)	Moderate ^{1,2}	RR 2.74 (1.77 to 4.24)	221 per 1000 384 more per 1000 (170 more to 716 more)	Study population
	Efficacy of treatment versus coconut oil plus neem oil assessed with: viability of embedded sand fleas Follow-up: median 7 days	100 (1 RCT)	⊕○○○ Very low ^{3,4}	OR 1.60 (0.70 to 3.57)	309 per 1000 108 more per 1000 (71 fewer to 306 more)	Study population

Undesirable effects		How substantial are the undesirable anticipated effects?		
JUDGMENT	RESEARCH EVIDENCE			ADDITIONAL CONSIDERATIONS
<input type="radio"/> Trivial <input checked="" type="radio"/> Small <input type="radio"/> Moderate <input type="radio"/> Large <hr/> <input type="radio"/> Varies <input type="radio"/> Don't know	<p>Adverse events of topical potassium permanganate are likely mild and transient. However, pain and itching are more frequent with potassium permanganate than with other interventions. In one trial, participants allocated to potassium permanganate were more likely to report an increase in pain (OR 3.6; 95% CI 1.1–12.1; $p = 0.043$) or an increase in itching (OR 2.6; 95% CI 0.86–7.50; $p = 0.090$) compared with participants allocated to coconut oil plus neem oil.</p>			Potassium permanganate is an oxidizing agent and used as disinfectant for topical treatment of suppurating lesions caused by fungal or bacterial infections. It can burn the skin if not carefully prepared to a 0.01% dilution.
Certainty of evidence				
JUDGMENT	RESEARCH EVIDENCE	Outcomes	Importance	Certainty of the evidence (GRADE)
<input checked="" type="radio"/> Very low <input type="radio"/> Low <input type="radio"/> Moderate <input type="radio"/> High <hr/> <input type="radio"/> No included studies	<p>Efficacy of treatment versus dineticonic assessed with: viability of embedded sand fleas Follow-up: median 7 days</p> <p>Efficacy of treatment versus coconut oil plus neem oil assessed with: viability of embedded sand fleas Follow-up: median 7 days</p>	<p>CRITICAL</p> <p>⊕⊕⊕○ Moderate^{1,2}</p> <p>CRITICAL</p> <p>⊕○○○ Very low^{3,4}</p>		

Values Is there important uncertainty about or variability in how much people value the main outcomes?	JUDGMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<p><input type="radio"/> Important uncertainty or variability</p> <p><input type="radio"/> Possibly important uncertainty or variability</p> <p><input type="radio"/> Probably no important uncertainty or variability</p> <p><input checked="" type="radio"/> No important uncertainty or variability</p>		No evidence was found. However, most individuals probably will place a higher value on treatment response than on the potential adverse events of treatment.	
			<p>Conducting trials with potassium permanganate is ethically inappropriate given the availability of more effective treatments.</p>

Balance of effects Does the balance between desirable and undesirable effects favor the intervention or the comparison?	JUDGMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
	<p><input type="radio"/> Favors the comparison</p> <p><input checked="" type="radio"/> Probably favors the comparison</p> <p><input type="radio"/> Does not favor either the intervention or the comparison</p> <p><input type="radio"/> Probably favors the intervention</p> <p><input type="radio"/> Favors the intervention</p> <hr/> <p><input type="radio"/> Varies</p> <p><input type="radio"/> Don't know</p>		

Resources required		
How large are the resource requirements (costs)?		
JUDGMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<input type="radio"/> Large costs <input type="radio"/> Moderate costs <input checked="" type="radio"/> Negligible costs and savings <input type="radio"/> Moderate savings <input type="radio"/> Large savings <input type="radio"/> Varies <input type="radio"/> Don't know	Data from one of the included trials: It was estimated from trial expenses that a single treatment with potassium permanganate costs KES 34 (USD 0.34) per patient plus an additional KES 6 (USD 0.06) for Vaseline application after the foot bath (total: KES 40 or USD 0.4 per patient).	
Cost-effectiveness		
Does the cost-effectiveness of the intervention favor the intervention or the comparison?		
JUDGMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
	No economic evaluation was found.	 <input type="radio"/> Favors the comparison <input type="radio"/> Probably favors the comparison <input type="radio"/> Does not favor either the intervention or the comparison <input type="radio"/> Probably favors the intervention <input type="radio"/> Favors the intervention <input type="radio"/> Varies <input checked="" type="radio"/> No included studies

Equity		What would be the impact on health equity?	
JUDGMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS	
<input type="radio"/> Reduced <input type="radio"/> Probably reduced <input type="radio"/> Probably no impact <input type="radio"/> Probably increased <input checked="" type="radio"/> Increased <hr/> <input type="radio"/> Varies <input type="radio"/> Don't know	<p>A systematic search of the literature showed the following:</p> <p>Tungiasis is endemic in low-income communities in tropical and subtropical countries.</p> <p>Disadvantaged populations may include:</p> <ul style="list-style-type: none"> Those living in precarious housing conditions, especially homes with earthen floors; Rural communities; Older persons; Children; Native communities. 		
Acceptability	Is the intervention acceptable to key stakeholders?	ADDITIONAL CONSIDERATIONS	
JUDGMENT	RESEARCH EVIDENCE		
<input type="radio"/> No <input checked="" type="radio"/> Probably no <input type="radio"/> Probably yes <input type="radio"/> Yes <hr/> <input type="radio"/> Varies <input type="radio"/> Don't know	<p>Topical potassium permanganate was generally acceptable.</p> <p>However, potassium permanganate is likely less acceptable than the alternatives.</p> <p>The increment in itching and pain may limit its acceptability.</p> <p>It produces a characteristic dark/purple color on the skin.</p> <p>Also, in one trial, when study participants were asked about their satisfaction, only 10/47 (21%) preferred potassium permanganate over the alternative treatment.</p>	<p>Potassium permanganate may be less acceptable in children.</p>	

Feasibility Is the intervention feasible to implement?		RESEARCH EVIDENCE		ADDITIONAL CONSIDERATIONS	
JUDGMENT					
<input type="radio"/> No					
<input type="radio"/> Probably no					
<input type="radio"/> Probably yes					
<input type="radio"/> Yes					
<input checked="" type="radio"/> Varies					
<input type="radio"/> Don't know					

A systematic search of the literature showed the following:

Barriers to implementing effective treatment may include:

- Social stigma;
- Lack of knowledge about prevention and control activities;
- Lack of knowledge about the zoonotic nature of tungiasis and insufficient animal control;
- Self-treatment of lesions;
- Normalization of tungiasis, as it may not be considered a health problem.

* The risk in the intervention group (and its 95% CI) is based on the assumed risk in the comparison group and the relative effect of the intervention (and its 95% CI).

1 The risk of bias was assessed using ROBINS-I and certainty of evidence was rated down two levels due to residual confounding.

2 Participants and study personnel were not blinded; however, certainty of evidence was not penalized further. It was judged unlikely that the lack of blinding may have affected the prognosis of participants or the measurement of the outcome.

3 Attrition bias cannot be ruled out: 19/119 (16%) of the fleas selected for observation were lost to follow-up.

4 The confidence interval around the absolute effect includes benefit, no effect and harm. It likely crosses at least two decision thresholds.
CI, confidence interval; GRADE, Grading of Recommendations Assessment, Development and Evaluation; OR, odds ratio; RCT, randomized controlled trial; RR, risk ratio.

SUMMARY OF JUDGMENTS

JUDGMENT					
DESIRABLE EFFECTS	Trivial	Small	Moderate	Large	Varies
UNDESIRABLE EFFECTS	Trivial	Small	Moderate	Large	Varies
CERTAINTY OF EVIDENCE	Very low	Low	Moderate	High	No included studies
VALUES	Important uncertainty or variability	Possibly important uncertainty or variability	Probably no important uncertainty or variability	No important uncertainty or variability	
BALANCE OF EFFECTS	Favors the comparison	Probably favors the comparison	Does not favor either the intervention or the comparison	Probably favors the intervention	Favors the intervention
					Varies
					Dont know

		JUDGMENT				
RESOURCES REQUIRED	Large costs	Moderate costs	Negligible costs and savings	Moderate savings	Large savings	Varies
COST-EFFECTIVENESS	Favors the comparison	Probably favors the comparison	Does not favor either the intervention or the comparison	Probably favors the intervention	Favors the intervention	Varies
EQUITY	Reduced	Probably reduced	Probably no impact	Probably increased	Increased	Varies
ACCEPTABILITY	No	Probably no	Probably yes	Yes	Varies	Don't know
FEASIBILITY	No	Probably no	Probably yes	Yes	Varies	Don't know

TYPE OF RECOMMENDATION

Strong recommendation against the intervention	Conditional recommendation against the intervention	Conditional recommendation for either the intervention or the comparison	Conditional recommendation for the intervention	Strong recommendation for the intervention
<input type="radio"/>	<input checked="" type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>

Question 9: Should hydrogen peroxide vs. no hydrogen peroxide be used in individuals with tungiasis (any severity)?**Patient or population:** individuals with tungiasis (any severity)**Setting:** outpatients**Intervention:** hydrogen peroxide**Comparison:** no hydrogen peroxide

No evidence was identified.

ASSESSMENT**Desirable effects**

How substantial are the desirable anticipated effects?

JUDGMENT

- Trivial
- Small
- Moderate
- Large

-
- Varies
 - Don't know

RESEARCH EVIDENCE

No evidence was identified.

JUDGMENT**RESEARCH EVIDENCE**

- Trivial
- Small
- Moderate
- Large

-
- Varies
 - Don't know

ADDITIONAL CONSIDERATIONS

Hydrogen peroxide is a chemical with known adverse effects: it can cause irritation to skin and eyes, and in high concentrations it can cause burns or blisters on the skin. Inhalation of hydrogen peroxide vapors or accidental ingestion may cause symptoms such as a cough, abdominal pain, or nausea.

Certainty of evidence What is the overall certainty of the evidence of effects?		RESEARCH EVIDENCE	JUDGMENT	ADDITIONAL CONSIDERATIONS
		No evidence of benefit. Moderate to high certainty of harm.		
	<ul style="list-style-type: none"> ● Very low <input type="radio"/> Low <input type="radio"/> Moderate <input type="radio"/> High <p><input type="checkbox"/> No included studies</p>			
Values Is there important uncertainty about or variability in how much people value the main outcomes?	RESEARCH EVIDENCE	JUDGMENT	ADDITIONAL CONSIDERATIONS	
		<ul style="list-style-type: none"> <input type="radio"/> Important uncertainty or variability <input type="radio"/> Possibly important uncertainty or variability <input type="radio"/> Probably no important uncertainty or variability <input type="radio"/> No important uncertainty or variability 		
Balance of effects Does the balance between desirable and undesirable effects favor the intervention or the comparison?	RESEARCH EVIDENCE	JUDGMENT	ADDITIONAL CONSIDERATIONS	
		<ul style="list-style-type: none"> <input type="radio"/> Favors the comparison <input type="radio"/> Probably favors the comparison <input type="radio"/> Does not favor either the intervention or the comparison <input type="radio"/> Probably favors the intervention <input type="radio"/> Favors the intervention <p><input type="checkbox"/> Varies</p> <p><input type="checkbox"/> Don't know</p>		

Resources required How large are the resource requirements (costs)?	
JUDGMENT	RESEARCH EVIDENCE
<input type="radio"/> Large costs <input type="radio"/> Moderate costs <input checked="" type="radio"/> Negligible costs and savings <input type="radio"/> Moderate savings <input type="radio"/> Large savings <input type="radio"/> Varies <input type="radio"/> Don't know	Retail prices of hydrogen peroxide (1 L) range between USD 15 and 20.
Cost-effectiveness Does the cost-effectiveness of the intervention favor the intervention or the comparison?	
JUDGMENT	RESEARCH EVIDENCE
<input type="radio"/> Favors the comparison <input type="radio"/> Probably favors the comparison <input type="radio"/> Does not favor either the intervention or the comparison <input type="radio"/> Probably favors the intervention <input type="radio"/> Favors the intervention <input type="radio"/> Varies <input checked="" type="radio"/> No included studies	No economic evaluation was found.

Equity What would be the impact on health equity?			
JUDGMENT	RESEARCH EVIDENCE	JUDGMENT	RESEARCH EVIDENCE
JUDGMENT	RESEARCH EVIDENCE	JUDGMENT	RESEARCH EVIDENCE
<input type="radio"/> Reduced <input type="radio"/> Probably reduced <input type="radio"/> Probably no impact <input type="radio"/> Probably increased <input type="radio"/> Increased	<p>A systematic search of the literature showed the following:</p> <p>Tungiasis is endemic in low-income communities in tropical and subtropical countries.</p> <p>Disadvantaged populations may include:</p> <p>Those living in precarious housing conditions, especially homes with earthen floors;</p> <ul style="list-style-type: none"> Rural communities; Older persons; Children; Native communities. 	<input type="radio"/> No <input type="radio"/> Probably no <input type="radio"/> Probably yes <input type="radio"/> Yes	<p>No evidence was found.</p>
<input type="radio"/> Varies <input checked="" type="radio"/> Don't know		<input type="radio"/> Varies <input checked="" type="radio"/> Don't know	

Feasibility Is the intervention feasible to implement?		JUDGMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<input type="radio"/> No				
<input type="radio"/> Probably no				
<input type="radio"/> Probably yes				
<input type="radio"/> Yes				
<input type="radio"/> Varies				
<input checked="" type="radio"/> Don't know				
A systematic search of the literature showed the following:				
Barriers to implementing effective treatment may include:				
Social stigma;				
Lack of knowledge about prevention and control activities;				
Lack of knowledge about the zoonotic nature of tungiasis and insufficient animal control;				
Self-treatment of lesions;				
Normalization of tungiasis, as it may not be considered a health problem.				

SUMMARY OF JUDGMENTS

JUDGMENT					
DESIRABLE EFFECTS	Trivial	Small	Moderate	Large	Don't know
UNDESIRABLE EFFECTS	Trivial	Small	Moderate	Large	Don't know
CERTAINTY OF EVIDENCE	Very low	Low	Moderate	High	No included studies
VALUES	Important uncertainty or variability	Possibly important uncertainty or variability	Probably no important uncertainty or variability	No important uncertainty or variability	
BALANCE OF EFFECTS	Favors the comparison	Probably favors the comparison	Does not favor either the intervention or the comparison	Probably favors the intervention	Don't know
RESOURCES REQUIRED	Large costs	Moderate costs	Negligible costs and savings	Moderate savings	Large savings

		JUDGMENT							
		Favors the comparison	Probably favors the comparison	Does not favor either the intervention or the comparison	Probably favors the intervention	Favors the intervention	Varies	Varies	No included studies
COST-EFFECTIVENESS									
EQUITY	Reduced	Probably reduced	Probably no impact	Probably increased	Probably increased	Increased	Varies	Varies	Don't know
ACCEPTABILITY	No	Probably no	Probably yes	Yes			Varies	Varies	Don't know
FEASIBILITY	No	Probably no	Probably yes	Yes			Varies	Varies	Don't know

TYPE OF RECOMMENDATION		Strong recommendation against the intervention			Conditional recommendation for either the intervention or the comparison			Conditional recommendation for the intervention		Strong recommendation for the intervention	
●	○				○			○		○	

Tungiasis, a neglected tropical disease caused by the sand flea *Tunga penetrans*, continues to affect millions of people in vulnerable communities across South America, the Caribbean, and sub-Saharan Africa. This condition causes severe pain, inflammation, disability, and social stigma, particularly among children, and can lead to long-term cognitive impairment. Despite its widespread impact, tungiasis remains largely neglected in global public health agendas.

This comprehensive technical guide, grounded in the latest scientific research, offers seven evidence-based recommendations for the effective management of tungiasis. The recommendations address the most effective treatments, such as the use of low-viscosity dimeticone, particularly for severe and mild tungiasis. They also discourage some practices like the use of hydrogen peroxide and potassium permanganate and non-professional mechanical extraction in severe cases, as this common practice carries a high risk of secondary infections and physical trauma. Alternative treatments such as coconut oil combined with neem oil are encouraged, especially in resource-limited settings. The use of topical ivermectin is also recommended when other treatments are not available. Furthermore, the importance of educational and community-based approaches that empower communities to reduce transmission and improve access to proper treatments is emphasized.

This guide aims to provide clinicians, public health professionals, policymakers, and community leaders with practical tools to treat tungiasis, reduce its burden on affected populations, and help prevent its spread. By following these recommendations, communities can move toward a more sustainable and effective response to this neglected disease.



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