

## **Review of 2022 World Health Organization guidelines on the control and elimination of schistosomiasis**

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## Summary

Schistosomiasis is a helminthiasis infecting up to 250 million people globally. In 2001, the World Health Assembly (WHA) 54.19 resolution defined a new global strategy for control of schistosomiasis through preventive chemotherapy programmes. This resolution culminated in the 2006 World Health Organization (WHO) guidelines that recommended empiric treatment by mass drug administration with praziquantel predominately to school-aged children in endemic settings at regular intervals. Since then, school-based and/or community-based preventive chemotherapy programmes have been scaled-up, and have reduced schistosomiasis-associated morbidity. Over the past 15 years, new scientific evidence, combined with a more ambitious goal of eliminating schistosomiasis as a public health problem and a parallel increase in the global donated supply of praziquantel have highlighted the need to update public health guidance worldwide. In February 2022, WHO published new guidelines with six recommendations to update the global public health strategy against schistosomiasis, including expansion of preventive chemotherapy eligibility from the predominant group of school-aged children to all age groups (2 years and older), lowering the prevalence threshold for annual preventive chemotherapy, and increasing the frequency of treatment. This article, written by the 2018-2022 Schistosomiasis Guidelines Development Group and its international partners, presents a summary of the new WHO guideline recommendations for schistosomiasis along with their historical context, supporting evidence, implications for public health implementation, and future research needs.

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### Key Points:

- ☐ Schistosomiasis is a helminth infection that affects an estimated 250 million people, primarily in low- and middle-income countries.
- ☐ The key public health strategy against schistosomiasis is preventive chemotherapy, which include the mass empiric treatment of school-aged children in endemic settings with praziquantel.
- ☐ New WHO guidelines for control and elimination of schistosomiasis were published in February 2022 with key changes in the public health strategy against schistosomiasis.
- ☐ Key changes in new WHO guidelines include expanding preventive chemotherapy programmes from only school-aged children to entire communities, lowering the prevalence

threshold to initiate preventive chemotherapy more equitably, and more frequent treatment in high risk settings.

▣ New WHO guidelines for schistosomiasis are supported by new scientific evidence and a more ambitious policy goal of approaching elimination of schistosomiasis and interruption of transmission.

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Article

Introduction

In 2001, the World Health Assembly (WHA) 54.19 resolution marked a historic step forward in public health policy for the global control of schistosomiasis,<sup>1</sup> a helminth infection infecting an estimated 250 million people, predominantly those residing in low- and middle-income countries in Africa.<sup>2,3</sup> This landmark resolution led to a new strategy against schistosomiasis designated ‘preventive chemotherapy’, which is achievable by mass drug administration (MDA) of the drug praziquantel to school-aged children and high-risk adults exposed to schistosomiasis, thereby averting future disease morbidity. Over the past 15-20 years, there has been considerable global scale-up of preventive chemotherapy, with consequential changes in epidemiology, and significant scientific advances in the field of schistosomiasis control.<sup>4,5</sup> The World Health Organization (WHO) 2021-2030 Roadmap for Neglected Tropical Diseases (NTDs) has supported more ambitious public health targets, including a goal for elimination of schistosomiasis as a public health problem (currently defined as <1% proportion of heavy egg patent intensity *Schistosoma* infections).<sup>5</sup> In February 2022, WHO published updated guidelines to renew guidance on the control and elimination of schistosomiasis.<sup>6</sup> Here, members of the 2018-2022 Schistosomiasis Guidelines Development Group and its international partners, outline the key updates in the new WHO guideline recommendations for schistosomiasis, their supporting evidence, public health relevance, and implications for implementation, and highlight future research needs.

Schistosomiasis is a helminth infection caused by blood flukes of the genus *Schistosoma*, which can cause either intestinal or urogenital forms of clinical illness. Infection occurs after exposure

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to freshwater that harbours cercariae (that have been released from intermediate host snails), the infectious stage of *Schistosoma* spp. that can directly penetrate human skin and then enter the

body.<sup>7</sup> Acute schistosomiasis (also known as “Katayama syndrome”) can cause an acute nonspecific presentation of fever, chills, rigors, and myalgias. Infection then progresses to the various forms of chronic disease.<sup>7</sup> Five *Schistosoma* species, *S. mansoni*, *S. japonicum*, *S. mekongi*, *S. guineensis*, and *S. intercalatum*, cause the human intestinal form of chronic illness. This ranges from sub-clinical illness to presentations of abdominal pain, diarrhoea, intestinal polyps, pulmonary hypertension, and periportal fibrosis, and subsequently portal hypertension (causing hepatomegaly, splenomegaly, and ascites).<sup>7</sup> In advanced cases of morbidity, *Schistosoma* eggs can transit throughout the body affecting the spinal cord, brain, testes, ovaries, skin, and eyes.<sup>8,9</sup> *Schistosoma haematobium* and hybrid forms cause the human urogenital form of chronic illness, which ranges from sub-clinical illness to presentations of haematuria, dysuria, hydronephrosis, infertility, risk of ectopic pregnancy, and is a known aetiological factor of squamous cell carcinoma of the bladder.<sup>7</sup> The urogenital form of illness may also increase susceptibility to sexually transmitted diseases such as HIV.<sup>10-13</sup>

The majority of the estimated 250 million people with schistosomiasis reside predominately in sub-Saharan Africa. Other geographic disease foci are found in Asia, Latin America, and the Middle East.<sup>2,3</sup> The global burden of schistosomiasis is estimated to cause 1.4-3.3 million disability-adjusted life years (DALYs) annually, largely due to morbidity associated with infection rather than premature deaths.<sup>2,14</sup> Studies have shown that the heaviest burden of the disease occurs in school-aged children, while recent surveys have increasingly highlighted the burden of infection in preschool-aged children, adolescents, and adults.<sup>7,15-19</sup> Recent global

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trends demonstrate a pattern of declining schistosomiasis morbidity, and to some extent, a reduction in the total number of people infected with *Schistosoma*. This reduction in global burden is largely related to MDA using praziquantel, improved water, sanitation, and hygiene (WASH), information, education, and communication (IEC), behavioural change, and snail control. In a recent geospatial analysis of available epidemiological data, the study estimated that the prevalence of schistosomiasis in school-aged children in sub-Saharan Africa declined from 23.0% in 2000-2010 to 9.6% in 2015-2019.<sup>2</sup> In another contemporaneous study, a large-scale analysis of cross-sectional data from nine national schistosomiasis control programmes found that some, but not all, countries experienced reductions in schistosomiasis prevalence in schoolaged children.<sup>20</sup> The prevalence and disease burden in other age groups have likely remained

more stable over time.

#### History of WHO policy and formulation of guidelines

The public health strategy of preventive chemotherapy for schistosomiasis, as first outlined in the 2001 WHA 54.19 resolution, involves widespread treatment of all school-aged children (ages 5-15 years) in affected geographic zones at high-risk for schistosomiasis with treatment administered at regular intervals (e.g., annually or biennially).<sup>1</sup> The WHA 54.19 resolution outlined a goal of achieving a minimum target of 75% coverage for preventive chemotherapy in at-risk school-aged children.<sup>1</sup> In 2002, a WHO expert committee published the first operational guidance for preventive chemotherapy for multiple NTDs, including schistosomiasis.<sup>21</sup> This was published alongside a 2002 WHO guidelines document on preventive chemotherapy against schistosomiasis with further clarification in a subsequent 2006 WHO document.<sup>22,23</sup>

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These previous guidelines outlined eligibility and frequency of preventive chemotherapy in the target population based on egg-patent prevalence of infection using stool and urine microscopy. In areas with 10-49% prevalence of schistosomiasis, these earlier WHO guidelines recommended preventive chemotherapy in school-aged children every other year.<sup>5</sup> In areas with 50% or higher prevalence of schistosomiasis, those WHO guidelines recommended annual preventive chemotherapy in school-aged children with consideration to treat broader age groups.<sup>5</sup> If prevalence was less than 10%, no preventive chemotherapy was recommended, although treatment twice during primary schooling could be considered in endemic settings. These guidelines outlined the opportunity to expand treatment from only school-aged children to other at-risk groups (e.g., fishermen, farmers of irrigation fields, car washers, etc.) either with empiric or selective individual treatments in high-risk settings.<sup>5</sup> WHO published updated guidance for preventive chemotherapy again in 2011.<sup>24</sup> In 2012, the WHA 65.21 resolution outlined a plan for the elimination of schistosomiasis.<sup>25</sup> This was followed by the London Declaration on NTDs that focused on increasing global drug donations to NTD treatment programmes, as well as the first WHO NTD Roadmap outlining its long term NTD public health strategy.<sup>26,27</sup>

In 2018, WHO commissioned a guidelines development group to create updated guidelines for the control and elimination of schistosomiasis that were publicly released in mid-February 2022.<sup>6</sup> These guidelines were published closely after the second WHO NTD Roadmap outlining new targets for public health control and elimination from 2021-2030.<sup>5</sup> Table 1 shows a summary of

the WHO policy history for schistosomiasis.

Motivation for new WHO guidelines for schistosomiasis

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During the past 10-15 years since the currently employed 2006 and 2011 WHO guidelines on public health control of schistosomiasis were published, there have been many influential changes that have indicated a need for updated, evidence-informed WHO guidelines on the global strategy for schistosomiasis.<sup>23,24</sup> First, the public health goal for schistosomiasis has changed. The original goal was focused on averting and reducing morbidity in school-aged children and preventing the most extreme forms of clinical illness. The WHA 65.21 resolution and WHO NTD roadmap outlined a more ambitious goal of eliminating schistosomiasis, meaning more attention to infection in all age groups and a focus on reducing and breaking transmission. This also highlighted the need to better define the goal of “elimination of schistosomiasis as a public health problem”, as articulated in prior WHO guidelines.<sup>5</sup> Second, there still remains a substantial burden of disease from schistosomiasis in certain regions. Despite the widespread implementation of WHO-recommended preventive chemotherapy strategy against schistosomiasis, ongoing transmission and high prevalence in many endemic settings (“persistent hot spots”) remain.<sup>28-30</sup> This informed the need to analyze data at sub-district levels (wards/communities) to monitor and track effective coverage of these “persistent hot spots” in intervention efforts, and prioritize them for additional intervention including improved WASH. Third, the global supply of praziquantel has increased over time. The original preventive chemotherapy guidelines were developed in the context of a limited supply of praziquantel, which led to prioritizing the use of drug resources to only the highest risk populations. However, the expanded global supply of donated praziquantel now allows for expanding treatment to more age- and risk-groups and for more frequent treatment.<sup>31</sup> Fourth, there has now been significant operational research studying optimal preventive chemotherapy delivery strategies.<sup>15</sup> In particular, there is an increasing body of literature to support the health effectiveness of

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expanding preventive chemotherapy to entire communities (including preschool-aged children and adults) instead of school-aged children alone, alongside precision targeting of treatment.<sup>17,32-34</sup> As part of the guidelines process, nine systematic reviews were commissioned or reviewed to address key questions in schistosomiasis public health control and elimination (Table 2).

## Search strategy and selection criteria

We did not conduct a formal systematic review for this review article.

The guideline development process adhered to the Grading of Recommendations, Assessment, Development and Evaluation (GRADE) approach.<sup>35</sup> Each recommendation was assigned a certainty of evidence (i.e., very low, low, moderate, or high) based on the quality of available evidence informing a recommendation. High certainty of evidence was supported by randomized controlled trials, while observational data imply low quality of evidence. Further considerations could increase or decrease the certainty of evidence. Each recommendation is also assigned a strength of recommendation (i.e., conditional or strong) based on the guideline committee assessment of confidence in a recommendation, with further consideration of additional implementation factors (e.g., equity, values and preferences, and resources). Based on the limited amount of randomized trial level data in the field of schistosomiasis, many of the recommendations were supported by lower certainty of evidence.

## Highlights of the new WHO guideline recommendations for schistosomiasis

The new 2022 WHO guidelines include six recommendations to outline the public health strategy for schistosomiasis as described in this section and Table 3.

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Recommendation 1: In endemic communities with prevalence of *Schistosoma* spp. infection  $\geq 10\%$ , WHO recommends annual preventive chemotherapy with a single dose of praziquantel at  $\geq 75\%$  treatment coverage in all age groups from 2 years old, including adults, pregnant women after the first trimester, and lactating women, to control schistosomiasis morbidity and advance towards eliminating the disease as a public health problem.

(Strong recommendation; certainty of evidence: moderate)

This recommendation focuses on defining a new approach to preventive chemotherapy for schistosomiasis. Historically, preventive chemotherapy has been predominantly recommended by WHO for the treatment of school-aged children. The evidence underscoring the selection of the prevalence thresholds was quite limited. These previous guidelines, currently in use, were influenced by the high prevalence of infection and disease morbidity in school-aged children, further influenced by a limited global supply of praziquantel resulting in the need to focus therapy on the highest risk groups. Over the past 5-10 years, there has been a growing body of literature that indicates the importance of subtle and chronic morbidity where infection



prevalence is only moderate or low,<sup>36-38</sup> as well as considerable prevalence of infection and disease morbidity in additional age groups of preschool-aged children, adolescents, and adults.<sup>17,32-34</sup> Furthermore, modelling studies have suggested that these additional age groups act as an “untreated reservoir” within at-risk communities, which contribute to community-level transmission and reinfection of school-aged children.<sup>19,39</sup>

In the new WHO guidelines, preventive chemotherapy is recommended for all individuals, 2 years of age and older, in settings with a *Schistosoma* spp. prevalence of 10% or higher. This recommendation fundamentally changes the approach to preventive chemotherapy against schistosomiasis through three key aspects: (i) it expands the eligible population for preventive chemotherapy from school-aged children to the entire community (2 years and older); (ii) it

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lowers the prevalence threshold for annual preventive chemotherapy from 50% to 10%; and (iii) it simplifies the guidelines to a single prevalence threshold rather than multiple thresholds. The key drivers of the decision to expand treatment eligibility to the entire community included: (i) the documented infection and morbidity in additional age groups (preschool-aged children, adolescents, and adults), including at lower prevalence;<sup>17,32-34,36-38</sup> (ii) the role of treating the entire community to reduce community-level *Schistosoma* spp. transmission; (iii) an increased global supply of praziquantel; (iv) the equity and feasibility; and (v) the evidence supporting the cost-effectiveness of community-wide treatment. The selection of a prevalence threshold for preventive chemotherapy has been an integral aspect of the programme strategy. In the new WHO guidelines, a single threshold of 10% prevalence of *Schistosoma* spp. to initiate preventive chemotherapy was chosen. In the absence of randomized trials comparing treatment outcomes initiated at various prevalence thresholds, a single threshold of 10% prevalence of *Schistosoma* spp. to initiate preventive chemotherapy was chosen. This threshold choice was influenced by cost-effectiveness modelling that balanced the cost of treatment with expected gains in terms of health outcomes and empirical data to support the presence of disease morbidity in lower prevalence settings.<sup>19,36-38,40</sup> This decision to lower the prevalence threshold to 10% was further supported based on considerations of public health impact and focus on equity and feasibility. A key systematic review included in the guidelines studied the safety of praziquantel amongst all age groups supporting its widespread use. Key challenges include the implementation of expanded preventive chemotherapy programmes with robust measurement of community level

treatment coverage.

Recommendation 2: In endemic communities with prevalence of *Schistosoma* spp. infection <10%, WHO suggests one of two approaches based on programmatic objectives and resources:

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(i) where there has been a programme of regular preventive chemotherapy, to continue the intervention at the same or reduced frequency towards interruption of transmission; or (ii) where there has not been a programme of regular preventive chemotherapy, to use a clinical approach of test-and-treat, instead of preventive chemotherapy targeting a population.

(Conditional recommendation; certainty of evidence: very low)

This recommendation focuses on the preventive chemotherapy strategy for *Schistosoma* spp. in low prevalence settings (<10% prevalence). Based on the prior guidelines, if prevalence of *Schistosoma* spp. infection was <10% at baseline, then no preventive chemotherapy would be recommended. However, a key challenging public health question is the management of a setting with prior *Schistosoma* spp. prevalence >10% that has undergone preventive chemotherapy and now has a *Schistosoma* spp. prevalence <10%. Prior guidance has recommended an option to conduct a prevalence survey after 5-6 years of preventive chemotherapy and reduce frequency of treatment if prevalence is reduced to 1-10%.<sup>24</sup> In this scenario, the new guidelines recommend either continuing preventive chemotherapy at the same frequency, based on the reasoning that transmission in this setting remains high, or continuing preventive chemotherapy at a lower frequency. If the decision is made to reduce frequency of preventive chemotherapy, close epidemiological monitoring is strongly encouraged, to ensure no rebound in prevalence. The evidence to support this recommendation is limited and this remains an area in need of further research.

Recommendation 3: In endemic communities with prevalence of *Schistosoma* spp. infection  $\geq 10\%$  that demonstrate lack of an appropriate response to annual preventive chemotherapy, despite adequate treatment coverage ( $\geq 75\%$ ), WHO suggests consideration of biannual (twice yearly) instead of annual preventive chemotherapy.

(Conditional recommendation; certainty of evidence: very low)

This recommendation focuses on the optimal frequency of preventive chemotherapy and addresses epidemiological variation in effectiveness of preventive chemotherapy between

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settings, with continued transmission in “persistent hot spots”. Historically, the frequency of preventive chemotherapy was based on a prevalence threshold. In settings with  $\geq 50\%$  *Schistosoma* spp. prevalence, WHO recommended annual preventive chemotherapy in schoolaged children. In settings with 10-49% *Schistosoma* spp. prevalence, WHO recommended preventive chemotherapy every other year in school-aged children. The key challenge that was observed in subsequently implemented preventive chemotherapy programmes was the existence of “persistent hot spots”, indicating heterogeneity in response to preventive chemotherapy in geographic settings that appeared epidemiologically similar at baseline.<sup>28,41,42</sup> The heterogeneity in treatment response among populations in geographic settings has made developing generalizable preventive chemotherapy recommendations challenging. In the new 2022 WHO guidelines, preventive chemotherapy is recommended universally to start at a frequency of annual treatment. However, after a minimum of two years of preventive chemotherapy, if a follow up prevalence survey indicates the prevalence in a given setting has not declined appropriately with treatment, then the guidelines provide an option to increase the frequency of preventive chemotherapy to twice yearly in order to obtain better prevalence control. This recommendation is novel for a public health guideline because of the application of adaptive decision-making, which uses an empiric trial of preventive chemotherapy to determine whether a setting remains a “persistent hot spot” that otherwise might be hard to detect. The guideline recommendation provides broad guidance on how to determine whether a prevalence reduction after treatment is appropriate, and is supported by re-analysis of a randomized preventive chemotherapy trial that uses change in prevalence over time to predict “persistent hot spots”.<sup>42</sup> The decision for a preventive chemotherapy programme to increase frequency to twice

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annually is ultimately a decision for each country programme. The evidence to support the criteria for prediction or identification of “persistent hot spots” remains limited, and hence, an area in need of further scientific inquiry.

Recommendation 4: WHO recommends that health facilities provide access to treatment with praziquantel to control morbidity due to schistosomiasis in all infected individuals regardless of age, including infected pregnant excluding the first trimester, lactating women, and preschoolaged children <2 years. The decision to administer treatment in children under 2 years of age should be based on testing and clinical judgement.

(Strong recommendation; certainty of evidence: moderate)

This recommendation focuses on access to praziquantel for clinical management of schistosomiasis in all age and at-risk groups, with specific acknowledgement of specific populations. Historically, the highlighted specific populations of pregnant women, lactating women, and young children (<2 years) were not specifically addressed in schistosomiasis guidelines. The key contribution of Recommendation 4 was to explicitly state that pregnant women (2nd and 3rd trimester) and lactating women were eligible for praziquantel administration. The only group that should be excluded from treatment based on drug safety concerns are pregnant women in their 1st trimester. Under this new recommendation, the decision to treat children under 2 years of age (with the forthcoming orally dispersible formulation of praziquantel, a mono-enantiomeric pediatric formulation), was deferred to clinical judgement of the health care provider.

Recommendation 5: WHO recommends WASH interventions, environmental interventions (water engineering and focal snail control with molluscicides) and behavioural change interventions as essential measures to help reduce transmission of *Schistosoma* spp. in endemic areas.

(Strong recommendation; certainty of evidence: low)

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This recommendation focuses on the role of complementary and essential public health strategies of WASH and molluscicide application for environmental snail control (vector control) to reduce transmission of *Schistosoma* spp., alongside preventive chemotherapy campaigns. WASH interventions for schistosomiasis focus on minimizing open defecation or urination in or near open freshwater bodies (to reduce the parasite load in the environment contributing to new infections) and minimizing people's exposure to contaminated freshwater (to minimize the odds of exposure to infection).<sup>43</sup> Snail control interventions are largely restricted to focal application of chemical molluscicides in freshwater bodies, with consideration for larger scale use of molluscicides based on local epidemiology. Chemical molluscicides can kill the snail intermediate hosts of *Schistosoma*, hence reducing population level transmission of new infections.<sup>44,45</sup> WHO has previously published operational guidance on the public health role and implementation recommendations for both WASH and snail control interventions.<sup>5,46</sup> Of note, the 2022 WHO guidelines do not provide detailed guidance on how to deliver these complementary interventions, and/or how to integrate with preventive chemotherapy

programmes. These details are available in published WHO technical manuals.<sup>5,46</sup>

Recommendation 5 reinforces the general importance of these complementary strategies, but provides no further guidance on specific implementation.

Recommendation 6: In communities approaching the interruption of transmission (defined as having no autochthonous human cases reported for 5 consecutive years), WHO suggests a verification framework that consists of:

1. Testing for *Schistosoma* infection in humans with a diagnostic that has high sensitivity and specificity. This may require the use of a two-step diagnostic process starting with a high sensitivity test confirmed with a second, high specificity test.
2. Testing for *Schistosoma* infection in snails with a diagnostic that has high sensitivity and specificity. This may require the use of a two-step diagnostic process starting with a high sensitivity test confirmed with a second, high specificity test.

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3. Testing for *Schistosoma* infection in non-human mammalian hosts, as applicable, with a diagnostic that has high sensitivity and specificity. This may require the use of a two-step diagnostic process starting with a high sensitivity test confirmed with a second, high specificity test.

(Conditional recommendation; certainty of evidence: low)

This recommendation focuses on defining a framework to verify interruption of transmission of *Schistosoma* spp. in a previously endemic setting. There has been no prior WHO guidance on how to determine whether a previously endemic setting has interrupted transmission and should be considered non-endemic for schistosomiasis. Given an increasing interest in interruption of transmission, Recommendation 6 outlines an initial general framework that country programmes can apply when interruption of transmission is believed to have occurred. The recommendation suggests a two-part testing framework of humans, snails (the intermediate host of *Schistosoma* spp.), and animal reservoirs to confirm that *Schistosoma* spp. infections are no longer present. The confirmation of *Schistosoma* spp. elimination in non-human animal hosts is especially important for *S. japonicum* and *S. mekongi*, but may also be important for other species. The recommendation outlines a two-part testing scheme with an initial high sensitivity test followed by a confirmatory test with higher specificity for optimal accuracy. Further guidance on the operational aspects of this verification process, including choice of diagnostic and sampling

approach, is intended to be forthcoming in WHO operational manuals.

A complete description of the guideline recommendations and their supporting evidence can be found in the published WHO guidelines on control and elimination of schistosomiasis.<sup>6</sup>

Future needs for research

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The new WHO schistosomiasis guidelines highlight several research needs. Preventive chemotherapy programmes will be challenged to reach entire communities in the face of systemic non-adherence, low coverage, hard-to-reach populations, lack of equity of drug distribution, management and identification of “persistent hot spots”, and other competing public health responses, as witnessed over the past 2 years with the COVID-19 pandemic. Operational research on these topics will be essential and the 10-year Schistosomiasis Consortium for Operational Research and Evaluation (SCORE) might serve as a role model.<sup>54</sup> Scientific inquiry on how to optimize surveillance programmes for detection of infection prevalence and disease morbidity with efficient and low-cost approaches will be needed, including female genital schistosomiasis and other morbidity outcomes. Further work to refine the criteria for implementation of snail control strategies and WASH, layered onto preventive chemotherapy, are required. This includes developing an evidence base on key aspects of WASH and approaches to snail control that have effectiveness to reduce *Schistosoma* spp. transmission. There is an urgent need to develop and validate new diagnostics with improved sensitivity and specificity for *Schistosoma* spp. infection in humans, animals, the snail intermediate host, and environmental samples to inform verification of elimination in previously endemic settings. Key threats to the success of preventive chemotherapy programmes would be development of praziquantel resistance or substantial contribution of animal reservoirs to community transmission, including species exhibiting some degree of hybridization<sup>47</sup>, and research on these topics will be important. Scientific investigation and investment into development of new antischistosomal

drugs and protective vaccines would further support elimination efforts. Capacity building and development of a strong surveillance system for schistosomiasis will further support efforts for elimination of schistosomiasis, alongside study into the risk factors for persistent

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transmission. Finally, as *Schistosoma* spp. transmission is further reduced in endemic settings,

targeted research into when and how preventive chemotherapy can be scaled down is needed.

## Conclusion

Schistosomiasis is a common helminthiasis that causes a considerable global burden, with the majority of disease burden concentrated in low- and middle-income countries in Africa. During the COVID-19 pandemic, country programmes for preventive chemotherapy were temporarily discontinued or delayed. Our hope is these guidelines can revitalize the public health fight against schistosomiasis. These new WHO guidelines have been developed to strengthen the public health strategy to reduce morbidity resulting from schistosomiasis and start transitioning towards the ultimate goal of elimination. New scientific findings and a shifting public health goal towards elimination have influenced key changes in the latest 2022 WHO guidelines on schistosomiasis, with changes in preventive chemotherapy recommendations that will greatly expand access to treatment. Global coordination will be needed from WHO, national governments and country programmes, pharmaceutical companies, non-governmental organizations, and other stakeholders to realize the full public health potential of these guidelines.

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## Tables and Figures

**Table 1. WHO policy history for schistosomiasis**

2001 WHA 54.19 resolution<sup>1</sup>

Outlined plan for widespread treatment of all school-aged children (ages 5-15 years) in affected geographic zones at high-risk for schistosomiasis with treatment administered at regular intervals (e.g.,

annually or biennially) with minimum 75% coverage.

2002 WHO technical report<sup>21</sup>

Publication of first operational guidance for preventive chemotherapy for multiple neglected tropical diseases, including schistosomiasis.

2006 WHO technical manual<sup>23</sup>

Publication of technical manual for treatment of helminths.

2011 WHO technical manual<sup>24</sup>

Publication of technical manual for treatment of helminths in school-aged children.

2012 WHA 65.21 resolution<sup>25</sup>

Outlined plan for elimination of schistosomiasis.

2012 London Declaration on Neglected Tropical Diseases<sup>26</sup>

Global agreement for drug donation for preventive chemotherapy programmes for neglected tropical

diseases, including schistosomiasis.

2012 First WHO NTD Roadmap<sup>27</sup>

Outlined 2020 targets for public health control and elimination of neglected tropical diseases, including

schistosomiasis.

2018 WHO commissioned guidelines development group for schistosomiasis

2021 Second WHO NTD Roadmap<sup>5</sup>

Outlined 2021-2030 targets for public health control and elimination of neglected tropical diseases, including schistosomiasis.

2022 New WHO guidelines for schistosomiasis<sup>6</sup>

Publication of new WHO guidelines on control and elimination of schistosomiasis.

**Table 2. List of systematic reviews commissioned for the 2022 WHO guidelines on control and elimination of schistosomiasis**

Review 1

Impact of preventive chemotherapy against schistosomiasis on disease morbidity in key population age groups<sup>48</sup>

Review 2

Optimal prevalence threshold for preventive chemotherapy against schistosomiasis to control morbidity

Review 3

Frequency of praziquantel for preventive chemotherapy to control morbidity<sup>49</sup>

Review 4

Safety of praziquantel for preventive chemotherapy against schistosomiasis in at-risk populations

Review 5

Chemical-based snail control against schistosomiasis in at-risk communities<sup>45</sup>

Review 6

WASH interventions and schistosomiasis in at-risk populations<sup>50</sup>

Review 7

Diagnostic tools for Schistosoma infection in humans to verify interruption of transmission<sup>51</sup>

Review 8

Diagnostic tools for detection of Schistosoma in snails and the environment to verify interruption of transmission<sup>52</sup>

Review 9

Diagnostic tools for Schistosoma infection in non-human animal hosts to verify interruption of transmission<sup>53</sup>

Note: systematic reviews without a reference are unpublished.

**Table 3. List of 2022 WHO guideline recommendations for control and elimination of schistosomiasis**

Recommendation 1

In endemic communities with prevalence of *Schistosoma* spp. infection  $\geq 10\%$ , WHO recommends annual preventive chemotherapy with a single dose of praziquantel at  $\geq 75\%$  treatment coverage in all age groups from 2 years old, including adults, pregnant women after the first trimester and lactating women, to control schistosomiasis morbidity and advance towards eliminating the disease as a public health problem.

Recommendation 2

In endemic communities with prevalence of *Schistosoma* spp. infection  $< 10\%$ , WHO suggests one of two approaches based on programmatic objectives and resources: (i) where there has been a programme of regular preventive chemotherapy, to continue the intervention at the same or reduced frequency towards interruption of transmission; or (ii) where there has not been a programme of regular preventive chemotherapy, to use a clinical approach of test-and-treat, instead of preventive chemotherapy targeting a population.

Recommendation 3

In endemic communities with prevalence of *Schistosoma* spp. infection  $\geq 10\%$  that demonstrate lack of an appropriate response to annual preventive chemotherapy, despite adequate treatment coverage ( $\geq 75\%$ ), WHO suggests consideration of biannual (twice yearly) instead of annual preventive chemotherapy.

Recommendation 4

WHO recommends that health facilities provide access to treatment with praziquantel to control morbidity due to schistosomiasis in all infected individuals regardless of age, including infected pregnant excluding the first trimester, lactating women and children aged  $< 2$  years. The decision to administer treatment in children under 2 years of age should be based on testing and clinical judgement.

Recommendation 5

WHO recommends WASH interventions, environmental interventions (water engineering and focal

snail control with molluscicides) and behavioural change interventions as essential measures to help reduce transmission of *Schistosoma* spp. in endemic areas.

#### Recommendation 6

In communities approaching the interruption of transmission (defined as having no autochthonous human cases reported for 5 consecutive years), WHO suggests a verification framework that consists of:

1. Testing for *Schistosoma* infection in humans with a diagnostic that has high sensitivity and specificity. This may require the use of a two-step diagnostic process starting with a high sensitivity test confirmed with a second, high specificity test.
2. Testing for *Schistosoma* infection in snails with a diagnostic that has high sensitivity and specificity. This may require the use of a two-step diagnostic process starting with a high sensitivity test confirmed with a second, high specificity test.
3. Testing for *Schistosoma* infection in non-human mammalian hosts, as applicable, with a diagnostic that has high sensitivity and specificity. This may require the use of a two-step diagnostic process starting with a high sensitivity test confirmed with a second, high specificity test.

WASH, water, sanitation, and hygiene