Guideline: Preventive chemotherapy to control soil-transmitted helminth infections in at-risk population groups

EXECUTIVE SUMMARY

The World Health Organization (WHO) estimates that infections with the main soil-transmitted helminths – the roundworm (Ascaris lumbricoides), the whipworm (Trichuris trichiura) and the hookworms (Ancylostoma duodenale and Necator americanus) – contribute 5.18 million disability-adjusted life-years worldwide in 2010. Globally, an estimated 820 million people are infected with roundworms, 460 million with whipworms and 440 million with hookworms.

Although each species has specific characteristics, these soil-transmitted helminthias are grouped together for control purposes, owing to: (i) similar geographical endemicity and at-risk groups that are affected; (ii) treatment by the same medicines; (iii) the same tools used for diagnosis; and (iv) similar mechanism of negative impact on human health (linked to the intensity of infection).

Purpose of the guideline

This guideline provides global, evidence-informed recommendations on preventive chemotherapy, as a public health intervention in areas endemic for soil-transmitted helminths, to decrease the worm burden of soil-transmitted helminth infection in children, adolescent girls, women of reproductive age and pregnant women, including those coinfected with HIV.

The recommendations contained in this guideline are intended for a wide audience, including policymakers and their expert advisers as well as technical and programme staff at government institutions and organizations involved in the design, implementation and expansion of programmes to control soil-transmitted helminth infections and nutrition-sensitive actions for a safe and hygienic environment to improve public health.

This guideline aims to help WHO Member States and their partners to make evidence-informed decisions on the appropriate actions in their efforts to achieve the United Nations Sustainable Development Goals and the global targets presented in the World Health Assembly resolution WHA66.12 on Neglected tropical diseases, the Comprehensive implementation plan on maternal, infant and young child nutrition, the Global strategy for women’s, children’s, and adolescents’ health (2016–2030), Water, sanitation and hygiene for accelerating and sustaining progress on neglected tropical diseases: a global strategy.

This publication is a World Health Organization (WHO) guideline. A WHO guideline is any document, whatever its title, containing WHO recommendations about health interventions, whether they be clinical, public health or policy interventions. A standard guideline is produced in response to a request for guidance in relation to a change in practice, or controversy in a single clinical or policy area; it is not expected to cover the full scope of the condition or public health problem. A recommendation provides information about what policy-makers, health-care providers or patients should do; it implies a choice between different interventions that have an impact on public health and that have ramifications for the use of resources. All publications containing WHO recommendations are approved by the WHO Guidelines Review Committee.

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Guideline development methodology

WHO developed the present evidence-informed recommendations using the procedures outlined in the **WHO handbook for guideline development**. The steps in this process included: (i) identification of priority questions and outcomes; (ii) retrieval of the evidence; (iii) assessment and synthesis of the evidence; (iv) formulation of recommendations, including research priorities; and planning for (v) dissemination; (vi) implementation, equity and ethical considerations; and (vii) impact evaluation and updating of the guideline. The Grading of Recommendations Assessment, Development and Evaluation (GRADE) methodology was followed, to prepare evidence profiles related to preselected topics, based on up-to-date systematic reviews. The Developing and Evaluating Communication Strategies to support Informed Decisions and Practice based on Evidence (DECIDE) framework, an evidence-to-decision tool that includes intervention effects, values, resources, equity, acceptability and feasibility criteria, was used to guide the formulation of the recommendations by the guideline development group.

The scoping of the guideline and the prioritization of the outcomes were done by the guideline development group – nutrition actions 2013–2014 (Geneva, 18–21 February 2013). The evidence-informed recommendations were developed and finalized at a meeting of the guideline development group – deworming (Geneva, 13–15 April 2016). Three options for types of recommendations were agreed, namely: (i) strong recommendation; (ii) conditional recommendation (recommended only in specific contexts); and (iii) not recommended. Five external experts served as technical peer reviewers of a preliminary version of this guideline.

Available evidence

The available evidence included five systematic reviews of randomized controlled trials (RCTs) that followed the procedures of the **Cochrane handbook for systematic reviews of interventions** and assessed the effects of preventive chemotherapy on controlling soil-transmitted helminth infections in preschool and school-age children, adolescent girls, women of reproductive age, pregnant women and individuals coinfected with HIV. All studies compared a group of participants who had received anthelminthic medicines for soil-transmitted helminth infections with a group that had received a placebo or no treatment. For the studies to be included in the reviews, co-interventions other than anthelminthic medicines had to have been used for both the control and intervention arms. The overall quality of the available evidence was very low to moderate for the critical outcomes of worm burden, weight gain and haemoglobin concentrations.
Additional reviews of evidence were presented in response to the complexities of evaluating preventive chemotherapy programmes using only RCT designs. Evidence contributing to the decision-making process came from reviews of the morbidity caused by soil-transmitted helminth infections, the direct effects and safety of anthelminthic treatment, the values and preferences of the target beneficiaries and end-users, and cost analyses of the delivery of preventive chemotherapy interventions.

A decision-making framework was used to lead deliberations and consensus decision-making. This included the following considerations: (i) the quality of the evidence across outcomes critical to decision-making; (ii) the balance of benefits and harms; (iii) values and preferences related to the recommended preventive chemotherapy intervention in different settings and for different stakeholders, including the populations at risk; (iv) the acceptability of the intervention among key stakeholders; (v) resource implications for programme managers in different settings; (vi) equity; and (vii) the feasibility of implementation of the intervention.

**Recommendations**

- **Preventive chemotherapy (deworming),** using annual or biannual\(^a\) single-dose albendazole (400 mg) or mebendazole (500 mg),\(^b\) is recommended as a public health intervention for all young children (12–23 months of age), preschool (24–59 months of age) and school-age children\(^1\) living in areas where the baseline prevalence of any soil-transmitted infection is 20% or higher among children, in order to reduce the worm burden of soil-transmitted helminth infections (**strong recommendation, low-quality evidence**).
  - \(^a\) Biannual administration is recommended where the baseline prevalence is over 50%.
  - \(^b\) A half-dose of albendazole (i.e. 200 mg) is recommended for children younger than 24 months of age.

- **Preventive chemotherapy (deworming),** using annual or biannual\(^a\) single-dose albendazole (400 mg) or mebendazole (500 mg), is recommended as a public health intervention for all non-pregnant adolescent girls (10–19 years of age) and non-pregnant women of reproductive age (15–49 years of age) living in areas where the baseline prevalence of any soil-transmitted helminth infection is 20% or higher among non-pregnant adolescent girls and non-pregnant women of reproductive age, in order to reduce the worm burden of soil-transmitted helminth infection (**strong recommendation, moderate-quality evidence**).
  - \(^a\) Biannual administration is recommended where the baseline prevalence is over 50%.

- **Preventive chemotherapy (deworming),** using single-dose albendazole (400 mg) or mebendazole (500 mg), is recommended as a public health intervention for pregnant women, after the first trimester, living in areas where both: (i) the baseline prevalence of hookworm and/or *T. trichiura* infection is 20% or higher among pregnant women, and (ii) anaemia is a severe public health problem, with a prevalence of 40% or higher among pregnant women,\(^a\) in order to reduce the worm burden of hookworm and *T. trichiura* infection (**conditional recommendation, moderate-quality evidence**).
  - \(^a\) For the most recent estimates of prevalence of anaemia, visit the WHO-hosted Vitamin and Mineral Nutrition Information System (VMNIS).

The current guideline updates and supersedes previous recommendations contained in the WHO publication *Preventive chemotherapy in human helminthiasis: coordinated use of anthelmintic drugs in control interventions: a manual for health professionals and programme managers,*\(^2\) reviewed at the Informal Consultation on Preventive Chemotherapy in Human Helminthiasis (Geneva, March 2006), and complements some of the operational guidance of *Helminth control in school-age children: a guide for managers of control programmes,*\(^3\) published by WHO in 2011.

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\(^1\) We defined school-age children as those between 5 and 12 years of age. Although many children unfortunately do not attend school, these ages are compulsory school years in most settings, providing with it an entry point to address the nutritional needs of this age group. In some settings the upper range may be 14 years of age.


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Rationale
During the deliberations, the guideline development group took into particular consideration the following evidence:

- The morbidity caused by the different soil-transmitted helminth species in infected individuals is well documented and severe;
- Those infected with soil-transmitted helminths benefit significantly from anthelminthic treatment in terms of a reduction in worm burden;
- Albendazole and mebendazole are well tolerated, with only minor and transient side-effects reported;
- Preventive chemotherapy to control soil-transmitted helminth infections is well accepted among programme beneficiaries and implementers; and
- Logistical difficulties and additional costs of alternative methods to identify and treat infected individuals are prohibitive.

Remarks
Preventive chemotherapy, or the periodic large-scale administration of anthelminthic medicines to populations at risk, can dramatically reduce the burden of worms caused by soil-transmitted helminth infections. In areas of varying soil-transmitted helminth endemicity, no average benefit of preventive chemotherapy was detected for outcomes related to morbidity, nutritional outcomes or development in the entire population (composed of infected and uninfected individuals).

However, a decreasing worm burden of soil-transmitted helminths decreases morbidity among individuals heavily infected by soil-transmitted helminths. Because preventive chemotherapy does not break the cycle of infection and reinfection, populations living in contaminated environments continue to be at risk of infection and need frequent administrations of anthelminthic medicines.

Long-term solutions to soil-transmitted helminthiases require improvements in water, sanitation and hygiene. Moreover, multisectoral, integrated programmes will be needed to maximize and sustain the benefits of a decreased worm burden of soil-transmitted helminth infections. Preventive chemotherapy is an important but insufficient part of a comprehensive package to eliminate morbidity due to soil-transmitted helminths in at-risk populations.

The remarks in this section are intended to guide implementation of the recommendations.

- As the prevalence and intensity of soil-transmitted helminth infections are related, only light-intensity infection and low morbidity are expected where the prevalence of any soil-transmitted helminth infection at baseline is lower than 20%. Large-scale preventive chemotherapy programmes are, therefore, not required in these situations.
- Delivering preventive chemotherapy to adolescent girls and women of reproductive age entails extra care and precaution in ensuring that women and girls receiving anthelminthic medicines are not pregnant. Policy-makers may decide to withhold preventive chemotherapy among adolescent girls and women of reproductive age when the pregnancy status or gestational age of women and girls is uncertain, or in areas where rates of unplanned pregnancies are high and coverage of antenatal care is low.
- Extra resources may be required for delivery of preventive chemotherapy to adolescent girls, who may not be easily reached within the existing infrastructure.
- Anthelminthic medicines can be given to individuals coinfected with HIV, who are otherwise eligible for inclusion in large-scale preventive chemotherapy interventions.

• Provision of adequate water, sanitation and hygiene services is fundamental to break the cycle of infection and reinfection and sustainably control soil-transmitted helminth infections. Collaboration between programmes for control of soil-transmitted helminth infections and water, sanitation and hygiene programmes is essential to ensure prioritization of water and sanitation services to areas that are endemic for soil-transmitted helminths.

• Deworming should be delivered together with promotion of health and hygiene, to reduce transmission by encouraging healthy behaviours, such as hand washing, use of footwear and proper disposal of faeces.

• Routine monitoring for effective coverage and evaluation of the impact of the intervention should be an integral part of preventive chemotherapy programmes to help inform the decision on continuation or cessation of the programme.

Research gaps
Discussions between the members of the WHO guideline development group and the external resource group highlighted the limited evidence available in some areas of knowledge, meriting further research on preventive chemotherapy to control soil-transmitted helminth infections, particularly in the following areas:

• diagnostic or proxy indicators, to identify households at risk and individuals infected with soil-transmitted helminths;

• alternative anthelmintic medicines (or combinations of existing ones) in the event that drug resistance against albendazole or mebendazole becomes a significant concern;

• estimation of the species-specific intensity of infection that is relevant to cause a specific morbidity related to nutrient absorption and utilization and growth;

• implementation research on innovative distribution systems to reach vulnerable groups such as adolescent girls, including equity considerations;

• the effects of co-interventions of anthelmintic medicines with other nutritional, environmental, water, sanitation or hygiene interventions on nutritional outcomes and reinfection rates;

• active identification and documentation of adverse effects in specific populations, such as individuals living with HIV (especially in children and those on antiretroviral therapy), breastfeeding mothers and their infants, pregnant mothers and their unborn babies, and infants (less than 12 months of age); and

• factors that influence compliance with large-scale preventive chemotherapy programmes, including the values and preferences of children, adolescent girls and adult women, as well as the prevailing social attitudes about treatment of soil-transmitted helminth infections and how health education can improve compliance rates.

Plans for updating the guideline
The WHO steering group will continue to follow research developments in the area of preventive chemotherapy in at-risk population groups, particularly for questions in which the quality of evidence was found to be low or very low. If the guideline merits updating, or if concerns arise about their validity, the Department of Control of Neglected Tropical Diseases and the Department of Nutrition for Health and Development will coordinate the guideline update, following the formal procedures of the WHO handbook for guideline development.1

As the guideline nears its 10-year review period, the Department of Control of Neglected Tropical Diseases and the Department of Nutrition for Health and Development at WHO’s headquarters (Geneva, Switzerland) along with its internal partners, will be responsible for conducting a search for appropriate new evidence.