Recommendation: pregnant women in the second or third trimester

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 more among pregnant women, and (ii) where 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*[b]*, moderate quality of evidence*).

[a] For the most recent estimates of prevalence of anaemia, visit the WHO-hosted Vitamin and Mineral Nutrition Information System (VMNIS).

[b] This is a conditional recommendation. A conditional recommendation is one for which the guideline development group concludes that the desirable effects of adherence probably outweigh the undesirable effects, although the trade-offs are uncertain. Implications of a conditional recommendation for populations are that, while many people would desire preventive chemotherapy, a considerable proportion would not. With regard to policy-makers, a conditional recommendation means that there is a need for substantial debate and involvement from stakeholders before considering the adoption of preventive chemotherapy (deworming), as a public health intervention for pregnant women.

Rationale

During the deliberations, the guideline development group took into particular consideration the following evidence that resulted in a conditional recommendation:

- the morbidity caused by the different soil-transmitted helminths is species-specific: hookworm and *T. trichiura* infections cause anaemia, which is particularly detrimental for pregnant women, while morbidity due to *A. lumbricoides* is less relevant for this group;
- in areas where anaemia is not a public health problem, the parasite control intervention is probably not necessary;
- albendazole and mebendazole are well tolerated, with no adverse events in pregnant women and their fetuses when given after the first trimester of pregnancy. Anthelminthic medicines must not be given during the first trimester;
- preventive chemotherapy could be implemented as part of routine antenatal care in settings in which there are existing infrastructure and maternal health programmes; and
- logistical difficulties and additional costs of alternative methods to identify and treat infected individuals can be prohibitive.

Overall, in areas endemic for hookworm and/or *T. trichiura*, it was considered essential to periodically treat all pregnant women after the first trimester for the purpose of reducing the worm burden in those who are moderately to heavily infected, and provide optimal conditions for a healthy pregnancy for both mother and child. This recommendation is consistent with the WHO recommendations on antenatal care for a positive pregnancy experience *(111)*.

Remarks

The remarks in this section are intended to guide implementation of the recommendation, based on the discussion of the guideline development group.

- Provision of safe 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 infection 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.
- Member States may consider this intervention for pregnant women after debate and involvement from stakeholders. They should base their decision on their context, health-system infrastructure and ability to monitor and evaluate results.

Effects and safety of preventive chemotherapy in the context of HIV infection

Given that there is significant geographical overlap between the prevalence of soil-transmitted helminths and HIV infection, a review of the safety of anthelminthic treatment in persons living with HIV, including those receiving antiretroviral therapy, was done. A systematic review from the Cochrane HIV/AIDS Group evaluated the effects of deworming medicines on adverse events among individuals coinfected with HIV and soil-transmitted helminths *(112)*.

The review authors searched for published and unpublished studies in CENTRAL, ClinicalTrials.gov, the Cochrane Library, Embase, MEDLINE, the WHO International Clinical Trials Registry Platform (ICRTP) and the WHO Global Health Library, in September 2015. They also searched databases listing conference abstracts, scanned reference lists of articles, and contacted the authors of included studies. The search included randomized controlled trials that compared deworming medicines with a placebo or no intervention in people living with HIV.

Eight trials were included in the review: three trials evaluated the effect of providing deworming medicines to all adults with HIV without knowledge of their helminth-infection status, and five trials evaluated the effects of providing deworming medicines to individuals living with HIV and confirmed helminth infections.

The review showed that treatment of confirmed helminth infections in individuals living with HIV may have short-term beneficial effects on the progression of HIV infection, although evidence of long-term benefit is lacking. There is no indication that deworming medicines confer additional risks in populations infected with HIV. Based on the lack of reports of other than mild adverse events during and after anthelminthic treatment, from programmatic surveillance in populations with a high prevalence of HIV infection and from a number of clinical trials conducted in people infected with HIV, anthelmintic therapy appears to be well tolerated in individuals living with HIV. There is no evidence of an adverse safety signal, although studies specifically designed to evaluate safety have not been conducted.

Based on the results and the discussion around this review, it was concluded by the guideline development group that anthelminthic medicines can be given to those coinfected with HIV, who are otherwise eligible for inclusion in large-scale preventive chemotherapy interventions.

IMPLEMENTATION OF THE GUIDELINE

Preventive chemotherapy, or the periodic large-scale administration of anthelminthic medicines to at-risk populations, can dramatically reduce the burden of worms caused by soil-transmitted helminth infections. This intervention can potentially decrease morbidity among individuals who are heavily infected by soil-transmitted helminths. Owing to the mechanism of transmission of soil-transmitted helminths, however, there is also a high reinfection rate. A systematic review and meta-analysis of literature showed a reinfection rate at 3, 6 and 12 months after treatment for *A. lumbricoides* of 26% (95% CI: 16% to 43%), 68% (95% CI: 60% to 76%), and 94% (95% CI: 88% to 100%), respectively. For *T. trichiura*, respective reinfection rates were 36% (95% CI: 28% to 47%), 67% (95% CI: 42% to 100%), and 82% (95% CI: 62% to 100%), and for hookworm, 30% (95% CI: 26% to 34%), 55% (95% CI: 34% to 87%) and 57% (95% CI: 49% to 67%) *(113)*. Because preventive chemotherapy does not break the cycle of infection and reinfection, populations living in environments conducive to hatching or embryonation of soil-transmitted helminth eggs or the development of larvae continue to be at risk of infection and need periodic administrations of anthelminthic medicines.

Long-term solutions to soil-transmitted helminthiases require improvements in water, sanitation and hygiene. A systematic review and meta-analysis on the effect of sanitation (access and use of facilities for the safe disposal of human urine and faeces) on infection with soil-transmitted helminths *(84)* showed that the availability and use of sanitation was associated with a significant protection against infection with soil-transmitted helminths (odds ratio [OR]: 0.51; 95% CI: 0.44 to 0.61) *(98)*. A further comprehensive systematic review that examined the effect of improved water, sanitation and hygiene on soil-transmitted infections showed that the likelihood of any soil-transmitted infection was less with use of treated water (OR: 0.46; 95% CI: 0.36 to 0.60), wearing of shoes (OR: 0.30: 95% CI: 0.11 to 0.83), hand washing before eating (OR: 0.38; 95% CI: 0.26 to 0.55), and hand washing after defecating (OR: 0.45; 95% CI: 0.35 to 0.58) *(97)*. The reviewers concluded that pooled estimates from meta-analyses indicated at least a 33% reduction in the odds of soil-transmitted helminth infection with individual water, sanitation and hygiene access or practices.

These reviews highlight that control of soil-transmitted helminth infections will need multisectoral and integrated programmes 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. A range of water, sanitation and hygiene services and practices reduce the incidence of soil-transmitted helminths, and have further been linked to improved nutritional outcomes *(114)*.

A logic model depicting the plausible relationship between inputs and expected sustainable development goals relevant to deworming is presented in Annex 3.

Implementation considerations

As this is a global guideline, Member States are expected to adapt the recommendation according to their setting and its feasibility. Neglected tropical diseases, public health nutrition and child health programmes that include preventive chemotherapy for the control of soil-transmitted helminths require supportive policies, supply-chain management and health-care services that enable the proper availability, access and distribution of anthelminthic medicines. WHO regional and country offices assist with these processes.

School-based control of soil-transmitted helminth infections has been used by many countries, and lessons learnt on planning, implementation and monitoring have subsequently improved the coverage of preventive chemotherapy among children *(2, 9, 115)*. Inclusion of younger age groups has promoted and expanded community-based services such as child health days, so that vulnerable infants and young children have access to large-scale programmes of preventive chemotherapy *(2)*.

Expanding the intervention to adolescent girls and women of reproductive age has the potential to dramatically increase the number of people eligible to receive preventive chemotherapy to control soil-transmitted helminth infections, and thus to increase the total cost of delivering services, especially in settings in which there are limited structures and programmes to reach this population. Member States that will adapt these guidelines to include this population should explicitly take into account the heterogeneity of adolescent girls and adult women in general (for instance, in their state of physical growth and social development), as well as the diversity within their country (for instance, in terms of the expected responsibilities in the family and community, the numbers out of school or out of work and the existing social norms).

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. This is of particular concern in areas where rates of unplanned pregnancies are high and coverage of antenatal care is low. Member States that will adapt preventive chemotherapy among adolescent girls and women of reproductive age should be able to regularly assess the worm burden in women and girls aged 15–49 years, in order to ensure the relevance of the intervention, as well as be able to determine the stage of gestation among those who are (knowingly or unknowingly) pregnant. If the pregnancy status or gestational age of women and girls is uncertain, preventive chemotherapy should be withheld.

Meaningful involvement of adolescent girls and women of reproductive age in formulating strategies to integrate preventive chemotherapy with other interventions can increase compliance. In addition, when there is significant geographical overlap between the prevalence of helminth and HIV infection, care should be taken in formulation of policies on preventive chemotherapy among adolescent girls and adult women that do not exclude individuals living with HIV. National and subnational strategic planning can help address challenges and direct actions, so that deworming treatment can be practicable, feasible and acceptable to adolescent girls and adult women.

Access to accurate knowledge and information about soil-transmitted helmiths and the control of these infections improves treatment coverage. It is thus important to ensure that relevant persons involved in the implementation of interventions, such as programme managers, teachers and health-care staff, are informed of the positive and possible adverse effects of preventive chemotherapy, as well as the values and preferences of the end-beneficiaries of the intervention. Developing awareness campaigns and educational materials that are especially suited to adolescent girls and key populations, such as parents of young children, may be useful in improving and sustaining compliance.

Engaging with multiple stakeholders and partners will be critical in strengthening implementation and sustaining gains in controlling soil-transmitted helminth infections. Working in collaboration with sectors involved in child and adolescent well-being; reproductive health; water, sanitation and hygiene; early childhood development and education; social marketing; and others can help ensure a comprehensive, cross-sectoral and more sustainable approach to controlling soil-transmitted helminths.

Regulatory considerations

The *WHO Model List of Essential Medicines* (EML) compiles medicines that satisfy the priority health-care needs of populations and are selected with due regard to disease prevalence, evidence on efficacy and safety, and comparative costs *(116)*. The WHO EML is, thus, used by countries to develop their own national essential medicines lists. In this context, albendazole chewable tablet (400 mg), mebendazole chewable tablet (100 mg) and mebendazole chewable tablet (500 mg) are listed in the sixth version of the *Model List of Essential Medicines For Children (116, 117)*. Albendazole is listed under intestinal anthelminthic and antifilarial therapeutic indication, and mebendazole as an intestinal anthelminthic medicine *(116)*.

Besides albendazole and mebendazole, the WHO EML includes ivermectin, levamisole and pyrantel as intestinal anthelminthics. This guideline specifically assessed the evidence and additional factors on albendazole and mebendazole to inform its recommendations.

Pharmacopoeial standards help ensure the quality and safety of essential medicines. The monographs for albendazole and mebendazole included in The International Pharmacopoeia provide publicly available quality standards, including a new test for the dissolution of the albendazole chewable tablets *(118)*.

Ethical and equity considerations

Ethical principles lead to consideration of whether an intervention produces benefits to individuals and communities, prevents harm, also at the individual and societal levels, and distributes health benefits across social groups; that is, how much an intervention contributes to health equity, and respects and promotes the exercise of human rights.

Helminthiases occur mostly in poor communities, where conditions for transmission are rife and where they may play an important role in contributing to poverty *(100)*. Poor individuals, families and communities characteristically live in degraded and high-risk environments lacking adequate housing, water supply and sanitation, resulting in close contact with pathogens, and where access to health services is limited. Anthelminthic treatment must be considered a necessary but insufficient intervention that contributes to breaking the cycle between helminth infection, illness and chronic poverty, and should be complemented by an important and necessary improvement in delivery of services.

Anthelminthic treatment is less likely to increase health equity if it is not accompanied by concurrent interventions that tackle the root cause of what led these populations to get infected: their living conditions. Large-scale preventive chemotherapy programmes may reduce health inequities if they involve an intervention that reduces disparities in levels of infection among population groups according to place of residence, income and other social stratifiers (e.g. caste, social group) *(99–101)*.

The promotion of women's health literacy and empowerment is essential and can increase the success of public health interventions, such as large-scale deworming *(100)*. This approach may contribute to a reduction of persistent health inequities with respect to helminth infections in women and children.

Monitoring and evaluation of guideline implementation

Monitoring and evaluation should be built into the implementation process, in order to provide important lessons for uptake and further implementation. A number of indicators are suggested for monitoring of soil-transmitted helminth infection control programmes *(2)*. The indicators are classified into: (i) process indicators (to determine whether organizational elements of the control programme are in place and are functioning properly); (ii) performance indicators (to assess whether the control programme reached its coverage goal); and (iii) impact indicators (to assess whether the health impact of the control programme has been reached). The two recommended impact indicators are the prevalence of soil-transmitted helminths (overall and by species), and the prevalence of the different classes of intensity of infection. These indicators are recommended to be collected at baseline and every 3 or 4 years.

For evaluation at the global level, the WHO Department of Nutrition for Health and Development has developed a centralized platform for sharing information on nutrition actions in public health practice implemented around the world. By sharing programmatic details, specific country adaptations and lessons learnt, this platform provides examples of how guidelines are being translated into actions. The Global database on the Implementation of Nutrition Action (GINA) *(4)* provides valuable information on the implementation of numerous nutrition policies and interventions.

RESEARCH GAPS

Discussions between the members of the WHO guideline development group and the external resource group highlighted the limited evidence available in some knowledge areas, meriting further research on preventive chemotherapy for the control of 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 althelminthic 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 cointerventions of deworming 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 very young infants (less than 6 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 around treatment of soil-transmitted helminth infections and how health education can improve compliance rates.

GUIDELINE DEVELOPMENT GROUPS

This guideline was developed in accordance with the WHO evidence-informed guideline-development procedures, as outlined in the *WHO handbook for guideline development (119)*.

WHO steering group

A WHO steering group (see Annex 4), led by the Department of Nutrition for Health and Development, was established with representatives of the departments of Control of Neglected Tropical Diseases; Essential Medicines and Health Products; HIV/AIDS; Service Delivery and Safety; Reproductive Health Research; and Public Health, Environment and Social Determinants, as well as the Special Programme for Research and Training in Tropical Diseases. The steering group guided the overall guideline development process, as well as the retrieval, assessment and summary of the evidence.

The steering group drafted the scope of the guideline and the key questions in PICO format; identified the systematic review teams and guideline methodologist; developed and finalized the planning proposal; helped with the selection of the guideline development group and the external resource group; oversaw the evidence retrieval, assessment and synthesis; collected and assessed disclosures of interest; and managed conflicts in consultation with the WHO Office of Compliance, Risk Management and Ethics. The steering group drafted the recommendation, based on the decisions of the guideline development group; drafted the final guideline, including management of the peer-review process; and oversaw the dissemination of the guideline. Regional advisers from the WHO regions also participated in the meetings of the guideline development group.

Guideline development groups

The scoping of the guideline, the drafting of the key questions in PICO format and the prioritization of the outcomes were done by the guideline development group – nutrition actions 2013–2014 (Geneva, 18–21 February 2013).

The steering group identified candidates for the guideline development group – deworming from the roster of WHO advisers and experts, and issued a call for expressions of interest (October 2015), recommendations from other WHO departments and results from literature reviews were also considered. Twenty persons were informally asked whether they were interested in becoming part of the guideline development group – deworming. Of those 20 persons, 16 gave a positive response. Those interested were then asked to submit their latest curriculum vitae and filled in declaration-of-interest forms.

A final guideline development group was established with 16 members, to advise WHO in the areas of epidemiology and control of neglected tropical diseases, infectious diseases, health systems, social-impact evaluation, nutrition, infant and maternal health care, paediatrics, bioethics and systematic reviews. There were 10 women and six men, representing the six WHO regions.

The guideline development group examined the evidence used to inform the recommendation and appraised it using the *Grading of Recommendation Assessment, Development and Evaluation* (GRADE) evidence profiles *(120, 121)*. They interpreted the evidence, taking in consideration the Developing and Evaluating Communication Strategies to support Informed Decisions and Practice based on Evidence (DECIDE) framework *(7)*, an evidence-to-decision tool that includes intervention effects, values, resources, equity, acceptability and feasibility criteria, to guide the formulation of the recommendations *(122, 123)*. The members of the guideline development group and their areas of expertise are listed in Annex 5.

External resource groups

The external resource group for this guideline was composed of nine persons identified by the steering group whose role was to provide valuable insights to the guideline development group on issues relevant to the topic. Their expertise included bioethics, hygiene and sanitation, costing and cost analyses, economics, infectious disease epidemiology, reproductive health and HIV/AIDS.

The external resource group provided valuable insights during the open sessions of the group discussions. They were not present during the closed-session deliberations of the guideline development group. That is, they participated in general discussions on the evidence and factors to consider for the crafting of the recommendations but did not contribute to the decision on their wording, direction or strength. The members of the external resource group are listed in Annex 6.

Systematic review teams

The following groups were commissioned to conduct systematic reviews relevant to the key questions identified during the guideline development group scoping meeting:

- Cochrane Infectious Diseases Group (deworming in children)
- Cochrane Pregnancy and Childbirth Group (deworming during pregnancy)
- Cochrane HIV/AIDS Group (deworming in populations living with HIV)
- Campbell Collaboration (externalities and synergistic effects with cointerventions including quasi-experimental studies for deworming in children; and deworming in non-pregnant adolescent girls and adult women).

The systematic review teams provided comprehensive, objective syntheses of the evidence for each of the key questions to inform the recommendations. They also assessed the quality of the body of evidence and developed the GRADE evidence profiles. These systematic reviews were presented at the guideline development group meeting (Geneva, April 2016). The members of the systematic review teams are listed in Annex 6.

Management of conflicts of interests

The steering group, in compliance with the WHO *Guidelines for declaration of interests for WHO experts (124)* and in collaboration with the Office of Compliance and Risk Management and Ethics, managed the potential conflicts of interests. All potential guideline development group members were asked to fill in and sign the standard WHO declaration-of-interests and confidentiality undertaking forms. Updated curriculum vitae were also required from the prospective members of the guideline development group, as they engage in their individual capacity and not as institutional representatives.

The steering group reviewed the declarations-of-interest statements in conjunction with the curriculum vitae for all guideline development group members. Information from the internet or media were gathered, in order to identify any public statements made or positions held by the prospective guideline development group members and experts on the issue of deworming. These were assessed for intellectual bias that may be perceived to, or actually, affect impartiality. All concerns or potential issues were discussed with the Office of Compliance, Risk Management and Ethics. All potential conflicts of interest were managed on a case-by-case basis.

The following members of the guideline development group were assessed to have no perceived or real conflicts of interests on the topic. They were asked to verbally declare their research and programme

experiences and sources of funding: **Dr Huda Mustafa Al Hourani; Dr Beverley-Ann Biggs; Professor Anbrasi Edward; Professor Heba El Laithy; Ms Monica Muti; Professor Malden Nesheim; Ms Ifeoma Uzoamaka Onoja; Dr Tech Chuan Voo.**

The following members of the guideline development group were assessed to have no perceived or real conflicts of interests on the topic, but did not attend the meeting of the guideline development group and therefore made no verbal declaration of research and programme experiences or sources of funding: **Ms Claudia Lema Dodobara; Professor Serge Paul Eholié.**

The members listed next had declared interests that were further discussed with the Office of Compliance, Risk Management and Ethics. They were assessed to merit conditional participation that allowed their involvement in the meeting after publicly disclosing their interests at the start of the meeting to all meeting participants, and in the guideline document. Aside from their research and programme experiences and sources of funding, they were asked to specifically declare the following:

Professor Nilanthi de Silva declared that she has been Chair of the WHO Working Group on Access to Quality-Assured Essential Medicines for Neglected Tropical Diseases and has been a member of the WHO Strategic and Technical Advisory Group for Neglected Tropical Diseases since May 2009. She is also a member of the WHO Regional Office for South-East Asia Regional Programme Review Group for lymphatic filariasis and soil-transmitted helminths.

Dr Fiona Fleming declared that she works for an organization receiving research support from the Department for International Development of the Government of the United Kingdom of Great Britain and Northern Ireland to a value of £35 million. She disclosed that this funding was for the implementation, monitoring and evaluation of integrated control of schistosomiasis and intestinal helminth infections in Sub-Saharan Africa.

Professor Theresa Gyorkos declared that she received approximately US$ 1000 from Children Without Worms as a current member of the Soil-Transmitted Helminthiasis Advisory Committee. The advisory committee meets annually to provide independent expert scientific and technical advice on prevention and control of soil-transmitted helminth infections to members of the Soil-Transmitted Helminth Coalition, a group composed of about 50 partners from multiple sectors who "share a vision for reducing intestinal worm infections to create a world in which children are healthy and develop to their full potential". The coalition membership includes Johnson & Johnson (manufacturer of mebendazole) and GlaxoSmithKline (manufacturer of albendazole), who financially support Children Without Worms, as secretariat to the Soil-Transmitted Helminthiasis Advisory Committee. She also declared being the principal investigator of a US$ 1.5 million ongoing grant awarded by the Bill & Melinda Gates Foundation. This grant was awarded to her after an open competition. The research topic is on postpartum deworming.

Professor Celia Holland declared that she has conducted extensive research on the topic of discussion and that she also serves as a member of the WHO advisory panel on parasitic diseases.

Dr Narcis Kabaterine declared that he has served as a consultant to Merck KGaA (manufacturer of praziquantel) for work related to schistosomiasis. This work is not related to soil-transmitted helminths but to another condition, schistosomiasis, which is caused by a different parasite and treated with different medicines.

Professor Harshpal Singh Sachdev declared that he had published a systematic review in the *British Medical Journal* in 2007 on the effect of deworming on haemoglobin, and two commentaries on the subject in 2015 (in the *Lancet* and the *Internal Journal of Epidemiology*), in which he stressed the importance of evidence.

Names and brief biographies of the guideline development group, along with a description of the objectives of the meeting, were published on the WHO website, for public notice and comment. No additional information on any interests or biases relating to the individuals being considered for membership of the guideline development group were brought to light from the public notice.

Identification of priority questions and outcomes

An initial set of questions to be addressed in the guideline was the starting point for formulating the recommendation. The questions were drafted by technical staff at the Evidence and Programme Guidance unit of the Department of Nutrition for Health and Development, based on the policy and programme guidance needs of Member States and their partners. The questions were discussed and reviewed by the steering group.

A meeting of the guideline development group – nutrition actions 2013–2014 (Geneva, 18–21 February 2013) was held to finalize the scope of the questions and to rank the outcomes and populations of interest for the recommendation on preventive chemotherapy to control soil-transmitted helminth infections in at-risk groups. The guideline development group discussed the relevance of the questions and modified them as needed. The group scored the relative importance of each outcome from 1 to 9 (where 7–9 indicated that the outcome was critical for a decision, 4–6 indicated that it was important and 1–3 indicated that it was not important). The final key questions on this intervention, along with the outcomes that were identified as critical for decision-making, are listed in PICO format in Annex 1.

Evidence identification and retrieval

Previous Cochrane reviews assessing the effect of using deworming medicines on nutritional outcomes in children were done in 2000 *(125)*, 2007 *(126)* and 2012 *(127)*. New trials since the publication of the last systematic review included a large trial among children published in 2013 *(128)* with over one million study participants. A previous trial from Kenya was also replicated and published recently [2015] *(129)*. In light of these important new trials, an update of the systematic reviews was contracted with the Cochrane Infectious Diseases Group, to systematically review the evidence for the critical health outcomes of deworming for soil-transmitted intestinal helminth infections in children.

A previous systematic review of the impact of deworming on the prevalence of anaemia among adult women included both pregnant and non-pregnant women *(130)*. Thus, two new systematic reviews, one focusing on pregnant women and another on non-pregnant adolescent girls and adult women, were commissioned from the Cochrane Pregnancy and Childbirth Group and the Campbell Collaboration, respectively.

A previous Cochrane systematic review of deworming treatment in persons coinfected with HIV and helminth infections was published in 2009 *(131)*. This earlier systematic review assessed the impact of treating helminth infections on the progression of HIV among people living with HIV/AIDS. An update of this systematic review was contracted from the Cochrane HIV/AIDS Group, the same group that published the earlier review, on evidence of the effect of preventive chemotherapy in children and adult non-pregnant women living with HIV on health outcomes and adverse events.

In order to assess the synergistic effects of co-interventions (such as micronutrient supplementation or hygiene interventions) and potential confounding factors or externalities (such as the prevalence of soil-transmitted infections or the baseline nutritional status of children), an additional systematic review was commissioned from the Campbell Collaboration, which included quasi-experimental and non-randomized studies.

Quality assessment and grading of evidence

Systematic reviews *(84, 85, 102, 107, 112)* based on the PICO questions were used to summarize and appraise the evidence. These reviews followed the procedures of the *Cochrane handbook for systematic reviews of interventions (132)*. Each study included in the systematic reviews was assessed for risk of bias. This was recorded and contributed towards the assessment of the overall quality of the evidence. During the discussion and deliberations, the steering group and the guideline development group carefully reviewed the quality, scope and study inclusion criteria for the systematic reviews. The relative weight given to the trials and non-randomized studies was taken into account when evaluating the quality assessment for each study. When possible, the findings were synthesized with a pooled estimate of effect. The results of the systematic reviews were presented to the guideline development group, along with an assessment of the confidence in the estimates of effect for the critical outcomes.

Evidence profiles were prepared according to the GRADE approach, to assess the overall quality of the evidence *(120, 121)*. The quality of evidence for each outcome was rated as "high", "moderate", "low", or "very low", based on a set of criteria including risk of bias, inconsistency, imprecision, indirectness and publication bias.

Formulation of recommendations

The draft recommendations were discussed at a meeting of the steering group and in consultation with the guideline development group (Geneva, 13–15 April 2016).

Three options for types of recommendations were agreed, namely:

- strong recommendation
- conditional recommendation (recommended only in specific contexts)
- not recommended.

The systematic review and the GRADE evidence profiles for each of the critical outcomes were used to draft the recommendations. An evidence-to-decision framework (based on the DECIDE framework was used to lead the discussion and decision-making *(122, 123)*.

The domains listed next were prepared by the steering group and discussed during the guideline development group meeting for each of the key PICO questions.

Quality of evidence

The overall degree of confidence in the estimates of effect as presented in the GRADE profile was considered in the drafting of the recommendations. The higher the quality of evidence across critical outcomes that is relevant to decision-making, the higher the likelihood is of a clear, positive recommendation. A conditional recommendation is likely to be warranted when the overall quality is rated "low" or "very low".

Balance of benefits and harms

The guideline development group evaluated the balance of desirable and undesirable consequences, including the magnitude of the effects and relative importance of these consequences. Where benefits clearly outweigh harms or vice versa, the greater the likelihood is of a recommendation in favour of or against the intervention, respectively. Uncertainty about the net benefits or harms often leads to a conditional recommendation.

Values and preferences

The relative importance of the outcome to the individuals or populations directly affected by the recommendation describes the values and preferences. The steering group performed a review of qualitative information on how end-users (children, adolescent girls, women of reproductive age and pregnant women) perceived soil-transmitted helminths, deworming and their effects. These were presented during the guideline development group meeting. When there is uncertainty or wide variability in the values and preferences of the target beneficiaries, a conditional recommendation may be warranted.

Acceptability

A review of qualitative information on how health-care workers and service providers perceive soil-transmitted helminths, preventive chemotherapy and their effects for each of the at-risk groups was done and presented during the guideline development group meeting. The higher the acceptability of the intervention among stakeholders, the more likely it is that an intervention will be clearly recommended. When it was deemed necessary to recommend an intervention that is associated with low acceptability, strategies to address concerns about acceptability during implementation were discussed.

Resource use

This relates to evaluation of how resource intensive and costly the intervention is to service users and health systems in different settings. A recommendation in favour of or against the intervention is likely where the resource implications are clearly advantageous or disadvantageous, whereas a conditional recommendation may be justified if the resource implications are uncertain.

Equity

An intervention is likely to be recommended if it will reduce health inequities among different groups of women and their families.

Feasibility

The steering group presented instances in which deworming was implemented in the at-risk groups in different settings, to highlight the feasibility of implementation and whether barriers exist. Where there is greater feasibility, the more likely it is that the intervention will be recommended.

Based on the discussions during the meeting, each recommendation was supported by a rationale, implementation considerations and research priorities.

Decision-making during the guideline development group meeting

The chairpersons, Dr Biggs and Professor Nesheim, were nominated at the opening of the consultation and the nominations were approved by the guideline development group.

The procedures for decision-making were established at the beginning of the meetings, including a minimal set of rules for agreement and documentation of decision-making. At least two-thirds of the guideline development group were present for an initial discussion of the evidence, and proposed recommendation and remarks. By secret ballot, each member of the guideline development group noted the direction and strength of each of the recommendations, using an online form specifically designed for this purpose. Abstentions were not allowed.

Once voting was complete, subsequent deliberations among the members of the guideline development group could take place. If there was no unanimous consensus (primary decision rule), more time was given for deliberations and a second round of online voting took place. If no unanimous agreement was reached, a two-thirds vote of the guideline development group was required for approval of the proposed recommendation (secondary decision rule). The results from voting forms will be kept on file by WHO for up to 5 years.

Document preparation and peer review

The responsible technical officer wrote the first draft of the guideline, with comments from the steering group. Technical editing and proofreading were done by a contracted party.

The final draft guideline was peer-reviewed by content experts, to provided technical feedback; identify errors of fact; ensure that there were no important omissions, contradictions or inconsistencies with scientific evidence or programmatic feasibility; and assist with clarifying the language, especially in relation to implementation, adaptation and contextual issues. The independent peer-reviewers were selected by the steering group. Eight potential peer-reviewers were approached after assessment of the declarations of interests, and five agreed. The list of peer-reviewers appears in Annex 8.

The steering group reviewed all comments and revised the document, in order to ensure clarity of the recommendation while maintaining consistency with the original meaning.

DISSEMINATION AND PLANS FOR UPDATING

Dissemination

The current guideline will be posted on the WHO website, including the WHO Nutrition website *(8)*, the WHO Neglected Tropical Diseases website *(9)* and the WHO e-Library of Evidence for Nutrition Actions (eLENA) *(10)*. In addition, it will be disseminated through a broad network of international partners, including WHO country and regional offices, ministries of health, WHO collaborating centres, universities, other United Nations agencies and nongovernmental organizations.

Plans for updating the guideline

The WHO steering group will continue to follow research developments in the area of preventive chemotherapy in at-risk 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 there are concerns about its validity, the Department of Control of Neglected Tropical Diseases will coordinate the guideline update, following the formal procedures of the *WHO handbook for guideline development (119)*.

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 headquarters (Geneva, Switzerland) along with its internal partners, will be responsible for conducting a search for new evidence.

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ANNEX 1. QUESTION IN POPULATION, INTERVENTION, CONTROL, OUTCOMES (PICO) FORMAT

A. Effects and safety of preventive chemotherapy in young children, preschool and school-age children

Should preventive chemotherapy (deworming medicines) be given for the control of soil-transmitted helminth infections, compared to not giving preventive chemotherapy, to all yound children 12–23 months of age, preschool 24–59 months of age and school-age children[1] living in areas that are endemic for soil-transmitted helminth infections, to improve nutrition and health? If so, at what dose and frequency?

Population:	**Young children 12–23 months of age, preschool children (4–59 months of age) and school-age children[1]** Subgroups • By baseline prevalence of any soil-transmitted helminth in the trial: < 20%, 20–49%, ≥ 50%, unknown/not reported • By anaemia prevalence in the study: anaemia, no anaemia, mixed/not reported • With screening: yes versus no • With concomitant HIV infection
Intervention:	**Deworming treatment (albendazole, mebendazole)** Subgroups: • By frequency: annual, biannual • By medicine: albendazole, mebendazole • By duration: 0–35 months, 36–72 months, ≥ 73 months • By concomitant iron supplementation: yes, no, unknown/not reported
Control:	**No intervention or placebo**
Outcomes:	• Worm burden (egg count per gram of faeces) • Anaemia (defined as haemoglobin concentration < 110 g/L for children aged 24–59 months and < 115 g/L for children aged 5–12 years, adjusted by altitude where appropriate); severe anaemia (defined as haemoglobin concentration < 70 g/L, adjusted by altitude where appropriate) • Iron deficiency (as defined by using ferritin concentrations < 15 µg/L) • Diarrhoea (three liquid stools or more per day) • Growth: Weight (weight-for-age z-scores) Wasting (weight-for-height z-scores) Stunting (length/height-for-age z-scores) Body-mass-index-for-age • Cognitive development and school performance (as defined by trialists)

[1] We defined school-age children as those between 5 and 12 years of age. Although many children unfortunately do not attend schools, 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.

B. Effects and safety of preventive chemotherapy in non-pregnant adolescent girls and women of reproductive age

Should preventive chemotherapy (deworming medicines) be given for the control of soil-transmitted helminth infections, compared to not giving preventive chemotherapy, to all non-pregnant adolescent girls and adult women (approximately 15–49 years of age) living in areas that are endemic for soil-transmitted helminth infections, to improve nutrition and health? If so, at what dose and frequency?

Population:	**Non-pregnant menstruating adolescents (10–19 years of age) and women of reproductive age (15–49 years)** Subgroups • By baseline prevalence of any soil-transmitted helminth in the trial: <20%, 20–49%, ≥50%, unknown/not reported • By anaemia prevalence in the study: anaemia, no anaemia, mixed/not reported • With screening: yes versus no • With concomitant HIV infection
Intervention:	**Deworming treatment (albendazole, mebendazole)** Subgroups: • By frequency: annual, biannual • By medicine: albendazole alone versus mebendazole alone versus combined treatment • By duration: 0–35 months, 36–72 months, ≥ 73 months • By concomitant iron supplementation: yes, no, unknown/not reported
Control:	**No intervention or placebo**
Outcomes:	• Worm burden (egg count per gram of faeces) • Anaemia (defined as haemoglobin concentration < 120 g/L for non-pregnant women, adjusted by altitude where appropriate); severe anaemia (defined as haemoglobin concentration < 70 g/L, adjusted by altitude where appropriate) • Iron deficiency (as defined by using ferritin concentrations < 15 µg/L) • Diarrhoea (three liquid stools or more per day) • Reinfection • All-cause morbidity (number of patients with at least one episode of any disease during the study period)

C. Effects and safety of preventive chemotherapy in pregnant women

Should preventive chemotherapy (deworming medicines) be given for the control of soil-transmitted helminth infections, compared to not giving preventive chemotherapy, to all pregnant women living in areas that are endemic for soil-transmitted helminth infections, for improving nutrition and health outcomes? If so, at what dose and frequency?

Population:	**Pregnant women** Subgroups • By baseline prevalence of any soil-transmitted helminth in the trial: < 20%, 20–49%, ≥ 50%, unknown/not reported • By anaemia prevalence in the study: anaemia, no anaemia, mixed/not reported • With screening: yes versus no • With concomitant HIV infection
Intervention:	**Deworming treatment (albendazole, mebendazole)** Subgroups: • By frequency: annual, biannual • By medicine: albendazole alone versus mebendazole alone versus combined treatment • By delivery system: clinic versus health days/weeks • By concomitant iron supplementation: yes, no, unknown/not reported
Control:	**No intervention or placebo**
Outcomes:	• Worm burden (egg count per gram of faeces) • Maternal anaemia at or near term (defined as haemoglobin concentration < 110 g/L at 34 weeks' gestation or more); moderate anaemia during the postpartum period (defined as haemoglobin concentration of 80–109 g/L); severe anaemia at any time during the second or third trimesters (defined as haemoglobin concentration < 70 g/L) • Maternal iron deficiency at or near term (as defined by trialists, based on any indicator of iron status at 34 weeks' gestation or more) • Reinfection • Maternal mortality (death while pregnant or within 42 days of termination of pregnancy) • Birthweight • Perinatal mortality (pregnancy losses of at least seven months' gestation and deaths to live births within the first seven days of life)

ANNEX 2. GRADE SUMMARY OF FINDINGS TABLES

A. Preventive chemotherapy in preschool and school-age children

Preventive chemotherapy in preschool and school-age children known to be infected with soil-transmitted helminths

Patient or population: preschool and school-age children known to be infected with soil-transmitted helminths
Setting: areas endemic for soil-transmitted helminths
Intervention: preventive chemotherapy (deworming medicines)
Comparison: placebo or no treatment

Outcomes	**Anticipated absolute effects*** (95% CI)		Relative effect (95% CI)	Number of participants (studies)	Quality of the evidence (GRADE)	Comments
	Without preventive chemotherapy	**With preventive chemotherapy**				
Haemoglobin (g/L) Follow-up: 9 weeks to 6 months	—	—	MD 1.0 g/dL (–6.5 to 8.6 g/L)	247 (2 studies)	⨁⊖⊖⊖ VERY LOW[1]	
Formal test on cognition	—	—	Not pooled	103 (2 studies)	⨁⊖⊖⊖ VERY LOW[2]	
Weight gain (kg) Follow-up: 1 to 6 months	—	—	MD 0.75 kg (0.24 to 1.26 kg)	627 (5 studies)	⨁⨁⊖⊖ LOW[3]	
Height gain (cm) Follow-up: 1 to 6 months	—	—	MD 0.25 cm (0.01 to 0.49 cm)	647 (5 studies)	⨁⨁⊖⊖ LOW[4]	
Body mass index (kg/m^2) Follow-up: 1 to 6 months	—	—	MD -0.20 kg/m^2 (–0.46 to 0.06 kg/m^2)	407 (1 study)	⨁⨁⊖⊖ LOW[5]	

Preventive chemotherapy (single dose) in all preschool and school-age children

Patient or population: all preschool and school-age children
Setting: areas endemic for soil-transmitted helminths
Intervention: preventive chemotherapy (deworming medicines)
Comparison: placebo or no treatment

Outcomes	**Anticipated absolute effects*** (95% CI)		Relative effect (95% CI)	Number of participants (studies)	Quality of the evidence (GRADE)	Comments
	Without preventive chemotherapy	**With preventive chemotherapy**				
Haemoglobin (g/L) Follow-up: 9 weeks to 6 months	—	—	MD 0.6 g/L (–0.5 to 1.7 g/L)	1005 (3 studies)	⨁⨁⨁⊖ MODERATE[6]	
Formal test on cognition	—	One trial reported that deworming had no effect, and the other that deworming reduces cognitive scores	Not pooled	1361 (2 studies)	⨁⨁⊖⊖ LOW[7]	
Weight gain (kg) Follow-up: 7 weeks to 1 year	—	—	MD -0.04 kg (–0.11 to 0.04 kg)	2719 (7 studies)	⨁⨁⨁⊖ MODERATE[8]	
Height gain (cm) Follow-up: 7 weeks to 1 year	—	—	MD –0.12 cm (–0.33 to 0.10 cm)	1974 (5 studies)	⨁⨁⨁⊖ MODERATE[9]	
Mortality (between the ages of 1–6 years)	27 per 1000	25 per 1000	RR 0.95 (0.89 to 1.92)	1005,135 (3 trials)	⨁⨁⊖⊖ LOW[10]	

Preventive chemotherapy (multiple doses) in all preschool and school-age children

Patient or population: all preschool and school-age children
Setting: areas endemic for soil-transmitted helminths
Intervention: preventive chemotherapy (deworming medicines)
Comparison: placebo or no treatment

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	Number of participants (studies)	Quality of the evidence (GRADE)	Comments
	Without preventive chemotherapy	**With preventive chemotherapy**				
Worm burden – *Ascaris* Assessed with: prevalence Follow-up: mean 12 months	403 per 1000	209 per 1000 (177 to 246)	RR 0.52 (0.44 to 0.61)	13 914 (22 studies)	⊕⊕⊖⊖ LOW[11]	
Worm burden – hookworm Assessed with: prevalence Follow-up: mean 12 months	481 per 1000	178 per 1000 (77 to 409)	RR 0.37 (0.16 to 0.85)	6214 (10 studies)	⊕⊕⊖⊖ LOW[12]	
Worm burden – *Trichuris* Assessed with: prevalence Follow-up: mean 12 months	591 per 1000	425 per 1000 (337 to 543)	RR 0.72 (0.57 to 0.92)	5053 (9 studies)	⊕⊕⊖⊖ LOW[13]	
Cognitive processing: short-term attention (converted to WISC IV working memory index, 100-point scale) Follow-up: one year	—	—	MD –0.23 points (–0.6 to 0.14 points)	4078 (3 studies)	⊕⊕⊕⊕ HIGH	
Weight gain (kg) Follow-up: one year	—	—	MD 0.09 kg (–0.04 to 0.20 kg)	35 430 (11 studies)	⊕⊕⊕⊖ MODERATE[14]	
Height gain (cm) Follow-up: one year	—	—	MD 0.07 cm (–0.10 to 0.24 cm)	6839 (9 studies)	⊕⊕⊕⊖ MODERATE[15]	
Proportion stunted Follow-up: measured at 1–2 years	411 per 1000	403 per 1000 (361 to 444)	RR 0.98 (0.88 to 1.08)	4286 (4 studies)	⊕⊕⊕⊕ HIGH	
Mortality Follow-up: 1–5 years	25 per 1000	24 per 1000 (22 to 26)	RR 0.95 (0.89 to 1.02)	Over 1 million (6 trials)	⊕⊕⊕⊕ HIGH	

*__The risk in the intervention group__ (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).
CI: confidence interval; RR: risk ratio; MD: mean difference.

GRADE Working Group grades of evidence

High quality: We are very confident that the true effect lies close to that of the estimate of the effect.

Moderate quality: We are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.

Low quality: Our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect.

Very low quality: We have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect.

[1] Downgraded for risk of bias (none of the trials adequately described allocation concealment), for inconsistency (high level of heterogeneity) and for indirectness (one of the trials showing large effects was from a highly endemic area with intense worm burden).

[2] Downgraded for serious risk of bias and for indirectness (two trials measured cognitive functioning but did not clearly report the changes in cognitive scores). Neither is easily generalized to other settings.

[3] Downgraded for risk of bias (none of the trials adequately described allocation concealment) and for inconsistency (high level of heterogeneity).

[4] Downgraded for risk of bias (none of the trials adequately described allocation concealment) and for inconsistency (high level of heterogeneity).

[5] Downgraded for risk of bias (none of the trials adequately described allocation concealment) and for inconsistency (high level of heterogeneity).

[6] Downgraded for risk of bias (none of the trials were classified as having low risk of bias).

[7] Downgraded for risk of bias (none of the trials were classified as having low risk of bias) and for indirectness (only two trials assessed this outcome and the results are not easily generalized to other settings).

[8] Downgraded for risk of bias (none of the trials were classified as having low risk of bias).

[9] Downgraded for risk of bias (none of the trials were classified as having low risk of bias).

[10] Downgraded for risk of bias (none of the trials described allocation concealment) and indirectness (the largest study was conducted in a low-prevalence area which may not be generalizable to other settings).

[11] Downgraded for risk of bias (major baseline imbalance and selective reporting of worm burden in some studies) and inconsistency (high level of heterogeneity).

[12] Downgraded for risk of bias (major baseline imbalance and selective reporting of worm burden in some studies) and inconsistency (high level of heterogeneity).

[13] Downgraded for risk of bias (major baseline imbalance and selective reporting of worm burden in some studies) and inconsistency (high level of heterogeneity).

[14] Downgraded for inconsistency (baseline imbalance and heterogeneity).

[15] Downgraded for inconsistency (high level of heterogeneity).

For details of studies included in the review, see references *(84, 85)*.

B. Preventive chemotherapy in non-pregnant adolescent girls and women of reproductive age

Patient or population: non-pregnant adolescent girls and women of reproductive age
Setting: areas endemic for soil-transmitted helminths
Intervention: preventive chemotherapy (deworming medicines)
Comparison: placebo or no treatment

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	Number of participants (studies)	Quality of the evidence (GRADE)	Comments
	Without preventive chemotherapy	**With preventive chemotherapy**				
Worm burden – *Ascaris* Follow-up: mean 6 months	327 per 1000	95 per 1000 (46 to 202)	RR 0.29 (0.14 to 0.62)	1498 (2 studies)	⊕⊕⊕⊖ MODERATE[1]	
Worm burden – hookworm Follow-up: mean 6 months	331 per 1000	106 per 1000 (60 to 195)	RR 0.32 (0.18 to 0.59)	1498 (2 studies)	⊕⊕⊕⊖ MODERATE[2]	
Worm burden – *Trichuris* Follow-up: mean 6 months	277 per 1000	213 per 1000 (180 to 252)	RR 0.77 (0.65 to 0.91)	1498 (2 studies)	⊕⊕⊕⊖ MODERATE[3]	
Anaemia (end haemoglobin level < 120 g/L) Follow-up: mean 6 months	398 per 1000	327 per 1000 (239 to 442)	RR 0.82 (0.60 to 1.11)	683 (3 studies)	⊕⊕⊖⊖ LOW[4]	
Severe anaemia (end haemoglobin level < 70 g/L) Follow-up: mean 6 months	–	–	RR 6.25 (0.34 to 115.15)	51 (1 study)	⊕⊖⊖⊖ VERY LOW[5]	
Iron-deficiency anaemia (ferritin levels < 12 µg/L) Follow-up: mean 6 months	464 per 1000	413 per 1000 (297 to 571)	RR 0.89 (0.64 to 1.23)	186 (1 study)	⊕⊕⊖⊖ LOW[6]	
All-cause morbidity – conjunctival xerosis Follow-up: mean 8 months	188 per 1000	188 per 1000 (45 to 793)	RR 1.00 (0.24 to 4.23)	32 (1 study)	⊕⊕⊖⊖ LOW[7]	

*__The risk in the intervention group__ (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).
CI: confidence interval; RR: risk ratio.

GRADE Working Group grades of evidence
High quality: We are very confident that the true effect lies close to that of the estimate of the effect.
Moderate quality: We are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
Low quality: Our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect.
Very low quality: We have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect.

1 Downgraded for risk of bias (blinding of participants and outcome assessors were not reported).
2 Downgraded for risk of bias (blinding of participants and outcome assessors were not reported).
3 Downgraded for risk of bias (blinding of participants and outcome assessors were not reported).
4 Downgraded for risk of bias (blinding of participants and outcome assessors were not reported) and for imprecision (confidence interval includes the null effect as well as appreciable benefit).
5 Downgraded for risk of bias (blinding of participants and outcome assessors were not reported) and for serious imprecision (small sample size and only one event).
6 Downgraded for risk of bias (blinding of participants and outcome assessors were not reported) and for imprecision (confidence interval includes the null effect as well as appreciable benefit).
7 Downgraded for risk of bias (randomization, allocation concealment and blinding of participants, personnel, outcome assessors were not reported) and imprecision (wide confidence intervals).

For details of studies included in the review, see reference *(102)*.

C. Preventive chemotherapy in pregnant women

Patient or population: pregnant women
Setting: areas endemic for soil-transmitted helminths
Intervention: preventive chemotherapy (deworming medicines)
Comparison: placebo or no treatment

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	Number of participants (studies)	Quality of the evidence (GRADE)	Comments
	Without preventive chemotherapy	**With preventive chemotherapy**				
Worm burden (all parasites)	60 per 1000	17 per 1000 (6 to 49)	RR 0.29 (0.10 to 0.81)	4788 (3 studies)	⊕⊕⊕⊖ MODERATE[1]	
Maternal anaemia in the third trimester (< 110 g/L)	341 per 1000	320 per 1000 (276 to 375)	RR 0.94 (0.81 to 1.10)	3266 (4 studies)	⊕⊕⊖⊖ LOW[2]	
Low birth weight	88 per 1000	88 per 1000 (69 to 112)	RR 1.00 (0.79 to 1.27)	3255 (3 studies)	⊕⊕⊕⊖ MODERATE[3]	
Perinatal mortality	27 per 1000	30 per 1000 (19 to 46)	RR 1.09 (0.71 to 1.67)	3385 (2 studies)	⊕⊕⊕⊖ MODERATE[4]	

*__The risk in the intervention group__ (and its 95% confidence interval) is based on the assumed risk in the comparison group and the __relative effect__ of the intervention (and its 95% CI).
CI: confidence interval; RR: risk ratio.

GRADE Working Group grades of evidence
High quality: We are very confident that the true effect lies close to that of the estimate of the effect.
Moderate quality: We are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
Low quality: Our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect.
Very low quality: We have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect.

[1] Downgraded for inconsistency (high level of heterogeneity).

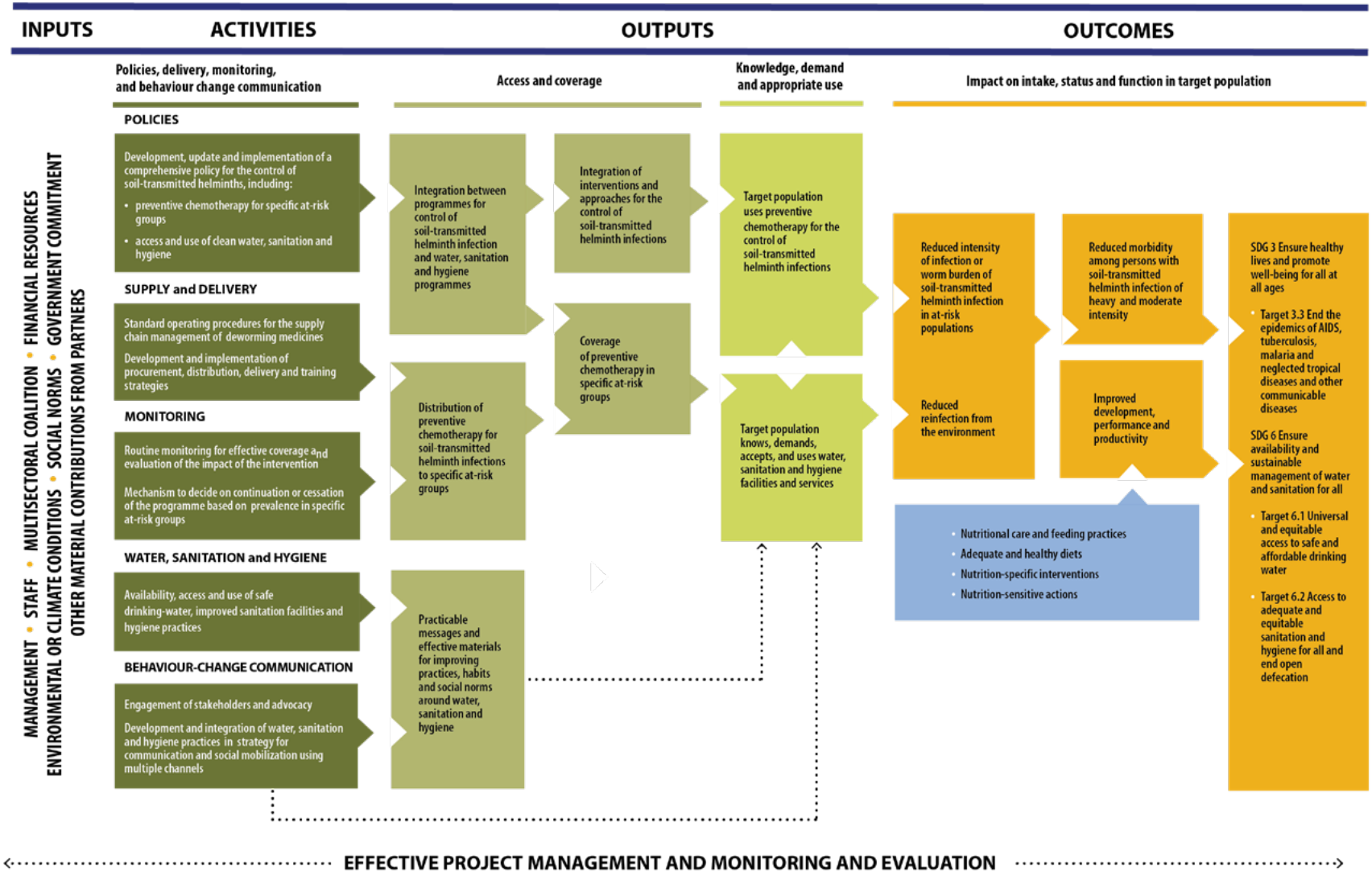
[2] Downgraded for risk of bias (high rate of attrition) and for inconsistency (high level or heterogeneity).

[3] Downgraded for risk of bias (unclear selection bias).

[4] Downgraded for indirectness (neither study was powered to capture perinatal mortality).

For details of studies included in the review, see reference *(107)*.

ANNEX 3. LOGIC MODEL FOR THE CONTROL OF SOIL-TRANSMITTED HELMINTH INFECTIONS



ANNEX 4. WHO STEERING GROUP

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ANNEX 5. WHO GUIDELINE DEVELOPMENT GROUPS

(Note: the areas of expertise of each guideline group member are given in italics)

Guideline development group – nutrition actions 2013–2014

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Ministry of Health
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Health programme management, food legislation, surveillance in primary health care

Dr Beverley-Ann Biggs

Head
International and Immigrant Health Group
Department of Medicine
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Micronutrient supplementation, clinical infectious diseases

Dr Norm Campbell

Professor
Departments of Medicine
Community Health Sciences and Physiology and Pharmacology
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Physiology and pharmacology, hypertension prevention and control

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National Maternal and Child Health Centre
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Programme implementation, midwifery

Dr Maria Elena del Socorro Jefferds

Team Lead, International Micronutrient Malnutrition Prevention and Control Programme
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Centers for Disease Control and Prevention
United States of America

Behaviour science, programme evaluation

Dr Luz Maria De-Regil

Chief Technical Adviser and Director
Research and Evaluation
Micronutrient Initiative
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Maternal and child nutrition, epidemiology, systematic reviews, programme implementation

Dr Heba El Laithy

Professor of Statistics and Head of Statistical Departments
Faculty of Economics
Cairo University
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Statistics, economics

Dr Rafael Flores-Ayala

Branch Chief, Nutrition
Centers for Disease Control and Prevention
United States of America

Nutrition and human capital formation, nutrition and growth, impact of micronutrient interventions

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National Health and Medical Research Council
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Policy-making, systematic reviews, evidence

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Department of Obstetrics and Gynaecology
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Obstetrics and gynaecology, clinical practice

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Breastfeeding, capacity-building on counselling and nutrition

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Food fortification, food science and technology, standards and legislation

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Children's Hospital Oakland Research Institute
United States of America

Micronutrients, maternal and child nutrition, dietary requirements

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Institute of Tropical Medicine
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Public health, food safety, laboratory methods

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Department of Paediatrics and Unit of Research on Health Services and International Health
Institute for Maternal and Child Health
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Paediatrics, malnutrition, infectious diseases, methods

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National Institute for Nutrition and Food Safety
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Malaria, international tropical diseases research and practice

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Global Alliance for Improved Nutrition
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Micronutrients, programmes, epidemiology

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Department of Experimental Pharmacology and Toxicology
University of Port Harcourt
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Diabetes

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Programme Officer
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Center for Research for Mothers and Children
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Micronutrients, programmes, infant feeding

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Instituto Nacional de Ciencias Médicas y Nutrición Salvador Zubiran
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Paediatrics, systematic reviews

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Paediatrics

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Regional Food Fortification Adviser
A2Z Project
East, Central and Southern African Health Community
United Republic of Tanzania

Food fortification technical regulations and standards, policy harmonization

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Health and Nutrition Officer
United Nations Children's Fund (UNICEF) Office in Skopje
The Former Yugoslav Republic of Macedonia

Programme implementation

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Independent international expert on global public health
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Hashemite University
Jordan

Nutrition counselling, chronic diseases, noncommunicable diseases

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Department of Medicine
University of Melbourne
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Micronutrients supplementation, clinical infectious diseases

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Professor of Parasitology and Dean of the Faculty of Medicine
University of Kelaniya
Sri Lanka

Medical parasitology, neglected tropical diseases

Ms Claudia Lema Dodobara**

Executive Director
Salud Sin Límites Perú
Peru

Medical anthropology, qualitative research on health

Professor Anbrasi Edward

Associate Scientist
Center for Refugee and Disaster Studies, Department of International Health
Johns Hopkins Bloomberg School of Public Health
United States of America

Health systems and community-based research

Professor Serge Paul Eholié**

Professor of Tropical and Infectious Diseases
Treichville University Teaching Hospital
Côte d'Ivoire

HIV, infectious diseases, noncommunicable diseases

Professor Heba El Laithy

Professor of Statistics
Faculty of Economics and Political Science
Cairo University
Egypt

Social impact evaluation, micro-data analysis

Dr Fiona Fleming

Senior Monitoring and Evaluation Manager Faculty of Medicine
School of Public Health
Imperial College London
United Kingdom of Great Britain and Northern Ireland

Control of infectious diseases, neglected tropical diseases

Professor Theresa Gyorkos

Professor
Department of Epidemiology, Biostatistics and Occupational Health
McGill University
Canada

Global health, parasite disease epidemiology, neglected tropical diseases

Professor Celia Holland

Professor of Parasitology
School of Natural Sciences
Trinity College Dublin
United Kingdom of Great Britain and Northern Ireland

Epidemiology and control of soil-transmitted helminths

Dr Narcis Kabatereine

Head of Vector Control Division
Ministry of Health
Uganda

Control of neglected tropical diseases

Ms Monica Muti

Nutrition Intervention Manager
Ministry of Health and Child Welfare
Zimbabwe

Nutrition, national implementation programmes

Professor Malden Nesheim

Professor Emeritus
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Cornell University
United States of America

Nutrition, nutritional consequences of neglected tropical diseases

Ms Ifeoma Uzoamaka Onoja

Principal Dietitian
University of Nigeria Teaching Hospital
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Nutrition and dietetics, infant and maternal healthcare

Professor Harshpal Singh Sachdev

Senior Consultant in Paediatrics and Clinical Epidemiology
Sitaram Bhartia Institute of Science and Research
India

Paediatrics, systematic reviews

Dr Teck Chuan Voo

Assistant Professor
Centre for Biomedical Ethics
National University of Singapore
Yong Loo Lin School of Medicine
Singapore

Research ethics, clinical ethics

** unable to attend in person

ANNEX 6. EXTERNAL RESOURCE GROUPS

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Meeting of the WHO guideline development group – deworming

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ANNEX 7. SYSTEMATIC REVIEW TEAMS

Systematic review 1

Deworming drugs for soil-transmitted intestinal worms in children: effects on nutritional indicators, haemoglobin, and school performance *(84)*

David C Taylor-Robinson[1], Nicola Maayan, Karla Soares-Weiser, Sarah Donegan, Paul A Garner

[1] Department of Public Health and Policy, University of Liverpool, Liverpool, Merseyside, United Kingdom of Great Britain and Northern Ireland

Systematic review 2

Deworming and adjuvant interventions for improving the developmental health and well-being of children in low- and middle-income countries: a systematic review and meta-analysis *(85)*

Vivian Andrea Welch[1], Shally Awasthi, Chisa Cumberbatch, Robert Fletcher, Jessie McGowan, Katelynn Merritt, Shari Krishnaratne, Salim Sohani, Shalini Suresh, Peter Tugwell, George A Wells

[1] Director, Methods Centre, Bruyere Research Institute; Assistant Professor, School of Epidemiology, Public Health and Preventive Medicine, University of Ottawa, Canada

Systematic review 3

Deworming for non-pregnant adolescent and adult women: a systematic review *(102)*

Vivian A Welch[1], Shalini Suresh, Elizabeth Ghogomu, Jessie McGowan

[1] Director, Methods Centre, Bruyere Research Institute; Assistant Professor, School of Epidemiology, Public Health and Preventive Medicine, University of Ottawa, Canada

Note: We report in this document a summary of the results from a recent systematic review (March 2016). The systematic review has been submitted for publication and is undergoing peer-review. A pre-publication summary is available from the Department of Nutrition for Health and Development, World Health Organization, Geneva, Switzerland (nutrition@who.int).

Systematic review 4

Effect of administration of antihelminthics for soil-transmitted helminths during pregnancy *(107)*

Rehana A Salam, Batool A Haider, Quratulain Humayun, Zulfiqar A Bhutta[1]

[1] Center for Global Child Health, Hospital for Sick Children, Toronto, Canada

Systematic review 5

Antihelminthics in helminth-endemic areas: effects on HIV disease progression *(112)*

Arianna Rubin Means[1], Paul Burns, David Sinclair, Judd L Walson

[1] Department of Global Health, University of Washington, Seattle, Washington, United States of America

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Note: The names and affiliations of peer-reviewers are provided here as an acknowledgement and by no means indicate their endorsement of the recommendations in this guideline. The acknowledgement of the peer-reviewers does not necessarily represent the views, decisions or policies of the institutions with which they are affiliated.

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