Reaching girls and women of reproductive age with deworming

Report of the WHO Advisory Group on deworming in girls and women of reproductive age

Rockefeller Foundation Bellagio Center, Bellagio, Italy
28-30 June 2017
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Additional financial support for the meeting was provided by WHO using grant funds from the Bill & Melinda Gates Foundation.
Every girl and every woman of reproductive age who is infected with soil-transmitted helminths has the right to be treated.

Because intestinal worm infections of moderate and heavy intensity, especially hookworm and whipworm infections, cause substantial morbidity in girls and women of reproductive age.

Because treatment is safe and effective at reducing morbidity, including during pregnancy (after the first trimester) and during breastfeeding.

Because girls and women of reproductive age living in areas endemic for soil-transmitted helminth infections who present to a health service should be treated on a case-by-case basis.

For logistic and cost-effective reasons, where the prevalence of soil-transmitted helminth infection in a community equals or exceeds 20%, targeted preventive chemotherapy of all girls and women of reproductive age in the community is recommended. Preventive chemotherapy targeted to this group at risk can be delivered through many different venues including schools, households, health facilities such as antenatal care clinics, and other appropriate venues.
Background

The World Health Organization (WHO) periodically convenes meetings and consultations in order to provide updated guidance to Member States on public health matters of particular global importance. In December 1994, WHO convened an informal consultation to address the increasingly urgent issue of hookworm infection and associated morbidity in women of reproductive age, a population that had been neglected for far too long. The report of this informal consultation, published by WHO in 1996, listed nine key research gaps, importantly expanding the research focus to include other parasite infections, in addition to hookworm infections, which impact the health and nutrition of girls and women of reproductive age (WHO, 1996). It also drew attention to the lack of specific empirical evidence on pregnant and lactating women. Since the preparation of this seminal report, WHO has published numerous documents and guidelines on parasite infections, on anaemia and on deworming that have included girls and women of reproductive age but, until now, none has specifically focused on this population. This 2017 meeting was convened in response, to remind the international community of the continuing importance of soil-transmitted helminth infections in girls and women of reproductive age and of the need to ensure their inclusion in all efforts aimed at reducing the morbidity associated with and transmission of these infections.

The Rockefeller Foundation is renowned for its visionary role and active participation in eliminating hookworm infection and disease from the United States in the early 1900s. This singular achievement is widely recognized as having established the public health system in the United States and for creating a global civic citizenry to address issues of global importance. Since the 1900s the Rockefeller Foundation has supported innovative and impactful ideas that have the potential to transform people’s lives for the better. One of its foremost concerns focuses on the theme of resilience. The notion of resilience captures the capacity of girls and women of reproductive age to overcome the adverse effects of hookworm and other parasitic infections. By hosting experts who all have contributed in one way or another to reducing the consequences of hookworm and other soil-transmitted helminth (Sth) infections in girls and women of reproductive age (at its Bellagio Center), the Rockefeller Foundation contributes to informed advocacy for public health action and research affecting those who are most vulnerable.
1. Introduction and meeting objectives

The WHO Advisory Group on deworming in girls and women of reproductive age convened a meeting of international experts at the Rockefeller Foundation Bellagio Center in Bellagio, Italy on 20–30 June 2017. The meeting was co-organized by Dr Antonio Montresor, WHO Department of Control of Neglected Tropical Diseases, and Professor Theresa Gyorkos, WHO Collaborating Center for Research and Training in Parasite Epidemiology and Control at the McGill University Department of Epidemiology, Biostatistics and Occupational Health. Professor Gyorkos chaired the meeting and Dr Layla Mofid was the meeting rapporteur. Annex 1 contains the list of participants and Annex 2 the meeting agenda.

Drs. Gyorkos and Montresor are the primary co-authors of this report and all participants are considered as co-authors.

The Bellagio Declaration (see above) was formulated by the Advisory Group and unanimously adopted at the meeting.

1.1 Overall meeting objectives

The overall objectives of the meeting were:

- to review the current evidence on the occurrence and health impact of soil-transmitted helminth (STH) infection in girls and women of reproductive age and to identify research gaps;
- to identify operational strategies to control STH infection in each of the different subgroups of girls and women of reproductive age (adolescent girls, pregnant women, lactating women and non-pregnant non-lactating women); and
- to define a plan of action to promote expanded control of STH infection in girls and women of reproductive age.

1.2 Sessional objectives

A total of 12 objectives were addressed in five sessions: introduction and orientation; evidence; lessons from the field; moving forward; and recommendations and next steps.

Session 1. Introduction and orientation

Objective 1: To understand the basis for including girls and women of reproductive age as a high-risk group for STH infections.

Objective 2: To appreciate the historical and current WHO policy of deworming interventions targeting girls and women of reproductive age.

Objective 3: To quantify the magnitude of the problem in terms of the numbers of girls and women of reproductive age at risk of STH infection.

Objective 4: To document the unmet need, in terms of deworming coverage, and barriers to implementation.
Session 2. Evidence

Objective 5: To review the strengths and weaknesses of the cumulative published and unpublished evidence on the effectiveness of deworming in girls and women of reproductive age.

Session 3. Lessons from the field

Objective 6: To review current country policies and practices regarding deworming targeting girls and women of reproductive age, with specific consideration of:
- 6.1 the main impediments to expansion;
- 6.2 successful approaches to reducing morbidity;
- 6.3 key messages for decision-makers to promote the intervention; and
- 6.4 the cost of the intervention.

Session 4. Moving forward

Objective 7: To explore strategies for delivery of deworming programmes.
- Objective 7.1: To discuss the advantages and disadvantages of dividing the population of girls and women into more homogeneous subgroups (i.e. adolescent girls, pregnant women, lactating women, and non-pregnant, non-lactating women) to enhance implementation and expansion.
- Objective 7.2: To identify and prioritize research gaps related to deworming strategies targeting girls and women of reproductive age.

Session 5. Recommendations and next steps

Objective 8: To formulate recommendations regarding actionable strategies for deworming interventions targeting girls and women of reproductive age.

Objective 9: To prioritize research gaps regarding deworming in girls and women of reproductive age.

Objective 10: To identify needs in terms of guidelines, manuals and other documentation to expand STH control in this risk group.

Objective 11: To plan the presentation of this meeting’s report to WHO and other scientific and policy audiences, as appropriate.

Objective 12: To set out a plan of action to monitor progress of the above objectives.
2. Discussion, by objective

Objective 1

To understand the basis for including girls and women of reproductive age as a high-risk group for STH infections

WHO identifies three population groups at high risk for STH infections: school-age children, preschool children, and girls and women of reproductive age, or WRA (WHO, 2006). The designation of high risk derives from an understanding of the disease burden attributable to STH infection, in addition to a consideration of other STH-attributable outcomes, including environmental contamination. For example, peak intensities of *Ascaris lumbricoides* infections are more characteristic of children than adults (Crompton, 2001); infected children have higher rates of school absenteeism than uninfected children (Thériault et al., 2014); and STH-contaminated environments are likely due more to the defecation habits of children than adults (Lanata et al., 1998; WHO, 2015). The basis for identifying girls and women of reproductive age as a high-risk group for STH infection stems from the impact of STH infections on biological requirements, nutritional deficits and co-morbidities present at specific stages during the reproductive lifespan. The clinical and epidemiological evidence for this is summarized below.

Clinical evidence

Since the publication of Cook’s review of helminth-attributable clinical manifestations (Cook, 1986), there has been sufficient scientific evidence of high quality linking STH infection (in particular, hookworm and *Trichuris trichiura* infections) with anaemia (Brooker et al., 2008; Bundy and Cooper, 1989; Gyorkos et al., 2011; Khuroo et al., 2010; Larocque et al., 2005; Smith and Brooker, 2010) and other outcomes (e.g. nutritional deficiencies) (Crompton, 1986; Yap et al., 2014). Blood loss is a direct consequence of hookworm and *T. trichiura* infections. Elegant studies in the 1960s provide a detailed assessment of the blood loss per hookworm (e.g. an average of 0.2 ml/day per *Ancylostoma duodenale* and an average of 0.04 ml/day per *Necator americanus* (Roche and Layrisse, 1966). Infection with either hookworm species or *T. trichiura*, especially moderate and heavy intensity infections, can exacerbate blood loss due to menstruation, pregnancy and childbirth (Crompton, 1993; Crompton and Whitehead, 1993; Stephenson et al., 2000a; 2000b). Chronic STH infection in malnourished populations can also adversely affect the immune system, increasing susceptibility to further infection among other outcomes (Abdoli and Pirestani, 2014; Behnke, 2006; Yap et al., 2014).

Epidemiological evidence

The prevalence of hookworm and *T. trichiura* infections varies widely between and within regions (Pullan et al., 2014) (Table 1). Globally, the magnitude of hookworm infection is larger than that of *T. trichiura* infection; however, in Latin America and the Caribbean, the magnitude of *T. trichiura* infection appears to be greater than that of hookworm infection. It should also be noted that of the two human hookworm species, *A. duodenale* is considered to be more geographically restricted to certain areas primarily in Africa and Asia, whereas *N. americanus* is considered to be more widespread, especially in the Americas (Palmer and Reeder, 2001). Human infection with the zoonotic hookworm *A. ceylanicum* is almost exclusively found in South-East Asia (Traub, 2013).
Table 1. Prevalence of hookworm and *Trichuris trichiura* infection by geographical region

<table>
<thead>
<tr>
<th>WHO region</th>
<th>Prevalence of infection (95% confidence interval)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Hookworm</td>
</tr>
<tr>
<td></td>
<td>Trichuris trichiura</td>
</tr>
<tr>
<td>Asia</td>
<td>7.5% (6.7–8.7%)</td>
</tr>
<tr>
<td></td>
<td>7.6% (6.6–8.7%)</td>
</tr>
<tr>
<td>Latin America and the</td>
<td>5.2% (4.4–6.1%)</td>
</tr>
<tr>
<td>Caribbean</td>
<td>12.3% (11.3–13.7%)</td>
</tr>
<tr>
<td>Sub-Saharan Africa</td>
<td>13.6% (12.9–14.6%)</td>
</tr>
<tr>
<td></td>
<td>11.6% (10.9–12.6%)</td>
</tr>
<tr>
<td>North Africa and the</td>
<td>1.0% (0.9–1.6%)</td>
</tr>
<tr>
<td>Middle-East</td>
<td>1.9% (1.6–2.4%)</td>
</tr>
<tr>
<td>Oceania</td>
<td>47.9% (44.7–51.0%)</td>
</tr>
<tr>
<td></td>
<td>6.4% (5.8–7.0%)</td>
</tr>
</tbody>
</table>


Note: the prevalence for Oceania is heavily influenced by Papua New Guinea, as countries with larger populations such as Australia are not included in the analysis.

There is a large body of evidence linking hookworm infection and anaemia in women of reproductive age. Brooker et al (2008) conducted a systematic review of 13 cross-sectional studies of hookworm infection and haemoglobin in pregnant women and found that even light intensity infections were associated with significantly lower haemoglobin levels compared with no infection. In addition, haemoglobin levels decreased as hookworm infection intensity increased in a dose-dependent manner. Studies published after this review (Makhoul et al., 2012; McClure et al., 2014) yielded similar findings. A systematic review in non-pregnant adults (mostly women) also showed a significant, dose-dependent association between higher intensities of hookworm infection and decreased haemoglobin levels (Smith and Brooker, 2010).

The evidence linking *T. trichiura* infection with anaemia and lower hemoglobin levels in pregnant women is less conclusive. Of six observational studies, one found associations between moderate or heavy *T. trichiura* infection and anaemia after adjusting for covariates including hookworm infection, whereas light infection was not associated with anaemia (Gyorkos et al., 2011). Another study found a significant association between *T. trichiura* infection and anaemia, but the range of infection intensities was not specified (Getachew et al., 2012). The remaining four studies included at most a small number of participants with infection of moderate intensity, and none with heavy intensity infection (Nurdiati et al., 2001; Muhangi et al., 2007; Ndyomugyenyi et al., 2008a; Makhoul et al., 2012). This pattern is similar to that observed in children: significant associations between *T. Trichuris* infection of moderate (≥ 5000 to < 10 000 eggs per gram [epg]) or heavy (≥ 10 000 epg) intensities and decreased haemoglobin levels (Robertson et al., 1992; Ramdath et al., 1995), and no association when all *T. trichiura* infection intensities are combined into one category and compared with no infection (e.g. Ezeamama et al., 2008; Suchdev et al., 2014).

Overall, the published evidence base linking anaemia and/or haemoglobin levels with hookworm and *Trichuris* infections in pregnant and non-pregnant women is of uncertain generalizability, as studies were conducted in settings with different STH prevalences and intensities. At the present time, there are no published data on STH infections and anaemia in study populations of adolescent girls or lactating women.
Objective 2

To appreciate the historical and current WHO policy of deworming interventions targeting girls and women of reproductive age

Since the publication of the Report of the WHO Informal Consultation on hookworm infection and anaemia in girls and women in 1996 (WHO, 1996) and the adoption by the Fifty-fourth World Health Assembly in 2001 of resolution WHA54.19 on schistosomiasis and soil-transmitted helminth infections, which advocated for preventive chemotherapy of all high-risk groups (WHA, 2001), WHO has included a recommendation for deworming programmes to include girls and women. Over time, deworming recommendations targeting girls and women of reproductive age have been included in guidelines or relevant documents from WHO and, when appropriate, within guidelines for integrated intervention programmes. In addition, when appropriate, specific subgroups of WRA have been prioritized. Some examples include the following documents:

Nutrition

School health
- School deworming at a glance (World Bank and WHO, 2003)

Neglected tropical diseases
- Preventive chemotherapy in human helminthiasis (WHO, 2006)
- Accelerating work to overcome the global impact of neglected tropical diseases: a roadmap for implementation (WHO, 2012a)
- Assessing the epidemiology of soil-transmitted helminths during a transmission assessment survey in the Global Programme for the Elimination of Lymphatic Filariasis (WHO, 2015a)
- Guideline: preventive chemotherapy to control soil-transmitted helminth infections in at-risk population groups (WHO, 2017)

Water, Sanitation and Hygiene (WASH)
- Preventing disease through healthy environments: a global assessment of the burden of disease from environmental risks (WHO, 2016)

Integrated public health intervention
- Improving nutrition outcomes with better water, sanitation and hygiene: practical solutions for policies and programmes (WHO, 2015b)

Maternal, neonatal, child and adolescent health
The most recent recommendations on deworming in girls and women of reproductive age have been published in the WHO guideline Preventive chemotherapy to control soil-transmitted helminth infections in at-risk population groups (WHO, 2017), which details the rationale for each recommendation. However, the guideline does not specifically mention lactating women. Rather, this subgroup of WRA is considered to be within that of the subgroup of non-pregnant adolescent girls and non-pregnant adult women. The document contains the following recommendations:

- **adolescent girls (non-pregnant)**
  Preventive chemotherapy (deworming), using annual or biannual single-dose albendazole (400 mg) or mebendazole (500 mg), as a public health intervention for all non-pregnant adolescent girls and women of reproductive age living in areas where the baseline prevalence of any soil-transmitted helminth infection is ≥ 20% among adolescent girls and women of reproductive age, in order to reduce the worm burden of STH (strong recommendation, moderate quality of evidence).

- **pregnant women, including pregnant adolescent girls (in the second or third trimester)**
  Preventive chemotherapy (deworming), using single-dose albendazole (400 mg) or mebendazole (500 mg), 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% among pregnant women, and (ii) where anaemia is a severe public health problem, with a prevalence of ≥ 40% among pregnant women, in order to reduce the worm burden of hookworm and *T. trichiura* infection (conditional recommendation, moderate quality of evidence).

- **non-pregnant adolescent girls and non-pregnant adult women**
  Preventive chemotherapy (deworming), using annual or biannual single-dose albendazole (400 mg) or mebendazole (500 mg), as a public health intervention for all non-pregnant adolescent girls and women of reproductive age living in areas where the baseline prevalence of any STH infection is ≥ 20% among adolescent girls and women of reproductive age, in order to reduce the worm burden of soil-transmitted helminths (strong recommendation, moderate quality of evidence).

This guideline underscores the need to treat girls and women of reproductive age in order to reduce STH-attributable morbidity. Similar to the strategy used to reduce morbidity in child populations, for cost-effective reasons, preventive chemotherapy for girls and WRA is recommended only in areas where STH endemicity equals or exceeds 20%. In those areas where the prevalence of hookworm and/or *T. trichiura* infections exceeds 20% (and where anaemia levels are also likely to be high), treatment of pregnant women (after the first trimester) should be considered a priority. The guideline does not specify the platform for the delivery of preventive chemotherapy, entrusting each country to identify those platforms most appropriate for reaching at-risk adolescent girls and adult WRA. Whenever possible, national and sub-national platforms that can be used to deliver multiple interventions should be used (e.g. antenatal clinics, women’s gathering sites).

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1 Refers to a prevalence of > 50% for STH infection or the source of data for the prevalence of anaemia (as appropriate).
2 Refers to the definition of the strength of the recommendation.
Objective 3

To quantify the magnitude of the problem in terms of the numbers of girls and women of reproductive age at risk of STH infection

Numbers attract attention. From Stoll and his Wormy World in 1947 to the numbers update provided by Pullan and colleagues 67 years later in 2014, to the yearly updates of numbers of children receiving deworming in the annual data reported in the WHO PCT (preventive chemotherapy and transmission control) databank (most recently to 2016), numbers have informed the goal and driven the progress of STH prevention and control activities (Stoll 1947; Pullan et al., 2014; WHO, 2017b). So, what are the numbers of WRA? How big is the challenge?

The numbers of girls and WRA at risk of STH infection have now been estimated at 688 million (Table 1) (Mupfasoni et al., 2018). This WHO-led group based their estimation on 2015 age- and sex-disaggregated population data from the United Nations World Population Prospects 2015 database (United Nations, 2015), data from the Global Atlas of Helminth Infection (www.thiswormyworld.org), data from the WHO PCT databank (WHO, 2015) and country-specific fertility rates (United Nations, 2015). Given the heterogenous nature of this population group, specific numbers were estimated for four subgroups: (i) adolescent girls; (ii) pregnant women (both adolescent and adult); (iii) lactating women (both adolescent and adult); and (iv) adult non-pregnant, non-lactating adult women (while fully appreciating the dynamic interface among subgroups in any one year).

<table>
<thead>
<tr>
<th>Subgroup</th>
<th>Numbers at risk of STH infection</th>
<th>Percentage (%) at risk of STH infection</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adolescent girls (15–19 y)</td>
<td>108 269 000</td>
<td>15.7</td>
</tr>
<tr>
<td>Pregnant women (15–49 y)</td>
<td>69 463 000</td>
<td>10.1</td>
</tr>
<tr>
<td>Lactating women (15–49 y)</td>
<td>69 463 000</td>
<td>10.1</td>
</tr>
<tr>
<td>Non-pregnant, non-lactating adult women (20–49 y)</td>
<td>440 947 000</td>
<td>64.1</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>688 142 000</strong></td>
<td><strong>100</strong></td>
</tr>
</tbody>
</table>

a Adolescent girls are considered a subgroup of women of reproductive age.

b Adapted from Mupfasoni et al (2017).

The majority of WRA are in the non-pregnant non-lactating subgroup (Table 2); however, in addition to numbers, there are other considerations that will inform a deworming programme. For example, the prevalence and intensity of hookworm and *T. trichiura* infections in an area are important, as is the prevalence of anaemia. Where the occurrence of anaemia and hookworm and *T. trichiura* infections is high (and, consequently, where the risk of both maternal and infant morbidity would be of concern), pregnant women might be of highest priority in planning a deworming
Together, the WHO South-East Asia and African regions have the highest numbers of each WRA subgroup, accounting for 74.7% of all STH at-risk WRA (Mupfasoni et al., 2018). Clearly, deworming programmes may need to target each WRA subgroup separately as each may have a different interface with routine health care services in a country (Mofid and Gyorkos, 2017). Given the potential capacity of a country’s health system to reach each of these WRA subgroups through existing health care services, pregnant and lactating women (20% of WRA) would be most likely to benefit if a new intervention such as deworming were to be added (for example, through antenatal and delivery care services for pregnant women, and through well baby clinics for lactating women). It is possible to reach adolescent girls through the education system (in partnership with the Ministry of Health) where school attendance in this age group is high, but it would be more challenging otherwise. Similarly, reaching non-pregnant, non-lactating adult women, the largest subgroup of WRA (i.e. 64%), would necessitate dedicated planning, additional resources and collaboration with other sectors.

Such planning and resources have been a hallmark of the Global Programme to Eliminate Lymphatic Filariasis (GPELF), where a community-based programme for delivery of treatment has successfully been implemented in the majority of the 72 countries where the disease is endemic (WHO, 2017c). GPELF included the administration of albendazole to everyone in the community, including non-pregnant WRA subgroups. Overall, 20% of all WRA in need of deworming for STH infections have received albendazole at least once per year through this community-based elimination programme. As LF prevalence decreases to low levels and community-based treatment is no longer required, new strategies will need to be considered to maintain a deworming programme for STH infections.

**Women of childbearing age (WRA)**

- Adult women (aged 20–49) neither pregnant nor lactating
- Adolescent girls (aged 15–19) neither pregnant nor lactating
- Pregnant women (aged 15–49) (2nd or 3rd trimester)
- Lactating women (aged 15–49)

**688 million needed preventive treatment in 2015**

Estimated percentage of each sub-group needing preventive chemotherapy for STH
Objective 4

To document the unmet need, in terms of deworming coverage, and barriers to implementation

Unmet need: deworming coverage

Some data are available on women receiving albendazole within GPELF, but as this programme devolves, and as deworming programmes will now be expanding treatment in girls and women of reproductive age, it will be important to monitor coverage by sex and age group. The WHO PCT databank in this regard would be a natural vehicle to assume this role.

Unmet need: barriers to implementation

Safety and efficacy concerns: Safety concerns refer to both those related to the girls and women themselves and also to those related to newborns and infants, in the case of deworming administration during pregnancy.

Adverse events associated with deworming in girls and women themselves have rarely been published, and usually only within the context of specific research studies (e.g. Keiser and Utzinger, 2008; Ndyomugyenyi et al., 2008). However, no serious adverse events have been reported (Ndyomugyenyi et al., 2008). For large-scale deworming programmes, there have been unpublished reports of mild side-effects in adolescent girls; for example, during a National Deworming Day in India. There is an overall appreciation, based on years and even decades of experience with deworming programmes, that, if any side-effects arise from administration of the deworming treatment, they are minor and transient (WHO, 2006). Moving forward, standard operating procedures for assessing and reporting adverse events may be advisable.

Adverse events related to newborn and infant outcomes following deworming treatment of the mother during pregnancy have been studied (details from the five randomized controlled trials conducted to date are shown in Table 3). No association has been reported between administration of mebendazole or albendazole and congenital abnormalities (e.g. de Silva et al., 1999; Gyorkos et al., 2006; Tørlesse and Hodges, 2001; Ndibazza et al., 2010); no association between mebendazole or albendazole administration and the frequency of miscarriages, stillbirths, or prematurity (de Silva et al., 1999; Gyorkos et al., 2006; Ndyomugyenyi et al., 2008; Tørlesse and Hodges, 2001); no association between mebendazole or albendazole administration and perinatal mortality (Gyorkos et al., 2006; Ndyomugyenyi et al., 2008); and no association between albendazole administration and incidence of malaria, diarrhoea or pneumonia (Webb et al., 2011). Benefits from maternal deworming accruing to newborns and infants have been reported in terms of a lower frequency of very low birth weight (Larocque et al., 2006); lower perinatal mortality (e.g. de Silva et al., 1999) and lower infant mortality at 6 months of age (e.g. Christian et al., 2004). Further research is required to assess the effect of maternal deworming treatment on the risk of eczema and the susceptibility to vaccines in infants (Mpairwe et al., 2011; Webb et al., 2011). Overall, therefore, this cumulative evidence suggests that benefits outweigh risks in terms of newborn and infant outcomes from maternal deworming.

Another safety issue concerns the identification of girls and women in the first trimester of pregnancy (when deworming medicines are not advised to be administered). WHO has recommended using the self-reporting of the date of the last menstrual period to
determine pregnancy status (WHO, 1994), but concerns have been raised about the accuracy of this self-report as an indicator of pregnancy (Gyapong et al., 2003). This concern clearly requires additional research attention, including qualitative research. In addition, there remain concerns about deworming during any trimester of pregnancy (Insetta et al., 2014), indicating a need for clearer guidelines and other supportive resources, especially for programme managers having responsibility for the deworming programmes. Such additional guidance would clarify questions related to the effects of deworming during pregnancy and during breastfeeding on both maternal and infant outcomes; deworming in conjunction with other interventions; the risk and reporting of adverse events; and the frequency of deworming during pregnancy, among others.

A more general type of concern related to both safety and efficacy is that of the quality of medicines. This concern is present for any deworming programme and for all target populations. Efforts to ensure that the medicines used in any deworming programme are of the highest quality require constant vigilance (e.g. confirmation of the source, adequate storage facilities and adequate precautions during transportation). Any concerns about reduced efficacy should be reported to the appropriate WHO Regional Office.

**Implementation platform concerns:** How to reach the different subgroups of girls and women of reproductive age poses a challenge. Adolescent girls who are enrolled in school can be reached through the formal school system. It may also be possible to use the school as a distribution point for other adolescent girls and for adult women. Reaching non-enrolled adolescent girls would require consideration of local cultural and labour practices (Mofid and Gyorkos, 2017; Stephenson et al., 2000b). Pregnant women and lactating women are perhaps the most easily reachable of the WRA subgroups as they are more likely to be in contact with the health care system (e.g. through antenatal clinics, delivery facilities and well baby clinics, among other opportunities). Non-pregnant and non-lactating adolescent girls and WRA can be reached through a number of community-based venues, including the workplace and marketplace, women’s groups, places of worship, volunteer groups, according to local customs.

Special circumstances will present additional challenges with respect to implementation. For example, additional recognition of potential risk and appropriate coordination of services may be required for displaced populations, for refugees and following natural catastrophes or other disasters. Every effort should be made to integrate deworming for girls and WRA into primary health care services and to extend such efforts into other relevant services as offered by other sectors (e.g. within the agricultural and labour sectors).
Objective 5

To review the strengths and weaknesses of the cumulative published and unpublished evidence on the effectiveness of deworming in girls and women of reproductive age

Published evidence on the effectiveness of deworming in girls and WRA comes mainly from randomized clinical trials (RCTs) and systematic reviews on deworming in pregnant populations. To date, there have been five published clinical trials of deworming in pregnant women (Table 3). (Note that the same trial produced results for five papers (Ndibazza et al (2010), Mpairwe et al 2011; Nampijja et al 2012, Webb et al 2011; 2012.) These have been included in three systematic reviews (Brooker et al., 2008; Imhoff-Kunsch and Briggs, 2012; Salam et al., 2015).

The individual studies presented in Table 3 all have some methodological limitations that limit their interpretation and contribution to effective deworming programme policy and implementation. First, the number of trials included in the evidence base is small. Second, of the five trials, four used albendazole and one used mebendazole. Further limitations include small sample sizes, concurrent administration of iron supplementation, variable periods of follow-up, different baseline prevalences (and intensities) of hookworm and T. trichiura infections, among others, calling into question the appropriateness of any cohesive summary of the data. The conclusions of the three systematic reviews reflect the uncertainty with which these data should be regarded.

Brooker et al (2008) reviewed two of the RCTs described in Table 3 (Torlesse et al., 2001) and Larocque et al., 2006), plus two non-randomized intervention trials and two observational studies. They concluded “there are insufficient data to quantify the benefits of deworming, and further studies are warranted”, but nevertheless recommended that “efforts (...) be made to increase the coverage of anthelmintic treatment among pregnant women”.

The Imhoff-Kunsch and Briggs (2012) systematic review included Torlesse and Hodges (2001), Elliott et al (2005), Larocque et al (2006) and Ndibazza et al (2010), along with observational studies. They concluded that “Although the current meta-analysis shows no clear benefit of deworming on MNCH [maternal, newborn and child health] outcomes, we believe there may nonetheless be a public health benefit to alleviating the burden of STH infections in pregnant women”.

Finally, the Cochrane review (Salam et al., 2015) included all studies described in Table 3. However, for the Ndibazza et al (2010) study, the secondary analysis restricted to women infected at baseline (that showed a significant effect of deworming) was not considered, nor was the lack of difference in the occurrence of infant eczema between hookworm-infected versus non-infected (Mpairwe et al., 2011). The conclusion of the review was that “The evidence to date is insufficient to recommend use of antihelminthic for pregnant women after the first trimester of pregnancy”.
### Table 3. Published clinical trials of albendazole or mebendazole in pregnancy

<table>
<thead>
<tr>
<th>Reference (location)</th>
<th>Baseline STH prevalence</th>
<th>Groups</th>
<th>Outcome*</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Torlesse and Hodges, 2000; 2001 (Sierra Leone)</td>
<td>Hookworm 66% T. trichiura 74 %</td>
<td>ALB or placebo in 2nd trimester</td>
<td>Hb in second and third trimester</td>
<td>No difference in anaemia; Hb decline smaller in ALB-treated (Δ = 6.6 g/L, p = 0.0034)</td>
</tr>
<tr>
<td>Elliott et al., 2005a; 2005b (Uganda)</td>
<td>Hookworm 38% T. trichiura 13%</td>
<td>ALB or placebo in 2nd trimester</td>
<td>Perinatal mortality; infant eczema &lt; 1 yr of age</td>
<td>No effect on perinatal mortality (5/49 vs 4/44); no effect on infant eczema</td>
</tr>
<tr>
<td>Larocque et al., 2006 (Peru)</td>
<td>Hookworm 46% T. trichiura 82%</td>
<td>MEB plus iron or placebo plus iron in 2nd trimester</td>
<td>Hb and anaemia in 3rd trimester; low birth weight; very low birth weight</td>
<td>No effect on Hb, anaemia or low birth weight; less very low birth weight in MEB-treated (0/479 vs 7/471; p = 0.007)</td>
</tr>
<tr>
<td>Ndyomugyenyi et al., 2008b (Uganda)</td>
<td>Hookworm 67% T. trichiura 5%</td>
<td>ALB, IVM, ALB + IVM or placebo in 2nd trimester</td>
<td>Hb and anaemia at 36 weeks of gestation</td>
<td>No difference in Hb or anaemia</td>
</tr>
<tr>
<td>Ndibazza et al., 2010 Mpairwe et al., 2011 Nampijja et al., 2012 Webb et al., 2011 Webb et al., 2012 (Uganda)</td>
<td>Hookworm 44% T. trichiura 9%</td>
<td>ALB or placebo in 2nd or 3rd trimester</td>
<td>Hb and anaemia at delivery; infantile eczema ≤ 1 yr of age; infant motor and neurocognitive functioning at 15 mo of age; HIV plasma viral load; infant response to immunizations and other infections</td>
<td>No effect on anaemia; among moderate/heavy hookworm infected lower risk of anaemia (OR = 0.45, 95% CI: 0.21, 0.98); more eczema in infants of ALB-treated mothers but not between hookworm infected and uninfected; no effect on infant motor or cognition functioning; no effect on HIV viral load; no effect on response to BCG, tetanus or measles immunizations; among hookworm-infected less IL-5 and IL-13 response to tetanus immunization</td>
</tr>
</tbody>
</table>

Hb, haemoglobin; ALB, albendazole (ALB in all studies was single dose (400 mg)); MEB, mebendazole single dose (500 mg)); IVM, ivermectin; IL, interleukin.

*Outcomes are maternal unless specified otherwise.
The experience gathered from the above review of evidence highlights two critical points:

- In RCTs that were aimed at assessing the impact of mass deworming, women were enrolled regardless of their infection status at baseline (with the exception of the Ndyomugenyi et al. (2008b) trial), thus diluting the intention-to-treat analysis of the effect of the treatment. Preventive chemotherapy is administered with the intent of providing treatment benefit to those who are infected (uninfected persons are treated because the programme is applied to the whole population for logistical and cost reasons). Measuring the benefits of the intervention on the entire treated group therefore is inappropriate as benefits will only accrue to those infected and not to those uninfected.

- The prevalence and intensity of STH infections varied greatly across studies. Of note, two RCTs (Torlesse and Hodges, 2001; Larocque et al., 2006) were conducted in populations where the prevalence of *T. trichiura* infection was higher than that of hookworm. The limited effectiveness of single-dose albendazole and mebendazole against *T. trichiura* (Moser et al., 2017) may explain the small impact of deworming in these studies.

In conclusion, published evidence from clinical trials conducted in pregnant women tends towards overall benefit rather than overall risk, with an additional benefit of deworming among those who are infected with hookworm and/or *T. trichiura*. Evidence from other sources, such as observational studies, pre-post research designs and time series analyses, among other designs, would contribute useful information.

Non-published evidence from several countries provides some additional detail and insight into country-specific aspects of policy-making, programme planning and programme implementation. Among the WRA subgroups, lactating women remain an understudied group. The only study conducted in this population to date found a mean length gain of 0.8 cm in 6-month old infants of mothers who received albendazole compared with infants of mothers who had received placebo (Mofid et al., 2015; Mofid et al., 2017). Overall, the meeting considered that, while there was a consensus that the state of the evidence requires strengthening, there was sufficient cumulative knowledge to support the recommendations put forth in the current WHO guideline (WHO 2017), as summarized above under Objective 2. The following research gaps were identified in order to further inform the guideline: (i) coherence of data from observational and longitudinal studies in terms of understanding the biological association between STH infection, deworming, and maternal and child outcomes; (ii) age and sex-disaggregated data from ongoing large-scale deworming programmes, ideally also including species-specific and drug-specific data on outcomes, and including the frequency of adverse events; (iii) data on cost-effectiveness of deworming programmes; (iv) data on the effect of co-infection; and (v) data from pharmacovigilance, including compliance at all levels (from supplier to distributors to the women themselves).
Objective 6

To review current country policies and practices regarding deworming targeting girls and women of reproductive age

Specific consideration should be given to objectives 6.1 the main impediments to expansion; 6.2 successful approaches to reducing morbidity; 6.3 key messages for decision-makers to promote the intervention; and 6.4 the cost of the intervention.

There has been little information in either the published or unpublished literature on deworming programmes specifically targeting WRA. The large-scale deworming programmes were initially focused on school-age children because this age group was at high risk of morbidity from STH infections; the infrastructure of schools made the programmes cost-effective; and the two pharmaceutical companies, GlaxoSmithKline and Johnson & Johnson, provided the single-dose deworming medicines (albendazole and mebendazole, respectively) free of charge.

The GPELF included WRA in its community-based treatment strategy, whereby all individuals in a household except pregnant women were eligible for deworming. It has been estimated that coverage rates for WRA within GPELF, on an annual basis, approximate 20% of all at-risk WRA.

There have been other reports of deworming in WRA, but these have either been within research projects or in limited geographical areas within a country. The lessons below from the representatives of five countries (Cambodia, Ecuador, India, Peru and Viet Nam) provide some additional context, especially in terms of challenges and opportunities.

Cambodia

The national preventive chemotherapy deworming programme began in 2005, initially targeting schoolchildren; as of 2007, preschool children have also been included (Ministry of Health, 2010). Data from 2013 to 2015 reported in the WHO PCT Databank show twice-yearly rounds of mebendazole administered to more than one million preschool children and over four million school-age children, representing a coverage of over 90% in both groups (WHO, 2015c). This programme is ongoing, with emphasis on maintaining high levels of coverage and in reaching children living in remote villages. The twice-yearly deworming programme is implemented in May and November, concurrently with the vitamin A distribution programme. In addition, deworming is integrated with other large-scale public health intervention programmes such as measles vaccination, the family planning programme and insecticide-treated net distribution. With expansion of the school-based deworming programme envisioned to include secondary schools and private schools, increasing numbers of adolescents will be reached. For WRA, it is recognized that there is a high prevalence of STH infection, especially hookworm, in women who live in rural villages and in women who work on plantations and in the garment industry, among other industries. In this regard, there are ongoing discussions with the Ministry of Labour and Vocational Training, in conjunction with the Ministry of Health, the Ministry of Education and the Ministry of Rural Development. Some private companies have proved to be effective partners in deworming activities as they want to maintain the health of their workers. The role of nongovernmental organizations...
in providing deworming is also recognized as a positive adjunct to governmental activities because of the traditional trust developed with villagers over time. Currently, it is estimated that coverage of deworming among WRA is in the order of 30%, with the expectation that this will rise to 50% in the short term. One strategy to reach WRA who work on plantations is to piggyback deworming onto malaria control activities. In addition to improving coverage in WRA are concerns related to updating the preventive chemotherapy reporting system; possible revision of intervention strategies in areas with STH, schistosomiasis and lymphatic filariasis co-endemicity; and a possible switch in deworming medicines from mebendazole to albendazole because of the important hookworm presence.

Ecuador
Deworming activities with annual albendazole administered to preschool and school-age children have been reported since 2003, with coverage rates for preschool children of 5.1% in 2003 rising to 45.4% in 2005, and for school-age children of 11.1% in 2003 rising to 85.0% in 2006. Between 2007 and 2008, no data were reported on coverage rates but by 2009 a coverage rate of 100% was reported for school-age children (PAHO, 2010; WHO, 2010). Since 2009, a programme targeted to schoolchildren has continued but with no available data on impact or coverage. Few data on STH endemicity were available prior to a national survey undertaken among schoolchildren during 2011–2012 in each of Ecuador’s three ecological zones (coast, Andean, and Amazon regions): the Amazon lowlands were found to have the highest prevalence of any STH infection (approximately 60%), of which 45.6% had moderate or heavy intensity infections (Chammartin et al., 2013; Moncayo et al., 2017 unpublished data). Although annual treatments with albendazole continue to be administered to children and provided through government-sponsored daycare facilities and schools, there are no deworming programmes targeting WRA beyond secondary school.

India
The national deworming programme began in 2009, with the federal government providing a dedicated budget for all the states and union territories for the implementation of a bi-annual deworming programme targeting preschool and school-age children. In 15 states, the bi-annual deworming programme was initially bundled with the vitamin A supplementation programme for children aged under five. In 2012, because of a high anaemia prevalence, a weekly iron and folic acid programme was started in adolescent girls and boys. As of 2013, the national strategy advocated for a combined deworming and iron supplementation programme to reach, in addition to children and adolescents, adult WRA. At this time, the states were able to implement the programme for the children and adolescents but not for the WRA. In 2015, based on the WHO predictive map of STH prevalence in the country, and informed by the success of the polio campaign, a fixed-day strategy was planned to reach children and adolescents in all the states and union territories. The first round of National Deworming Day was implemented in 10 states and one union territory, those jurisdictions having an adequate supply of albendazole on hand. Simultaneously, a national prevalence survey was started to support the evidence-based policy for deworming in the 1–19 year age group. With results from the national prevalence survey, a bi-annual deworming strategy was implemented in 34 states and union territories where the STH prevalence was found to be more than 20% and annually in 2 states (Madhya Pradesh and Rajasthan) with less
than 20% prevalence. The initial uptake of the National Deworming Day strategy varied among the states but both coverage and expansion (e.g. to include private schools) have been increasing in subsequent years. As of February 2017, more than 75 million deworming treatments have been provided to children and adolescents up to 19 years of age. The implementation of a deworming programme targeting WRA has been more challenging, despite the national initiative. The major programmatic challenges include drug procurement, a huge target population, and the lack of prevalence data and a monitoring mechanism, among others. Currently, an additional focus is to implement a deworming programme for pregnant women (Ministry of Health and Family Welfare, 2014). Guidance from the national level includes integrating the deworming programme with other interventions such as safe water and sanitation interventions and nutrition intervention programmes, depending on activities in each state. The aim will be to monitor (with a well-defined, measureable and state-harmonized indicator) state programmes in order to obtain state-level coverage estimates (from a standard type of registry) and to learn from the implementation experience in each state.

**Peru**

Up until 2011, there were no documented national deworming programmes and Peru was in the process of mapping areas of STH endemicity (Saboya et al., 2011; 2013). Data in the WHO PCT Databank indicate that, between 2011 and 2015, approximately 850 000 preschool and 2 000 000 school-age children were considered in need of preventive chemotherapy for STH infections, but no data are provided on the numbers targeted or treated (WHO, 2015c). The leadership of the Pan American Health Organization (PAHO) in organizing several pan-American events (e.g. a workshop on STH in preschool children in Washington DC in 2011; the 2013 promotion meeting in Bogota) and several international events hosted in the Region of the Americas (e.g. ICOPA XIII (the International Congress of Parasitology in Mexico City in 2014) have contributed to a heightened awareness of STH infection and disease burden in the country. From 2012 to 2014, Loreto, the largest region of Peru and perhaps the most STH-endemic, initiated a school-based deworming programme and achieved coverage rates as high as 60% despite overwhelming challenges (Rodriguez Ferrucci et al., 2016). In 2013, the Ministry of Health of Peru ratified a resolution calling for the inclusion of deworming during pregnancy, as of 35 weeks’ gestation, in endemic areas (MINSA, 2013). Recently, the Ministry of Health has recognized the high prevalence of anaemia and STH in children and has developed a Plan of Action (2017–2020) to provide deworming treatment for its approximately 3.5 million children at risk of STH infection in the country (MINSA, 2017). Although there has been no report on the uptake of these new initiatives, deworming is recognized as an important public health intervention addressing population groups at highest risk of STH-attributable morbidity.

**Viet Nam**

The goal of the national deworming strategy is centred around reducing anaemia, primarily so that women would enter pregnancy with robust iron stores. Because the overall prevalence of hookworm was assumed to be 20–50%, and because hookworm infection exacerbates anaemia, a pilot deworming programme, using albendazole, targeted to non-pregnant women, was initiated in 2006 in two districts of one province, in addition to weekly iron-folic acid supplementation (Casey et al., 2013). A baseline survey confirmed the high prevalence of STH and hookworm (84% and
76%, respectively) and also a high prevalence of anaemia (approximately 40%). The deworming programme was administered by the health system through community health care workers and included periodic monitoring with occasional adherence and cost surveys (Casey et al., 2010; 2011; 2013). The monitoring component of the programme was able to establish that the overall impact of the deworming programme after six years was mostly observed in the elimination of moderate and heavy intensity infections, with a decrease in both overall STH prevalence and a decrease in anaemia prevalence (Casey et al., 2017). Adherence was estimated at 85% over the six years of the monitoring. Where sustained decreases in anaemia were not observed, reasons included lack of access to deworming medicines and a high turnover of workers. With this pilot experience, deworming in non-pregnant women was scaled up to 10 provinces in 2010, with the expectation to expand to 20 provinces by 2020. While the intervention has been included in the national nutrition plan, the monitoring component has been dropped, as has the weekly iron-folic acid supplementation, because of high costs.

Based on these and other country experiences, the following observations were made.

Objective 6.1  Impediments to expansion
- Uncertainty about why governments are not scaling up despite knowledge (WHO 2017 guidelines will be helpful in this regard).
- Women may be unaware of the risk of STH infection and/or STH-related symptomatology.
- Women and health workers may be concerned about side-effects, despite the existence of national guidelines for deworming girls and WRA.
- Health workers are overstretched.
- Supply chain for delivery of medicines can be a challenge.
- There is a lack of information and capacity of health workers to capture and transmit appropriate information.
- Deworming in pregnant women is mentioned in national guidelines but no details are provided.

Objective 6.2  Successful approaches to reducing morbidity
- Girl-to-girl interaction can be helpful where non-enrolled girls can be brought to school (India).
- The lead may be best if from the Maternal and Child sector rather than from the Neglected Tropical Disease sector (depends on internal organization, tradition, resources, among others).
- Leadership is needed from state/government ministers (including those in sectors other than health).
- In Bangladesh and India, in addition to primary schools, preventive chemotherapy is now implemented in secondary schools.
- Need to tap medical specialists and other appropriate health professionals (e.g. nurses, midwives) to be champions (specific training is required for health professionals).
• Need to consider existing preventive chemotherapy campaigns which reach girls and WRA so that deworming can be integrated (e.g. into school-based campaigns, iron supplementation and other micronutrient supplementation programmes, nutrition initiatives, especially those that are household-based).
• Donated medicines reduce cost and assure quality.
• Experience from GPELF can inform the continuation of its STH deworming component with respect to programme implementation; explore re-directing of funds and donations from GPELF to STH deworming programmes as countries succeed in eliminating LF.
• Document progress in reducing morbidity to encourage continued implementation.
• Ensure individual case management is available for those seeking medical attention.

Objective 6.3  Key messages for decision-makers to promote the intervention
• Integrate multiple interventions from various sectors as much as is possible, especially those targeted towards girls and WRA (e.g. vaccination or WASH campaigns).
• Include adolescents in school-based deworming programmes (as in the Philippines).
• Offer appropriate training for health staff.
• Ensure commitment from all partners involved.
• Develop appropriate educational materials (tailored to target population), for different health professionals, documenting benefits of deworming; consider “notes” for easy referral.
• Develop a specific protocol to guide programme managers and health workers when the deworming programme includes pregnant women.
• Produce social mobilization and marketing tools to improve education and information; especially important preceding an event like a national deworming day or other activity and for adequately informing the public about perceived side-effects.
• Need to maintain data flow from sub-national to national-level programmes.
• Consider prioritizing those most vulnerable (e.g. WRA in rural areas).
• Consider promoting deworming together with WASH activities that are targeted to girls and WRA.

Objective 6.4  The cost of the intervention
• At present, deworming medicines are donated and these are provided free of charge for schoolchildren.
• Cost estimates to expand deworming programmes to include girls and WRA have not yet been developed (research gap), but this is recognized as providing key information for decision-makers to plan and expand programme implementation.
• Consider transfer of funds from LF to STH control.
Objective 7
To explore strategies for delivery of deworming programmes

Objective 7.1
To discuss the advantages and disadvantages of dividing the population of girls and women into more homogeneous subgroups (i.e. adolescent girls, pregnant women, lactating women, and non-pregnant, non-lactating women) to enhance implementation and expansion

There was a consensus that WRA is not a homogenous group but includes several subgroups that are distinct in terms of biology (susceptibility and response to infection), behaviour (socio-cultural exposure to infection) and access to, and use of, deworming treatment (interface with government and non-government providers). WHO recognizes the following different subgroups in its 2017 guidelines: adolescent (non-pregnant) girls, pregnant adolescent girls and adult women, and non-pregnant adolescent girls and adult women (WHO 2017a). Lactating women are sometimes also recognized as a distinct group (Mupfasoni et al., 2018). Advantages were seen in acknowledging the challenges of each subgroup with respect to targeting programme planning, implementation and monitoring, where the features of each subgroup merited separate consideration. For example, adolescent girls may be frequently out of school and therefore not easily reached by school-based deworming programmes; pregnant women need to be identified to avoid receiving deworming in their first trimester, but could more easily be reached through antenatal clinics; lactating women were perceived to be more easily reached through well baby clinics, and non-pregnant non-lactating adult women were perceived to be more difficult to reach, or more costly to reach, than the other subgroups. It was recognized that different countries have different strategies and platforms to reach each subgroup and that these should be encouraged so that no group is left behind. For example, India’s deworming programme includes girls up to 19 years of age in its secondary school programme. And for those adolescent girls who are no longer in school, a community-based approach is being implemented through the Anganwadi Centres.

The following additional considerations were noted for each subgroup in terms of implementation of a deworming programme and to expanding the programme. One common consideration for all subgroups was the need to address the question of cost-effective methods for identifying pregnant women in the first trimester of pregnancy.

Adolescent girls
- Prioritize vulnerable girls within this group (i.e. those from low socioeconomic status, rural, high prevalence areas)
- Create specific creative messaging

Pregnant women
- Ensure integration with other programmes whenever possible (e.g. nutrition programmes)
- Explore the possibility of drug donations for this subgroup
Non-pregnant women
• Explore integration with existing community-based platforms

Lactating women
• Provide deworming treatment in the early postpartum period as a cost-effective intervention within routine postpartum care

All subgroups
• Prioritize WRA from low socioeconomic status, rural and high prevalence areas
• Review existing programmes and platforms that reach out to girls and WRA to assess how deworming might be integrated
• Put into place a reporting system appropriate for the platform(s) that will be used for each subgroup to monitor coverage and other indicators
• Put into place a monitoring system for each subgroup
• Produce practical guidelines to assist programme managers in the planning, implementation and monitoring of programmes for each subgroup
• Include representative WRA populations in disease monitoring surveys
• Put into place a process for reporting adverse events
• Develop health education interventions to increase public awareness and demand
• Provide standard definitions for adverse events and for any other indicator that will be used in reporting (to assist programme managers)

Objective 7.2
To identify and prioritize research gaps related to deworming strategies targeting girls and women of reproductive age

There is little documented information on strategies and platforms that have been effective in reaching girls and WRA. The following information and research gaps have been identified. Empirical evidence addressing these gaps would facilitate a more evidence-informed choice of implementation. (An example from Viet Nam provides insight on this approach (Phuc et al., 2009)). Due to the heterogeneous nature of this population group, after gaps which pertain to all subgroups, are listed those gaps that are pertinent to each subgroup. These lists will require prioritization and refinement in order to appropriately direct investment to areas of greatest need.

Information and research gaps identified as relevant to all WRA subgroups

Clinical
• Investigate the effect of STH infection and treatment on allergies and response to vaccines in children.
• Investigate the effect of STH infection and treatment on microbiota of WRA and their children.
Epidemiological

- Encourage use of standard measurements for improved comparisons over time and in different settings (e.g. specifying specific timepoints for outcome evaluation, including measurement of species-specific intensity levels; assessing programme impact among infected persons; using standard diagnostic tools (or testing new ones); using standard numerator and denominator definitions for reporting coverage and other outcomes).
- Investigate preferences of the girls and women themselves with respect to delivery and monitoring aspects of the deworming programme in their community.
- Summarize current knowledge on the epidemiology of STH infections in WRA.
- Develop mathematical models to evaluate prevention and control strategies targeting different WRA subgroups.
- Consider separately mapping out the different species of hookworm infection.
- Develop a practical exclusion protocol for excluding girls and women in the first trimester of pregnancy (including self-reporting).
- Summarize the epidemiology of STH-related determinants of morbidity, disease burden and mortality in WRA, and especially in pregnant women and newborns.
- Summarize the epidemiology of neglected tropical diseases in WRA.
- Obtain evidence on impact from randomized studies (maternal and infant outcomes).
- Obtain evidence on impact from observational studies (maternal and infant outcomes).
- Obtain evidence on value of pre-pregnancy deworming and, where appropriate, in conjunction with family planning medication.

Diagnostics

- Develop new diagnostics (for STH and Strongyloides infections; to define Strongyloides burden in WRA in various settings; to appreciate differential effects and impact on morbidity of the different hookworm species; quantitative results will be especially important for measurement of intensity of infection).

Treatment

- Obtain evidence on factors affecting distribution chain from supplier to WRA.
- Obtain evidence from pharmacovigilance.
- Obtain evidence on efficacy of medicines.
- Obtain evidence on value of more than one dose during pregnancy (after the first trimester).
- Investigate quality of medicines purchased through the private sector and ways to encourage quality-assured medicines.
Communication

- Investigate effect of various communication strategies and practices on behaviour changes.
- Evaluate delivery models to reach female workers.
- Evaluate use of mobile technology (e-health) for tracking coverage and reporting of side-effects.
- Identify ways to translate evidence into policy.
- Identify factors influencing the health system in programme uptake and implementation.
- Identify ways to foster exchange between research and policy communities to inform both.
- Consider framing an ideal protocol for specific research gaps.

Policy/guidelines

- Develop a consensus around effective interventions to address STH infections and STH-related morbidity in WRA.
- Evaluate financing options for deworming plus or minus concurrent supplementation packages.
- Estimate cost-effectiveness of deworming programmes targeting WRA.

Information and research gaps identified as particularly relevant to: adolescent girls

- **Priority research gaps**
  - identifying adolescent girls who are pregnant in the first trimester
  - how to reach adolescent girls (including perceptions and barriers)
  - mobility and re-infection potential
- **Other research gaps**
  - qualitative/social research to elicit preferences, trust issues, preferred delivery platforms, etc.
  - operational/implementation research on comparisons among platforms (in terms of costs, role of parents/guardians, etc.)
  - use of social media for targeting messages
  - creative communications
  - creating/encouraging “change leaders”.

Information and research gaps identified as particularly relevant to: pregnant women

- **Priority research gaps**
  - how to translate guidelines into practice?
  - benefits/risks of deworming with respect to birth outcomes and health of the newborn
• Other research gaps
  - perceptions of pregnant women and health care workers towards safety and benefits of deworming (promote acceptability)
  - how to change perceptions and behaviours
  - apply lessons learnt from the GPELF
  - efficacy of benzimidazoles in pregnant women
  - alternative treatment regimens (other than single-dose benzimidazoles).

Information and research gaps identified as particularly relevant to: Lactating women
• Priority research gaps
  - generating more data on safety and adverse events in the children
• Other research gaps
  - additional studies on drug and metabolites in breast milk
  - qualitative research on barriers to accepting deworming for mothers, caregivers and health professionals
  - more data on efficacy in lactating women
  - more observational epidemiological studies on benefits to mothers and children
  - concurrent nutritional status of lactating women
  - qualitative research about women’s feelings about taking drugs in pregnancy and during lactation.

Information and research gaps identified as particularly relevant to: non-pregnant non-lactating women
• Priority research gaps
  - cost-effectiveness of the deworming intervention plus or minus including iron folic acid supplementation using different delivery systems/platforms
  - how to identify women in the first trimester of pregnancy.
Objective 8
To formulate recommendations regarding actionable strategies for deworming interventions targeting girls and women of reproductive age

The following considerations were identified as being of importance in developing strategies to reach the different subgroups of WRA. They would also inform the reporting of coverage. For each subgroup, special attention is required for appropriate information, education and communication (IEC) materials and activities. In particular, there should also be an awareness of the global normative process and of wider financing processes and policies that may already be operating (each with its own existing momentum) and in which deworming could be integrated.

Adolescent girls
- use schools as a platform to reach adolescent girls not enrolled in school
- include secondary schools in programmes
- piggyback onto HPV (human papillomavirus) immunization and other appropriate adolescent health programmes
- messaging should be specific to this subgroup.

Pregnant women
- link with iron supplementation and IPTp (interruption treatment in pregnancy) for malaria
- identify more effective ways to provide iron supplementation
- identify ways to report on deworming
- identify ways to manage the deworming programme by trimester
- integrate deworming into nutrition programmes
- ensure that health workers are adequately trained in deworming, including specialists
- determine possibility of pica (geophagia) and, if appropriate, add to messaging.

![Distribution of estimated 26.7 million pregnant women, by WHO region](image)
Lactating women
- provide deworming immediately after delivery in the postpartum period or within a short time after delivery.

Adult non-pregnant non-lactating women
- assess value of private market in buying quality-assured anthelminthics.
- use existing platforms
- need to develop a protocol to identify women in the first trimester of pregnancy so they are excluded from treatment until their second trimester
- iron supplementation programmes to ensure robust pre-pregnancy iron stores
- include deworming in pre-conception care packages, when appropriate.

All girls and women of reproductive age
- add WRA to the WHO PCT database
- incorporate deworming into essential health care packages
- whenever possible, find ways to include deworming in WASH activities
- integrate deworming into other programmes offered by the health sector itself and by other government sectors
- reinforce concept of deworming as a public health intervention (over and above deworming as a clinical patient-based intervention)
- include deworming as a public health intervention in the medical, nursing and other appropriate training curricula
- use numbers of each WRA subgroup to inform strategic planning in each endemic country
- prioritize WRA in humanitarian settings (such as refugee camps)
- take into account possible provision of deworming by nongovernmental organizations.
**Objective 9**

**To prioritize research gaps regarding deworming in girls and women of reproductive age**

The following research gaps were identified, several of which would benefit from multi-country research:

- cost–effective identification of women in the first trimester of pregnancy;
- empirical evidence on safety for deworming programmes targeting each subgroup;
- effectiveness of drug combinations, especially where *Trichuris* prevalence is high;
- more effective ways to provide iron supplementation (less frequently than weekly?);
- importance of co-infections (not only with other helminth infections);
- empirical evidence of impact of maternal STH infections on health of infants and children;
- empirical evidence on the impact of maternal STH infection on lactation performance;
- persistence of infection over time after different intervention cycles;
- influence of population subgroups as reservoirs of infection;
- longitudinal characterization of probability of treatment throughout the lifespan (from preschool children to end of reproductive period to older age);
- identification of priority subgroups within the large group of non-pregnant, non-lactating women; and
- comparative value of using determinants other than age to differentiate subgroups (in the general WRA population or within each subgroup).
Objective 10

To identify needs in terms of guidelines, manuals and other documentation to expand STH control in this risk group

- Preventive chemotherapy guidelines should include information on:
  - goals and process and progress indicators
  - epidemiology-informed choice of medicine
  - frequency of deworming
  - how to measure efficacy
  - how to know if resistance has emerged
  - role of T. trichiura in causing anaemia
  - instructions on use (with food, etc.)
- consider mapping STH prevalence and intensity for girls and WRA;
- include documentation written specifically for the girls and WRA themselves (with their participation in the development of the documentation);
- contain documentation specifically for programme managers;
- include reviews of other WHO guidelines to ensure that, if they refer to the deworming intervention, they contain the latest up-to-date recommendations (e.g. nutrition guidelines, etc.), and to verify the need to mention deworming, if appropriate (e.g. in continuum of care documentation, etc.);
- contain documentation linking the benefits of deworming in girls and WRA to achieving the United Nations Sustainable Development Goals;
- countries should decide if they need additional documentation over and above WHO guidelines, especially if different platforms will be used for deworming distribution;
- documentation should include specific protocols for monitoring and evaluation standards emphasizing the reporting of age-disaggregated data;
- contain documentation for the reporting of adverse events;
- verify language on manufacturer’s brochure to allow for public health use; and
- clarify deworming drug use in clinical case management, community case management and public health applications (and add relevant information to existing guidance and forms).
Objective 11

To plan the presentation of this meeting’s report to WHO and other scientific and policy audiences, as appropriate

This report will be circulated to all appropriate audiences, initially to all WHO regional offices and relevant WHO departments: Department of Maternal, Newborn, Child and Adolescent Health; Department of Public Health, Environmental and Social Determinants of Health; Department of Reproductive Health and Research; Department of Nutrition for Health and Development; Department of Human Resources for Health; and the Special Programme for Research and Training in Tropical Diseases. It will be published online on the WHO website and the full report will be available in English, with summaries in all six official WHO languages.

In addition, this report will be shared with WHO partners including UNICEF, Children Without Worms, the Bill & Melinda Gates Foundation, the STH Advisory Committee on Soil-transmitted Helminths, the STH Coalition, the Task Force for Global Health, the Coalition for Operational Research on NTDs, Johnson & Johnson, GlaxoSmithKline, Nutrition International, the Canadian Partnership for Women and Children’s Health, and the Rockefeller Foundation, among others.

Excerpts or summaries from this report will form the basis for a Viewpoint in PLoS Neglected Tropical Diseases and similar brief communications will be submitted to other appropriate scientific peer-reviewed journals.

Finally, content from this report will be developed into a PowerPoint presentation and published online in pdf format for public use.
Objective 12

To set out a plan of action to monitor progress of the above objectives

The following six-step plan of action was envisioned:

1. Ensure the report is circulated to all potential audiences.
2. Develop a slate of documentation.
3. Agree on basic indicators for monitoring progress.
4. Provide technical support to countries in planning, implementing and monitoring.
5. Collect data on coverage and other indicators including adverse events.
6. Publish and share data, by country, by region.
3. Recommendations

The following are the summary recommendations from this WHO Advisory Group meeting:

- Deworming should be available and accessible to girls and women of reproductive age in all STH-endemic areas.
- Where the prevalence of any STH infection equals or exceeds 20%, deworming programmes should include girls and women of reproductive age.
- The necessary guidance should be developed and provided to deworming programme managers specifically for deworming targeting girls and women of reproductive age.
- Consideration should be given to providing deworming treatment to girls and women of reproductive age, and especially pregnant women, in as cost-effective a manner as possible (including donations).
- WHO should specify, for each WRA subgroup, coverage goals, morbidity reduction goals, and goals for any other process or impact indicator, with milestone timepoints.
- The current reporting system for adverse events should be reviewed to ensure collection of data from WRA subgroups.
- All deworming programmes targeting girls and women of reproductive age should be monitored periodically using standard indicators of process and impact.
- The research community should take note of the research gaps identified in order to provide rigorous empirical evidence to inform future policies and goals.
4. Research priorities

The following are the priority research topics identified during this WHO Advisory Group meeting:

- Determine the effectiveness of deworming programmes on reducing morbidity in adolescent girls and adult women of reproductive age.
- Estimate the impact (added value) of deworming programmes targeting girls and women of reproductive age on the overall goal of eliminating STH disease burden and on both maternal and infant outcomes.
- Update the global epidemiology of STH prevalence, intensity, morbidity and disease burden in girls and women of reproductive age.
- Investigate practical and cost-effective ways in which first trimester pregnancies can be identified.
- Explore ways in which social media and mobile technologies can contribute to optimizing programme coverage.
References


• Pan American Health Organization. Control y eliminacion de cinco enfermedades desatendidas en America Latina y el Caribem 2010-2015. Analisis de avances,
prioridades y líneas de acción para filariasis linfática, esquistosomiasis, oncocercosis, tracoma y helmintiasis transmitidas por el contacto con el suelo [Control and elimination for five neglected diseases in Latin America and the Caribbean 2010-2015. Analysis of progress, priorities and action plans for lymphatic filariasis, schistosomiasis, onchocerciasis, trachoma and soil-transmitted helminthiases]. Washington (DC): Pan American Health Organization, 2010 (in Spanish).

• Phuc TQ et al (2009). Lessons learned from implementation of a demonstration program to reduce the burden of anemia and hookworm in women in Yen Bai Province, Viet Nam. BMC Public Health. 9:266.


## Annexes

### Annex 1. List of participants

<table>
<thead>
<tr>
<th>Experts</th>
<th>Contact Information</th>
</tr>
</thead>
</table>
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<tbody>
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<tr>
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</table>
### Experts

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<tr>
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### Observers

<table>
<thead>
<tr>
<th>Organization</th>
<th>Representation</th>
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<tbody>
<tr>
<td>Bill &amp; Melinda Gates Foundation</td>
<td>One representative (Dr Simon Brooker)</td>
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<tr>
<td>GlaxoSmithKline</td>
<td>One representative (Dr Mark Bradley)</td>
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<tr>
<td>Children Without Worms</td>
<td>One representative (Dr Rubina Imtiaz)</td>
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<tr>
<td>Johnson &amp; Johnson</td>
<td>One representative (Ms Cori Vail)</td>
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## Annex 2. Agenda

### Day 1 - Wednesday, 28 June 2017

<table>
<thead>
<tr>
<th>Time</th>
<th>Session</th>
<th>Presenter(s)</th>
<th>Materials</th>
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<tbody>
<tr>
<td>8:30–9:00</td>
<td><strong>1. Welcome and introduction</strong></td>
<td>Montresor, Gyorkos</td>
<td>Introduction ppt</td>
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<tr>
<td></td>
<td>a. Welcome (5)</td>
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<td>b. Introduction (5)</td>
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<tr>
<td>9:00–9:10</td>
<td><strong>2. Meeting orientation and objectives</strong></td>
<td>Montresor, Gyorkos</td>
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<tr>
<td></td>
<td>a. Meeting objectives (10)</td>
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<td></td>
<td>b. Expected outcomes (10)</td>
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<td>9:10–9:20</td>
<td><strong>3. WRA as a high-risk group</strong></td>
<td>Montresor, Mupfasoni, Vercruysse, Gilbert, Knopp/Kupka/Lincetto</td>
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<tr>
<td></td>
<td>a. Clinical evidence (10)</td>
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<td>b. Number of WRA and PC coverage (10)</td>
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<td>c. Safety and efficacy (10)</td>
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<td>d. Epidemiological evidence (10)</td>
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<td>e. Integrated interventions (10)</td>
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<td>a. Adolescent girls</td>
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<td>b. Non pregnant women</td>
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<td>c. Pregnant women</td>
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<td>d. Lactating women</td>
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<td>10:10–10:30</td>
<td>Coffee break</td>
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<tr>
<td></td>
<td>a. Systematic reviews (30)</td>
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<td>b. Discussion (10)</td>
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<td>c. On-going field studies (30)</td>
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<td>d. Discussion (10)</td>
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<td></td>
<td>e. General Discussion (20)</td>
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<td>f. Identification of Research Gaps (20)</td>
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<tr>
<td>11:00–13:00</td>
<td>Lunch break</td>
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<td>13:00–14:00</td>
<td><strong>6. Lessons from countries having deworming policies or programs targeting WRA</strong></td>
<td>Casapia, Khieu, Deb, Biggs, Cooper</td>
<td>Peru policy, Cambodia policy, India programme, Viet Nam programme, Ecuador programme</td>
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<tr>
<td></td>
<td>a. Peru (20)</td>
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<td>b. Cambodia (20)</td>
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<td>c. India (20)</td>
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<td>d. Viet Nam (20)</td>
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<td>e. Ecuador (20)</td>
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<td>14:00–15:40</td>
<td><strong>7. Pluses and minuses of deworming programs targeting WRA</strong></td>
<td>Belizario, Insetta et al., 2014, Phuc et al., 2009, Gyapong et al., 2003</td>
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<tr>
<td></td>
<td>a. Philippines (10)</td>
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<td>b. Others to be considered (10)</td>
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<td>14:00–15:40</td>
<td>Coffee break</td>
<td>All</td>
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<td><strong>8. General discussion</strong></td>
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<tr>
<td>Time</td>
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<td>Presenter(s)</td>
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<tr>
<td>09:00-09:30</td>
<td>9. Recap from Day 1</td>
<td>Montresor</td>
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<td>09:30-11:30</td>
<td>10. Breakout sessions</td>
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<tr>
<td></td>
<td>a. Breakout 1: Strategies for deworming programmes targeting adolescent girls; and identification of research gaps</td>
<td>Belizario Rapporteur 1: Imtiaz</td>
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<td>b. Breakout 2: Strategies for deworming programmes targeting pregnant women; and identification of research gaps</td>
<td>Biggs Rapporteur 2: Gilbert</td>
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<td>11:30-12:00</td>
<td>Coffee break</td>
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<td>11:30-13:00</td>
<td>11. Breakout sessions, continued, with crossover of participants</td>
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<td></td>
<td>a. Breakout 1: Strategies for deworming programmes targeting non-pregnant women; and identification of research gaps</td>
<td>Vercruysse Rapporteur 3: Brooker</td>
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<td>b. Breakout 2: Strategies for deworming programmes targeting lactating women; and identification of research gaps</td>
<td>Cooper Rapporteur 4: Mofid</td>
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<tr>
<td>13:00-14:00</td>
<td>Lunch break</td>
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<td>14:00-16:00</td>
<td>12. Report from Breakout 1</td>
<td>Rapporteurs 1-4</td>
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<tr>
<td></td>
<td>Strategies for deworming programs targeting all subgroups of WRA: adolescent girls; pregnant women; non-pregnant women; lactating women</td>
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<td>16:00-16:30</td>
<td>Coffee break</td>
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<tr>
<td>16:30-17:30</td>
<td>13. Report from Breakout 2</td>
<td>Rapporteurs 1-4</td>
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<td></td>
<td>Research priorities: adolescent girls; pregnant women; non-pregnant women; lactating women</td>
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<td>Time</td>
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<tr>
<td>09:00-09:15</td>
<td><strong>14. Recap from Day 2</strong></td>
<td>Montresor Gyorkos</td>
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<tr>
<td>09:15-10:15</td>
<td><strong>15. Recommendations for actionable deworming strategies targeting all subgroups of WRA:</strong> adolescent girls; pregnant women; non-pregnant women; lactating women</td>
<td>All</td>
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<tr>
<td>10:15-11:00</td>
<td><strong>16. Recommendations for research priorities, including monitoring and evaluation and in PELF-endemic areas:</strong> adolescent girls; pregnant women; non-pregnant women; lactating women</td>
<td>All</td>
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<tr>
<td>11:00-11:30</td>
<td>Coffee break</td>
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<tr>
<td>11:30-13:00</td>
<td><strong>17. Remaining issues, and next steps</strong></td>
<td>All</td>
<td></td>
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<tr>
<td>13:00-15:00</td>
<td>Lunch break</td>
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