Soil-Transmitted Helminthiasis Advisory Committee (STHAC) Annual Meeting 2023

Meeting Report & Recommendations

This document details discussions and presents priority action items discussed during the October 18th, 2023 meeting.

CWW | A program of THE TASK FORCE FOR GLOBAL HEALTH

THE SOIL-TRANSMITTED HELMINTHIASIS ADVISORY COMMITTEE

The Soil-Transmitted Helminthiasis Advisory Committee (STHAC) is an independent group of experts in policy, strategy, research, and program implementation related to soil-transmitted helminthiasis (STH) control. Individual STHAC members specialize in child health, clinical medicine, diagnostic sciences, education, epidemiology, parasitology, public health program implementation, spatial statistics, and water, sanitation, and hygiene. Children Without Worms (CWW) is the secretariat of the STHAC.

The STHAC holds an annual meeting to address current programmatic and technical issues relevant to the global campaign to control STH. While considering the latest research, the STHAC formulates guidance to support the World Health Organization (WHO), the STH Coalition, partners, implementers, pharmaceutical donors, and researchers.

The 2023 meeting participants included the STHAC members and observers listed below:

STHAC MEMBERS

1. Matthew Freeman
2. Khumbo Kalua
3. Alejandro Krolewiecki
4. Bruno Levecke
5. Hadley Matendechero Sultani
6. Rachel Pullan
7. Lisa Rotondo
8. Jürg Utzinger (Chair)

MEETING OBSERVERS

1. David Addiss
2. Paul Emerson
3. Catherine Gordon
4. Jennifer Keiser
5. Jonathan King
6. Lynn Leonard
7. William Oswald
8. Karen Palacio
9. Monzur Patwary
10. Mariana Stephens
11. Judd Walson
12. Tijana Williams
13. Violetta Yevstigneyeva

CONTENTS

ACRONYMS

CWW	Children Without Worms
MHII	Moderate-to-heavy intensity infection
preSAC	Preschool-aged children
SAC	School-aged children
STH	Soil-transmitted helminthiasis
STHAC	Soil-Transmitted Helminthiasis Advisory Committee
WHO	World Health Organization

2023 ANNUAL MEETING

The annual meeting of the Soil-Transmitted Helminthiasis Advisory Committee (STHAC) was held on October 18, 2023, in person in Chicago, Illinois, USA, and virtually. Eight STHAC members and thirteen observers attended (Appendix A). A detailed description of the proceedings is provided in this report.

OPENING SESSION

The STHAC Chair, Prof. Jürg Utzinger, opened the meeting by welcoming the members and invited observers to introduce themselves. He presented an overview of the approved official annotated for this year's meeting agenda (Appendix B).

SESSION I: TOWARDS A RESEARCH AGENDA TO SUPPORT IMPROVED MONITORING AND EVALUATION

Before the meeting, an online survey about soil-transmitted helminthiasis (STH) research priorities was sent to the STHAC. The members were asked to review a list of 18 research questions previously identified (Appendix C). Staff from Children Without Worms (CWW) developed these questions based on conversations with various STH stakeholders, such as program managers and implementing partners. STHAC members were asked to rank questions by priority status and were invited to list any additional important research questions. CWW staff compiled the results.

The session began with an overview of the process for identifying the priority research questions. The online survey received responses from eight out of the nine STHAC members. Questions were categorized into the following priority statuses:

- Three were identified as the highest priority;
- Four were identified as a high priority;
- Three were identified as priority; and
- Eight were identified as not a priority.

Respondents identified eight other research questions of interest. The sections below list the questions by priority status and the new questions proposed by members.

The presentation of the survey results was followed by a group discussion to determine use cases, ideal setting, funding, and focus points for the highest priority research questions. Appendix D summarizes the discussions of this session. High priority questions were also briefly discussed.

HIGHEST PRIORITY

1. Are there areas where the program efficacy could be enhanced using a different drug or drug combination?
2. Are school-aged children (SAC) prevalence and moderate-to-heavy intensity infection (MHII) estimates similar in community- vs. school-based surveys (i.e., Are school-based surveys a valid proxy for community prevalence among SAC)?
3. Are SAC prevalence and MHII estimates measured in school-based surveys similar to those for preschool-aged children (preSAC) and women of reproductive age (i.e., Are school-based surveys a good proxy for preSAC and women of reproductive age)?

HIGH PRIORITY

1. Thinking about post-endemic surveillance, are there examples of a surveillance system that has been put in place? Has the system detected a signal of recrudescent prevalence or morbidity?
2. For there to be a *Strongyloides* program, there needs to be an understanding of its geographical distribution. Are there any examples of school or community prevalence surveys to assess *Strongyloides* among SAC?

3. Thinking about thresholds to change the frequency of preventive chemotherapy and the reduced sensitivity of Kato-Katz in low prevalence settings, would it save monitoring and evaluation resources to make treatment decisions on MHII rather than any prevalence?
4. Thinking about intervention units in which there have been several years of deworming, are there data that would support the development of a definition of a 'hot spot' or 'geographical area smaller than a district with persistent transmission and elevated risk of morbidity' that would trigger an enhanced preventive chemotherapy response at the sub-district level (i.e., When STH prevalence becomes heterogeneous, can we reliably leave no one behind and target those still at risk)?

PRIORITY

1. Can reading a single slide per sample save resources (personnel time, laboratory time, consumables) during prevalence surveys? From existing data, is it possible to calculate the cost savings?
2. Regarding diagnostics for MHII, what is the added sensitivity of reading duplicate versus single Kato-Katz slides (i.e., What is the risk of misclassifying a district as <2% MHII if only one slide is read)?
3. For school-based surveys, is the methodology of 50 children (selected at random) from each of 5 schools from a homogenous geographic area (or district) routinely used (i.e., In current practice, is the methodology for school-based surveys standardized and comparable or different between regions within a country and between countries)?

OTHER RESEARCH QUESTIONS IDENTIFIED

1. What are the uses, results, and obstacles for implementing drug efficacy trials?
2. What guidance should be offered to areas where low [drug] efficacy is determined?
3. How should anthelminthic resistance be included in surveillance activities?
4. How have countries successfully mainstreamed into health systems? - What are the impacts at each stage of the project cycle–on planning, mass drug administration coverage, target populations, data availability, drug ordering, etc.? What are the opportunities and challenges?
5. What opportunities are there to integrate into routine services (e.g., Child Health Days in Uganda)?
6. How does 'country-led' mass drug administration compare to 'implementing partner-led' mass drug administration (e.g., on coverage, infection, morbidity (however measured), community acceptance)?
7. How do countries make decisions to change the treatment approach? How do they use survey results to do so?
8. Is there any indication that treating x [not specified] times during school-age years leads to inferior outcomes than annual/biannual treatment?

SESSION II: INTEGRATING NEW TREATMENTS AND STRATEGIES IN STH CONTROL AND ELIMINATION

This session aimed to discuss novel treatments and strategies for STH control and elimination, including strongyloidiasis. Two presentations were delivered, each followed by an open discussion involving members and observers.

PRESENTATION 1: THE FUTURE ROLE OF EMODEPSIDE IN HUMAN STH CONTROL AND ELIMINATION

TITLE

Emodepside, an alternative anthelminthic

PRESENTER

Prof. Jennifer Keiser, Swiss Tropical and Public Health Institute

SUMMARY

The presentation included an overview of the four World Health Organization (WHO)-recommended treatments for STH: mebendazole, albendazole, pyrantel pamoate, and levamisole. Mebendazole and albendazole show low efficacy against *Trichuris* in preventive chemotherapy programs, prompting the need for alternative treatments.

A comprehensive multi-country study funded by the Gates Foundation compared the cure rates of albendazole with albendazole-ivermectin combination across different regions (Côte d'Ivoire, Lao People's Democratic Republic (PDR), Pemba Island). In stark contrast with Lao PDR and Pemba Island, the combination did not have high cure rates in Côte d'Ivoire due to a distinct genetic strain of *Trichuris*.

Emodepside, a cyclo-octa-depsipeptide dewormer used in cats and dogs, is being considered by the Swiss Tropical and Public Health Institute as a potential solution. Lab tests they conducted several years ago demonstrated excellent activity against *Trichuris* and hookworm. It was possible to move forward as Drugs for Neglected Diseases Initiative engaged in the onchocerciasis field with Bayer, and they did the Phase 1 study. They did a Phase 1 study with single ascending doses and multiple ascending doses, and they defined the safe dose to use. It was observed that there are no major safety concerns in humans.

After persistent communications with Bayer, Swiss Tropical and Public Health Institute received the tablets and subsequently conducted Phase 2a trials on Pemba Island (where there is still a high prevalence of *Trichuris*), testing varying doses of Emodepside (5-30 milligrams). Results highlighted exceptional efficacy against *Trichuris*, with a 95% cure rate at 15 milligrams.

The presentation addressed adverse events associated with Emodepside, including mild occurrences of headache, blurred vision, and dizziness. Notably, these events were transient, resolving within 24-48 hours. All findings were published in The New England Journal of Medicine, receiving recognition from Antonio Montresor (WHO) and the journal's editorial team.

Building on the Phase 2a findings, a more extensive Phase 2b trial confirmed Emodepside's effectiveness against hookworm infections. A Swiss Tropical and Public Health Institute statistician advised that the focus shifted solely to a comprehensive hookworm study. After extensive deliberation, the decision was made to conduct a study comparing Emodepside at 30 milligrams to albendazole at 400 milligrams to treat hookworm infections in almost 300 participants, with approximately 150 individuals in each arm. This study, recently completed on Pemba Island, confirmed the outcomes observed in the Phase 2a trial, demonstrating a cure rate exceeding 95% and an almost 100% reduction in egg count with the 30-milligram Emodepside dosage.

In this study, instances of co-infections with *Trichuris* were observed. Impressively, there was a high cure rate of nearly 98%, reflecting promising outcomes. Regarding adverse events, at the 30-milligram dosage of Emodepside, there were notable occurrences of dizziness and vision blur at both the 3-hour and 24-hour intervals, affecting approximately 30-40% of the participants. Albendazole demonstrated better tolerance at this dose. Nevertheless, adverse events attributed to either Emodepside or albendazole were found to subside after 48 hours.

OBSERVATIONS/RECOMMENDATIONS

Swiss Tropical and Public Health Institute has successfully entered into a contractual agreement with Bayer, driven by Bayer's enthusiasm upon reviewing the results. In this partnership, Bayer would be responsible for developing Emodepside at the FDA as a new treatment for STH, CMC, extended Phase I studies, and all regulatory aspects. Conversely, Swiss Tropical and Public Health Institute will take on the crucial responsibilities of funding and conducting the Phase 3 trial. This strategic alliance signifies a significant step forward in advancing Emodepside's development and potential approval for the treatment of STH. Swiss Tropical and Public Health Institute is currently seeking funds for the Phase 3 trial, where the team is deliberating on the optimal dosage. There is a dependency on the 15-milligram formulation, but considering adverse events, discussions are underway to shift towards either 15 or 30 milligrams potentially. The collaborative efforts with Bayer and the promising Phase 2 results position Emodepside as a potential breakthrough in STH treatment. The ongoing discussions on dosage and use cases reflect the commitment to advancing this research to its next critical phase.

During the discussion session, the focus shifted to framing Emodepside within the context of highly effective free drugs for specific species. Bayer's commitment to producing and marketing the drug at a social price rather than as a donation was emphasized, with discussions revolving around a $1 cost.

Some concerns were discussed about adverse effects, particularly in light of WHO's experience with triple-drug therapy (for lymphatic filariasis) and the issues faced with the 30-milligram dosage. The comparison was drawn to lymphatic filariasis, where familiar drugs aligned with the elimination agenda were already donated—the question of prioritizing *Strongyloides* populations at risk and ethical considerations for promoting drugs with potential side effects.

The consensus leaned towards the 15-milligram dosage, with the cost considerations. The idea of seeking additional support during development from STHAC and WHO, particularly if needed during collaboration with Bayer, was proposed. The need for different advocacy tools to raise trial funds is crucial, and it is too early to discuss access and donation. There was a recommendation to focus on adverse effects, expressing concerns about eye vision issues. Dr. Khumbo Kalua volunteered to support Phase 3, and there was a collective agreement on the importance of reducing harm at the population level, especially concerning potential adverse effects like blurred vision.

PRESENTATION 2: CONSIDERATIONS FOR INTEGRATING STRONGYLOIDIASIS INTO STH CONTROL PROGRAMS

TITLE

Considerations for integrating strongyloidiasis into STH control programs

PRESENTER

Dr. Catherine Gordon, QIMR Berghofer Medical Research

SUMMARY

The presentation described the integration of strongyloidiasis control into STH control programs. It outlined the global prevalence of *Strongyloides*, estimating 600 million cases predominantly in Southeast Asia and the Western Pacific.

In her presentation, Dr. Gordon emphasized the challenges in diagnosis due to the unique life cycle and the limitations of traditional methods like Kato-Katz or Formol-Ether Concentration. The life cycle involves larvae in feces, free-living stages, tracheal migration, and residence in the small intestine. While chronic infection is common, immunosuppression can lead to hyperinfection with severe symptoms and mortality.

Symptoms include diarrhea, abdominal pain, urticaria, and complications like bacterial sepsis and malabsorption. A Cambodia study linked *Strongyloides* to growth stunting and malnutrition in children, highlighting its socio-economic impact. Diagnostic challenges include false negatives in chronic cases.

Ivermectin is the preferred treatment, but its global availability varies. The absence of a vaccine and standardized diagnostics complicates control efforts. Risk factors align with other STH, emphasizing the importance of mass drug administration. Dr. Gordon suggested incorporating *Strongyloides* control into existing programs, such as those for lymphatic filariasis or scabies.

She noted that community engagement is crucial for successful mass drug administration implementation, supported by studies in the Philippines. The potential of a new drug, moxidectin, and combination drugs targeting both STH and *Strongyloides* were mentioned.

The presentation concluded with a one-health approach for a new program in Australia involving community engagement, mass drug administration with ivermectin, diagnostics including wastewater testing, health education, and exploring potential zoonotic transmission in dogs. It showcased the need for a comprehensive, community-oriented approach to address the challenges posed by *Strongyloides*, emphasizing tailored strategies and improved healthcare infrastructure.

OBSERVATIONS/RECOMMENDATIONS

Discussions noted the findings of a study where there was no difference between a single dose and having multiple doses, which is the same case with scabies. This means that *Strongyloides* control programs have already been underway in Africa, via the lymphatic filariasis and onchocerciasis programs. This presents an opportunity to look at communities involved in biannual onchocerciasis treatments compared to other communities.

It was noted that a critical component for integration into STH is diagnostic. During the discussion, several interesting points were raised, such as the inquiry about the status of the rapid diagnostic tests (it was mentioned that Professor Rahmah Noordin is developing a Brugia Rapid Test with higher sensitivity and specificity than the commercial ELISA test). Regarding its usefulness in a post-treatment setting, IgG would start to reduce after six months. This discussion suggested that collaborating with the group developing the rapid diagnostic test and validating it would be ideal.

A participant noted that the immunochromatographic strip is being tested in Salta and that they are willing to share the study protocol. Members suggested involving the WHO Diagnostics Technical Advisory Group subgroup on STH for input and to determine the needed evaluation. It was noted that Dr. Gordon does communicate with the WHO Diagnostics Technical Advisory Group and that an STHAC member chairs the STH subgroup.

Participants also highlighted the importance of a comprehensive approach involving water, sanitation, and hygiene components and behavior change (not just preventive chemotherapy) in addressing strongyloidiasis. The group emphasized the need for greater engagement with health systems to address *Strongyloides* effectively and differently from other NTDs.

Finally, a suggestion was made for longitudinal sentinel site surveillance after lymphatic filariasis treatment has been withdrawn, looking at *Ascaris, Trichuris*, and *Strongyloides*, done by multiple partners in multiple contexts simultaneously using a standardized protocol.

SESSION III. OTHER BUSINESS

Jürg Utzinger and Paul Emerson moderated this session. Two topics were discussed: the Lancet Global Health Viewpoint submission and the 2024 STHAC membership.

LANCET GLOBAL HEALTH STH VIEWPOINT SUBMISSION

It was noted that the opinion piece “Need for a paradigm shift in soil-transmitted helminthiasis control: Targeting the right people, in the right place, and with the right drug(s)” has gone through multiple drafts and several rounds of review. Dr. Emerson indicated that putting together the opinion piece and capturing a consensus opinion was considerably more challenging than writing up a scientific study. The current version of the piece incorporated feedback from all stakeholders (countries, academic, and research groups) while maintaining the critical message. It was also good to receive positive feedback from the representatives of WHO and the pharmaceutical companies in their personal capacities.

The next steps for the piece would be to add remaining references and submit it to Lancet Global Health, where it will likely undergo the peer review process. If the submission is unsuccessful, PLOS NTD will be considered the alternative journal. It was emphasized that individuals who support the piece should sign the author consent form. If not in agreement, individuals are encouraged to withdraw their names. There was a consensus to submit the piece without further discussion to avoid returning to square one. CWW will complete all required documents and circulate them once submitted.

2024 STHAC MEMBERSHIPS

This year, Lisa Rotondo and Theresa Gyorkos will depart from the STHAC. The departure of Theresa, who is retiring, and Lisa, due to competing priorities, was considered an opportunity to bring fresh perspectives and skills.

There was an overview of the current membership status and the criteria for selecting new members. Geographical coverage was considered essential, as was representation from academics, country programs, and donors. Achieving a gender balance was mentioned. The need for complementarity in skills and interests was highlighted, with consideration given to individuals who could add depth to the group. Several potential candidates were suggested during the discussion.

It was decided that the next step would entail developing a one-page document outlining the strengths and complementarity of potential members. Following this, an email would be sent to all STHAC members containing the one-pager and a link to an online voting poll to identify the top two candidates. The STHAC planned to identify the best-fitting candidates through this poll and then reach out to possible candidates.

CLOSING SESSION

The final session began with the announcement that Paul Emerson would step down from CWW Director effective January 1, 2024, noting that he would continue as the ITI Director, another Task Force for Global Health program. He will be mentoring Kristin Sullivan (CWW Public Health Advisor) to act as Director during the transition period while Mariana Stephens continues as the Deputy Director.

During the pandemic, there has been a shift towards virtual meetings and the financial constraints participants face. It was discussed that future STHAC Annual Meetings should continue to be held in conjunction with conferences such as the COR NTD and ASTMH annual conferences to increase in-person participation.

Jürg announced that he has been on the STHAC for the highest number of years and would like to step down as the Chair at the end of 2024. Therefore, the chair position will be open for 2025 to those within the STHAC. He proposed that Basel could be considered the venue for one of the following advisory committee meetings (aligning with a WHO meeting) and requested the Vice Chair to work with him. He reiterated that a two-day meeting involving a group of this size is ideal for a very enriching discussion.

CWW will circulate all the presentations and relevant published manuscripts. The final version of the Lancet viewpoint will be distributed to the authors for their confirmation and signature.

CWW will send a link to sign up for the STH Coalition listserv. Several exciting projects are on the horizon, including a 2024 newsletter and a March 2024 meeting in collaboration with the NTD NGO Network (NNN) Schistosomiasis & STH Disease Specific Group.

Jürg suggested that reports from meetings like the STHAC Annual Meeting are typically published in PLOS NTD. It was decided that an outline would be developed, followed by a list of contributors for different sections.

The meeting was closed by Jürg with thanks to all STHAC members and observers for their attendance, talks, and presentations, which were all very informative and insightful.

APPENDIX A: PARTICIPANTS

2023 Annual Meeting of the STHAC

Wednesday, October 18th, 2023 | 8:30–15:00 EDT (Chicago)

Hyatt Regency Hotel–Addams Room; Third Floor (West Tower)

ROLE	NAME	EMAIL
STHAC members	Matthew Freeman	matthew.freeman@emory.edu
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	Lisa Rotondo	lrotondo@rti.org
	Jürg Utzinger (Chair)	Jürg.utzinger@swisstph.ch
Meeting observers	David Addiss	daddiss@taskforce.org
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APPENDIX B: AGENDA

2023 Annual Meeting of the STHAC

Wednesday, October 18th, 2023 | 8:30–15:00 EDT (Chicago)

Hyatt Regency Hotel–Addams Room; Third Floor (West Tower)

TIME	TOPIC	PRESENTER(S)
Welcome and Administrative Announcements		
8:30–9:00	Coffee and tea	
Session I: Towards a Research Agenda to Support Future STH M&E		
9:00–12:00	Jürg Utzinger will welcome participants and outline the objectives for the meeting. Mariana Stephens will run through the housekeeping notes. Many of us have been involved in developing the new M&E guidelines for STH and SCH. Not all the guidance is based on published evidence. Agnostic to where data are collected or who leads the research, we would like to develop a prioritized research agenda to support (or refute) the guidelines. We are calling this "Towards a research agenda to support future STH M&E." Publishing the agenda may help research institutions raise funds against the questions. Paul Emerson will present the findings from the prioritization exercise, and Jürg will lead the discussion on the topics. STHAC members will review and discuss the STH Research Questions and draft the STH research agenda for PLOS NTD.	Jürg Utzinger Mariana Stephens Paul Emerson
Break		
12:00–13:00	Lunch Break	
Session II: Integrating New Treatments and Strategies in STH		
13:00–15:00	The control of trichuris has presented challenges for the STH program since it is less responsive to albendazole/mebendazole. Jennifer Keiser will provide an overview of the potential role of emodepside in trichuris control–see the paper attached. Catherine Gordon will present "Considerations for integrating strongyloidiasis into STH control programs." Any Other Business: • Lancet Global Health STH Viewpoint Piece–author forms • 2024 Membership Closing of the Meeting Jürg will review the outcomes of the 2023 Annual Meeting of the STHAC, declare the next official meeting date, and close the meeting for the day.	Jennifer Keiser Catherine Gordon Paul Emerson Jürg Utzinger

APPENDIX C: PRE-MEETING RESEARCH QUESTION PRIORITIZATION SURVEY

Prior to the annual meeting, the STHAC members received a set of STH-related monitoring and evaluation research questions to review and prioritize. They were tasked with prioritizing these questions based on their significance in enhancing the monitoring and evaluation of STH control programs. Below are the 18 questions categorized and their priority status based on member evaluations:

#	PRIORITY	RESEARCH QUESTION
SUB-DISTRICT ASSESSMENTS		
1	High priority	Thinking about intervention units in which there have been several years of deworming, are there data that would support the development of a definition of a 'hot spot' or 'geographical area smaller than a district with persistent transmission and elevated risk of morbidity' that would trigger an enhanced preventive chemotherapy response at the sub-district level (i.e., When STH prevalence becomes heterogeneous, can we reliably leave no one behind and target those still at risk)?
2		Is there any experience modifying school-based surveys to get a more granular or sub-district prevalence estimate (i.e., Is the school-based survey methodology modifiable to identify hotspots)?
DRUG TYPE		
3		Are there examples of the drug being tailored to the dominant species (e.g., are women of reproductive age specifically targeted where hookworm prevalence is high, or is albendazole/ivermectin (or other combination therapy) being used where *Trichuris* prevalence is high)?
4	Highest priority	Are there areas where the program efficacy could be enhanced using a different drug or drug combination?
DIAGNOSTICS		
5	High Priority	Thinking about thresholds to change the frequency of preventive chemotherapy and the reduced sensitivity of Kato-Katz in low prevalence settings, would it save monitoring and evaluation resources to make treatment decisions on MHII rather than any prevalence?
6	Priority	Regarding diagnostics for MHII, what is the added sensitivity of reading duplicate versus single Kato-Katz slides (i.e., What is the risk of misclassifying a district as <2% MHII if only one slide is read)?
7	Priority	Can reading a single slide per sample save resources (personnel time, laboratory time, consumables) during prevalence surveys? From existing data, is it possible to calculate the cost savings?
8		Thinking about diagnostics for MHII, what experience is there in using methods other than Kato-Katz to estimate eggs/gram of feces (i.e., Are we committed to using 19th-century technology in the 21st century)? If so, how do they correlate to duplicate Kato-Katz results?
9		Is there any knowledge and experience of quality control reading a subsample of duplicate Kato-Katz slides? If so, do you use a standard methodology, and how has quality control affected the classification of a district (i.e., Is there a current standardized methodology for quality control supported by evidence)?
SURVEY DESIGN		
10	Highest Priority	Are SAC prevalence and MHII estimates similar in community- vs. school-based surveys (i.e., are school-based surveys a valid proxy for community prevalence among SAC)?
11	Highest Priority	Are SAC prevalence and MHII estimates measured in school-based surveys similar to those for preSAC and women of reproductive age (i.e., are school-based surveys a good proxy for preSAC and women of reproductive age)?

(continued)

#	PRIORITY	RESEARCH QUESTION
12		Are SAC prevalence and MHII estimates measured in community-based surveys similar to those for preSAC and women of reproductive age (i.e., are community-based surveys a good proxy for preSAC and women of reproductive age)?
13	Priority	For school-based surveys, is the methodology of 50 children (selected at random) from each of 5 schools from a homogenous geographic area (or district) routinely used (i.e., In current practice, is the methodology for school-based surveys standardized and comparable or different between regions within a country and between countries)?
14		Are schistosomiasis-driven *S. mansoni* school surveys routinely quantifying STH ova or just indicating their presence/absence?
15		There is ambiguity in the interpretation of prevalence data and confidence intervals (particularly since it can be argued that school-based SAC surveys violate the principle of random sampling and would have particularly wide confidence intervals to account for that). Are there countries where the point prevalence from community- or school-based surveys has been used to guide treatment frequency? Are there countries where the upper 95% confidence interval from a prevalence estimate has been used?
SURVEILLANCE		
16	High Priority	Thinking about post-endemic surveillance, are there examples of a surveillance system that has been put in place? Has the system detected a signal of recrudescent prevalence or morbidity?
17		Thinking about post-endemic surveillance, is there any experience of recrudescence and shifting program activities from surveillance back to preventive chemotherapy?
STRONGYLOIDIASIS		
18	High Priority	For there to be a *Strongyloides* program, there needs to be an understanding of its geographical distribution. Are there any examples of school or community prevalence surveys to assess *Strongyloides* among SAC?

APPENDIX D: DISCUSSION SUMMARY OF HIGHEST AND HIGH-PRIORITY RESEARCH QUESTIONS

2023 Annual Soil-Transmitted Helminthiasis Advisory Committee (STHAC) meeting session summary: Establishing a priority research agenda to support soil-transmitted helminthiasis control program monitoring and evaluation

Date:	Wednesday, October 18, 2023
Time:	9:00 am – 12:00 pm
Location:	Addams Room, Hyatt Regency Hotel, Chicago
Description:	During this session, members sought to establish a priority research agenda to support soil-transmitted helminthiasis control program monitoring and evaluation. Members discussed research questions of interest and identified lead investigators to explore how each question could be addressed.
Chairs:	Jürg Utzinger, Swiss Tropical and Public Health Institute Paul Emerson, Children Without Worms
Rapporteurs:	Mariana Stephens, Children Without Worms Monzur Patwary, Children Without Worms

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Session rationale. During 2022 and 2023, several Soil-Transmitted Helminthiasis Advisory Committee (STHAC) members and observers supported the World Health Organization (WHO) in developing monitoring and evaluation guidelines for soil-transmitted helminthiasis (STH) and schistosomiasis control programs. However, the STH community acknowledged that evidence to support some recommendations was limited or non-existent. To address these gaps, the STHAC aimed to establish a research agenda to generate evidence to substantiate (or challenge) the existing recommendations. The STHAC also believed that documenting these critical research needs might aid organizations in securing the funds required to conduct studies and generate essential evidence.

Pre-meeting survey. Before the meeting, STHAC members participated in an online survey on STH research priorities. Children Without Worms (CWW) staff compiled and formulated suggested priority research questions based on their work and insights gathered from various partners, including country collaborators, academics, and World Health Organization staff. During the survey, STHAC members were asked to prioritize the proposed research questions and introduce any new ones not listed.

Of the 18 research questions presented in the pre-meeting survey, three were selected by members as a priority for discussion during the session:

1. Are there areas where the program efficacy could be enhanced using a different drug or drug combination?
2. Are school-aged children (SAC) prevalence and moderate-to-heavy intensity infection (MHII) estimates similar in community- vs. school-based surveys?
3. Are SAC prevalence and MHII estimates measured in school-based surveys similar to those for preschool-aged children (preSAC) and women of reproductive age?

Session outcomes. The outcomes of the discussions are summarized in Tables D1 and D2 below. Table D1 presents the three highest priority questions addressed during the session and outlines current and future areas for research. Table D2 summarizes the discussions around four other high-priority questions the STHAC discussed.

Table D1. Summary of STHAC session discussion for highest priority research questions

#	USE CASE	RELEVANT PREVIOUS AND ONGOING WORK	POSSIBLE RESEARCH SETTING	POSSIBLE FUNDER (RELATIVE COST*)	PROPOSED NEXT STEP(S)
1	Are there areas where the program efficacy could be enhanced using a different drug or drug combination?				
a	Enhance the effectiveness of deworming programs with ivermectin supplementation for *Trichuris trichiura* control in high-prevalence areas	Monitor in 5-6 districts the effect of combination therapy (ivermectin plus albendazole) vs. single-dose albendazole where the local government has procured ivermectin. Relevant work: – Efficacy and safety of co-administered ivermectin and albendazole in school-aged children and adults infected with *Trichuris trichiura* in Côte d'Ivoire, Laos, and Pemba Island, Tanzania: a double-blind, parallel-group, phase 3, randomized controlled trial (https://www.thelancet.com/journals/laninf/article/PIIS1473-3099(21)00421-7/fulltext)	In Rwanda, the END Fund is exploring a pilot project to support the Rwanda Biomedical Center for a small pilot involving combination treatment (albendazole + ivermectin) for *T. trichiura*. Few areas with community-led total sanitation are also being looked at to assess the differential impact of an integrated control approach (preventive chemotherapy plus water, sanitation, and hygiene vs. preventive chemotherapy alone)	WHO ($$$$)	Dr. Rachel Pullan (London School of Hygiene & Tropical Medicine) to develop a ~500-word piece about identifying areas with persistent *T. trichiura* infections from new impact surveys. She will analyze modeling work to determine improvement gains from combination treatment.
b	Enhance the effectiveness of deworming programs by using albendazole instead of mebendazole in areas with high hookworm prevalence	A 2023 clinical trial (involving Dr. Bruno Levecke (Ghent University)) in Cambodia prompted the national program to change from mebendazole to albendazole. Relevant works: – Efficacy and safety of co-administered ivermectin and albendazole in school-aged children and adults infected with *Trichuris trichiura* in Côte d'Ivoire, Laos, and Pemba Island, Tanzania: a double-blind, parallel-group, phase 3, randomised controlled trial (https://www.thelancet.com/journals/laninf/article/PIIS1473-3099(21)00421-7/fulltext) – Analysis of the population-level impact of co-administering ivermectin with albendazole or mebendazole for the control and elimination of *Trichuris trichiura* (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4946157/)	Not specified	Bill & Melinda Gates Foundation ($$$$$)	Dr. Alejandro Krolewiecki (Argentina Ministry of Health) and Dr. Bruno Levecke to develop a ~500-word piece about issues such as programming/political realities, limited funding, and drug resistance.

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#	USE CASE	RELEVANT PREVIOUS AND ONGOING WORK	POSSIBLE RESEARCH SETTING	POSSIBLE FUNDER (RELATIVE COST*)	PROPOSED NEXT STEP(S)
2	Are SAC prevalence and MHII estimates similar in community- vs. school-based surveys (i.e., are school-based surveys a valid proxy for community prevalence among SAC)?				
	Enhance program monitoring by better understanding the difference in prevalence between attending and non-attending children after multiple years of school-based control	Dr. Judd Walson (Johns Hopkins) will provide school attendance data from Deworm3 countries (India, Malawi and Benin). There are also data from Mozambique and Kenya. Relevant works: – Post-intervention epidemiology of STH in Bangladesh: Data to sustain the gains (https://journals.plos.org/plosntds/article?id=10.1371/journal.pntd.0008597)	Explore existing data (India, Malawi, Benin, Mozambique, and Kenya)	None identified ($)	Dr. Judd Walson, Dr. Khumbo Kalua (Blantyre Institute for Community Outreach), and Dr. Rachel Pullan will assign a PhD student to systematically review available literature and communicate with country representatives.
3	Are SAC prevalence and MHII estimates measured in school-based surveys similar to those for preSAC and women of reproductive age (i.e., are school-based surveys a good proxy for preSAC and women of reproductive age)?				
	Enhance program monitoring by better understanding the differences in prevalence by age group and species	Data from CWW-supported community surveys in Bangladesh and Uganda exist. Preliminary findings indicate that SAC can be a reasonable proxy for preSAC and women of reproductive age, except hookworm among women of reproductive age. Data are also available from Deworm3 countries. Relevant work: – Prevalence and intensity of soil-transmitted helminth infections in Uganda: Results from population-based prevalence surveys in five districts (https://journals.plos.org/plosntds/article?id=10.1371/journal.pntd.0011605)	Explore existing data (Bangladesh, Uganda, India, Malawi and Benin)	None identified ($$)	Not specified

**Relative cost: $ = Low; $$ = Moderate; $$$ = Moderately High; $$$$ = High; $$$$$ = Extremely High*

Table D2. Summary of STHAC session discussion for high-priority research questions

#	QUESTION
1	Thinking about post-endemic surveillance, are there examples of surveillance systems that have been put in place? Has the system detected a signal of recrudescent prevalence or morbidity?
	Participants discussed concerns about the prioritization of surveillance efforts in NTD programs, with questions raised about its significance compared to the primary goal of reducing prevalence. It was stated that NTD program managers echoed these concerns while reviewing the monitoring and evaluation manual. Participants indicated several STHAC members looked at these (surveillance) issues during a COR-NTD breakout session. One member suggested that stool collection may not be optimal and that latrine and water systems proxies may be preliminary indicators that can be used before diagnostics. A participant inquired about detecting recrudescence in lymphatic filariasis programs and suggested they explore potential opportunities for integration. During the discussion, a participant shared a case where a child with an obstructed bowel was initially undiagnosable through scans. It was only after surgical intervention that the presence of *Ascaris* was identified. The point raised was that if severe morbidity is becoming rare to the extent of being unrecognizable by physicians, there is a crucial role in reporting severe morbidity from clinical facilities. Participants agreed on the importance of clinical facility reporting, noting that laboratories routinely report notifiable diseases. They emphasized that even if the data are crude, they can potentially be utilized to identify hotspots in areas experiencing recrudescence. Participants also deliberated on the role of serology, particularly in the context of schistosomiasis surveillance in China. A key highlight was the recognition that decent serology is available for *Strongyloides*, and it is anticipated that the upcoming WHO guideline may suggest serology as the primary diagnostic test. Regarding the current status of serology, there was consensus that it should evolve towards a multiplex approach integrated into health surveillance systems. The suggestion was made to start with microscopy and progressively transition to more sophisticated multiplexing serodiagnostics. Finally, the discussion highlighted a unique opportunity for the NTD community to address issues at a policy level. Participants recognized that policymakers often lack awareness of the importance of NTDs, relegating them to a low priority. Advocacy for local ownership, involving governments in taking responsibility, was emphasized. The suggestion was to analyze data collected over the years to understand changes in prevalence and identify additional interventions beyond mass drug administration, such as improving water provision, behavior change, enhancing literacy rates, and promoting school attendance. There was consensus on the need for clear and directed advocacy, recognizing that asking countries to take ownership involves major modifications to existing programs, presenting a significant challenge for local governments. The critical question of who bears the financial responsibility for programming was acknowledged, especially without substantial external funding. The importance of solid advocacy was underscored, particularly for sustaining deworming efforts through access to domestic financing.
2	For a *Strongyloides* program to exist, an understanding of its geographical distribution is needed. Are there any examples of school or community prevalence surveys that assess *Strongyloides* among SAC?
	Participants highlighted the lack of sufficient estimates to comprehend the burden of *Strongyloides*, emphasizing the absence of countrywide prevalence surveys. Mention was made of a recently concluded significant study in South America, ongoing research in Malaysia and Sri Lanka, and upcoming studies in Australia. When questions arose regarding the morbidity associated with *Strongyloides*, participants emphasized the importance of not underestimating the attributable morbidity. The discussion underscored a collective recognition that while acknowledging this significance, there is a clear need for more evidence to understand the morbidity associated with these infections. It was suggested that, during surveys, efforts should be made to incorporate *Strongyloides* using appropriate, standardized diagnostic methods. Examples were shared regarding school and community surveys conducted by academic groups (rather than control programs). The discussion identified serology as a potential critical diagnostic for such surveys and stressed the importance of accurate laboratory tests. The possible use of hookworm prevalence as a surrogate marker for *Strongyloides* prevalence was highlighted. The feasibility of analyzing modeled data was acknowledged, though participants noted it was imperfect. Concerns were raised about using geostatistical modeling due to the complexity of *Strongyloides* and its environmental stage. However, participants expressed openness to exploring this approach.

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#	QUESTION
3	Thinking about thresholds to change the frequency of preventive chemotherapy and the reduced sensitivity of Kato-Katz in low prevalence settings, would it save monitoring and evaluation resources to make treatment decisions on MHII prevalence rather than any intensity prevalence?
	Participants discussed the possibility of countries applying for validation of elimination as a public health problem while still qualifying for drug donations, as the overall prevalence may not have been reduced. The Kato-Katz thick smear technique was acknowledged as a valuable tool for MHII, but concerns were raised about its diminishing usefulness as prevalence and intensity of infection decreases. The suggestion was made that, being over 60 years old, the Kato-Katz thick smear technique might be more suitable for automation, especially in the context of MHII.
4	Thinking about intervention units in which there have been several years of deworming, are there data that would support the development of a definition of a 'hot spot' or 'geographical area smaller than a district with persistent transmission and elevated risk of morbidity' that would trigger an enhanced preventive chemotherapy response at the sub-district level (i.e., When STH prevalence becomes heterogeneous, can we reliably leave no one behind and target those still at risk)?
	The discussion focused on the challenges and considerations of implementing deworming programs at the sub-district level. The theoretical efficiency of sub-district implementation was acknowledged, particularly for more informed decision-making. However, challenges were noted, particularly with the existing complexities faced in implementing programs at the district level. It was pointed out that data are expected to become available to allow exploration of the spatial distribution. One member suggested that moving to the sub-district level would amount to programs returning to 'square one.' Additional emphasis was put on the significance of granularity in deworming efforts. The suggestion was made to consider reaching, say, 20,000 individuals as adequate rather than conducting extensive monitoring and evaluation across entire areas with millions of people in a district. The key question raised was how to transition towards this more precise approach, ensuring that medication is targeted to areas in need and avoiding unnecessary treatment for those who do not require it. Additional discussion focused on the potential use of MHII prevalence to guide treatment decisions rather than any intensity infection prevalence. One participant felt detecting true hotspots would be much easier if we used a cutoff based on MHII prevalence. A participant stated that because *Ascaris*/*Trichuris* eggs survive for long periods in the soil and there is a free-living form of *Strongyloides*, the notion of using programs to achieve elimination is overly ambitious. As such, the program's focus should be to reduce gross morbidity (i.e., MHII). It was noted that infection intensity does not jump rapidly. To go from a light infection (which may not even be noticed) to a severe morbidity situation, one must be infected ten to hundreds of times. The discussion also highlighted a potential conflict with the WHO Road Map, where achieving elimination as a public health problem is based on achieving MHII below 2% among children. However, if the prevalence of any intensity infection is above 2%, programs may still need to allocate drugs regardless of the association with the disease. Concerns were raised by some members who pointed out that stopping all treatment might control morbidity despite high prevalence, but there is a risk of recurrence if treatment is halted. This emphasized the need for a robust surveillance system to monitor and respond to potential recrudescence after treatment cessation.