

STH Advisory Committee
Operational Research Sub-Committee Teleconference
September 9, 2015

Participants

Individual	Organization
Lauren Abrams	CWW
David Addiss	CWW
Laura Appleby	PCD
Alison Bettis	LCNTDR
Jason Cantera	PATH
Katie Gass	NTD-SC
Charles Mwandawiro	KEMRI
Rachel Pullan	LSHTM
Helen Storey	PATH
Judd Walson	UW

Meeting summary

The operational research sub-committee is charged with tracking and sharing information on STH operational research, as well as identifying, discussing, and highlighting STH research priorities and issues on behalf of the STH Coalition and the STH Advisory Committee. The topics discussed on the September 9 teleconference were related to recommendations of the 2014 STH Advisory Committee meeting, with the exception of the last item on the Cochrane review.

1. Operational research on how best to accelerate drug coverage and improve reporting in order to achieve WHO global treatment targets for 2020 (Gass)

The NTD Support Center (NTD-SC) is working with collaborators on 3 projects related to improving drug coverage and reporting:

- a) A study in Cambodia aims to determine which age group can provide reliable information on deworming and whether parents can be a proxy for whether children received deworming in school. *The NTD-SC is looking for 1-2 country partners with upcoming school based distributions.*
- b) The NTD-SC and collaborators recently completed coverage surveys (based on aggregated coverage of 2 opportunities for deworming for children 24-60 months of age) for 3 districts in Honduras in order to make recommendations to WHO regarding which coverage survey methodology is most feasible. In these districts the two deworming opportunities were preschool and community-based drug distributions. The results show that the drug delivery system was working well. Approximately 80% of PSAC were offered deworming, and there was 55% compliance (those who were offered pills who swallowed them). The primary reason for not swallowing was that they had been

dewormed independently, i.e., had received unprogrammed deworming. 80% of all children surveyed had received *at least* one dose of unprogrammed deworming. They are holding a meeting in mid-October with national Ministry of Health officials. Results should be published after that meeting, hopefully by the end of 2015.

- c) As mentioned during the last teleconference, the NTD-SC is piloting a coverage supervision tool, an in-process self-monitoring tool for program managers that can be used internally and inexpensively. It is a quick tool that utilizes a lot quality assurance sampling (LQAS) strategy to classify coverage as likely to be above or below a target threshold. In addition this tool can be used to identify reasons for noncompliance, areas for mop up, and to supervise community drug distributors. It has been implemented in Ethiopia for LF and onchocerciasis and will be implemented next in Nigeria. It has not yet been tested in a school-based setting.

Discussion

- Ethiopia is about to roll out a large school-based deworming through the MOH. Laura Appleby (PCD) will put Katie Gass in touch with Mike French from SCI.
- The NTD-SC is putting out a position statement with WHO, which will encourage the use of coverage surveys for NTDs to better understand how much deworming is taking place and to understand reporting and issues of noncompliance. The aim is to create momentum around doing coverage surveys. They are also putting guidelines and recommendations for different tools at program managers' disposal.

- 2. Validate in the field the utility of WHO guidelines on assessing STH drug efficacy. Develop and deploy molecular markers to assess the potential emergence of drug resistance and**
- 3. Operational research to identify and deploy new drug regimens, formulations, and drug combinations for STH control. The results of these studies should be incorporated into ongoing epidemiologic modeling (Addiss on behalf of Brooker)**

The Bill & Melinda Gates Foundation is keenly interested in the issues of drug resistance and new drug combinations and regimens. More information on these items may be available at the October 24-25 meeting of the STH Advisory Committee.

Discussion

- It would be useful to develop guidelines for what phenotypic resistance might look like to help program managers identify where resistance might be occurring.

- 4. Operational research on the magnitude, patterns, and importance of unprogrammed deworming (Addiss)**

Unprogrammed deworming is deworming not sponsored by government deworming programs. CDC and KEMRI have [published a paper](#) on this from Kibera, Kenya, where unprogrammed deworming was high. David has just published a [commentary](#) on this issue. This issue is largely unique to STH because of the widespread availability of inexpensive generic deworming medication. Accurate coverage for self-

treatment and treatment delivered by small NGOs is hard to get a handle on. Children Without Worms is working with WHO on the NGO Deworming Inventory to assess the extent of NGO-sponsored deworming in 2013 and 2014. Drug coverage surveys are done for STH, assessment of unprogrammed deworming should be included. There is no standard set of questions that have been field tested and validated, but we should move in that direction. We (CWW and NTD-SC) hope to have the input from social scientists to standardize questions on unprogrammed deworming that could be used on coverage surveys.

Discussion

- PCD may have data on unprogrammed deworming in Ethiopia. They will share their experience.
- It would be interesting to stratify the results by gender. It has been suggested that girls may be disproportionately represented in those getting dewormed outside of school because they are less likely to go to school. Understanding the motivations for deworming is important, both to understand what's driving this now and what can continue to drive individual treatment when the drug donations are eventually withdrawn.
- Coverage surveys of other NTDs that target children can be used to assess unprogrammed deworming for STH in addition to STH coverage surveys.
- It would be interesting (and important) to know the accuracy of self-reported unprogrammed deworming. Some initial work is being done to assess this.

5. Research to refine and field-test PCR diagnostic assays as well as evaluation of programmatic costs associated with them (Addiss on behalf of Williams)

A study of the performance of PCR with "spiked" stool specimens is underway with Steve Williams, Rojelio Mejia and Alejandro Krolewiecki. The spiking of stool samples with eggs has been done and they are about to isolate the DNA from each sample for PCR. This will give very detailed information on the sensitivity and specificity of the PCR tests in a way that has never been done before.

Tom Nutman at the NIH has been processing hundreds of stool samples from Africa and has been using Williams's primers and probes.

Williams's group is submitting a paper for publication this week on the performance of the multi-parallel PCR test on samples from Timor. The specificity was good: the *Ancylostoma duodenale* test did not detect *Ancylostoma ceylanicum* in the samples. They have now developed a new PCR assay for regions that have ceylanicum. The submitted paper will also describe the latest version of the multi-parallel PCR for hookworm species, *Ascaris*, *Trichuris* and *Strongyloides*.

Williams's group has designed the primers and probes to add *Schistosoma mansoni* to the test. They are obtaining field samples and will report on this soon.

Dr. Williams will have a more complete report and the results of the spiking study at the STH Advisory Committee meeting in October.

Discussion

- Update from PATH – we are pursuing three work streams: (1) a field friendly, isothermal nucleic acid amplification technology (NAAT) using the RPA chemistry; (2) a rapid diagnostic test to detect STH antigens; and (3) a simple stool sample preparation method. For the NAAT development, we are now optimizing multiplex assays for *Ascaris*, *Trichuris* and the two hookworm species. The multiplex RPA assays will be tested on STH-positive stool samples (verified by Kato-Katz and PCR). Next steps are to improve the limit of detection (LOD) performance, as well as evaluate the assays against more stool specimens. We are grateful to Jun Belizario for the stool specimens that we have received. The goal is to eventually convert the assays into a commercially available kit. For the antigen detection RDT development, we are continuing the characterization of the antibodies to their utility as diagnostic reagents. We are collaborating with Maria Elena Bottazzi and Bin Zhan at Baylor University on this effort. For sample preparation development, we are evaluating currently available tools so that we can bench-mark new field friendly methods for DNA extraction procedures under development.

6. “State of the art” review from Emory University Center for Global Safe Water on the importance of environmental monitoring for STH control (Addiss)

A year ago the NTD SC provided funding for a review of environmental sampling for STH. Philip Collender and colleagues at Emory University have completed this review. A manuscript has been accepted for publication in *Trends in Parasitology*. CWW and NTD-SC is planning a ½ day symposium to review the findings and discuss their implications. **Continue the innovative work being done by investigators at the London Centre for NTD Research on epidemiologic modeling of STH transmission breakpoints as well as further elucidation of R_0 for STH species and its correlation with indicators that are measurable in field settings (Pullan)**

Worm expulsions were done in 6 communities and involved 150-200 individuals in each community. Reinfection studies are also underway on all those individuals by comparing egg counts at baseline and at 3, 6, and 12 months after deworming. The data will be used to inform epidemiologic models.

Coverage surveys have also been done, including both school-based and community treatment. The community based surveys covered a population of 80,000 individuals in over 80 clusters, with a target of 60 households per cluster. They are trying to capture information on who received deworming treatment as part of the program and outside the program.

They also are going into the communities to do qualitative assessment on what factors influence compliance. That will be completed over the next few months.

The study is scheduled for 30 months (2 years of intervention). Community-based arms will receive 2 or 4 rounds and then they’ll follow up for a full 30 months so all individuals will be tracked for the same amount of time.

Discussion

- It would be useful to see the questions being asked on unprogrammed deworming in this study and to see how they compare with those from other studies to get a sense of which questions work and what type of information they yield.

7. Operational research to assess - in various epidemiologic and programmatic settings - the potential rebound of STH prevalence and intensity in persons not targeted by school-based programs as a result of the transition from community-based LF program to school-based STH programs (Addiss on behalf of Lammie)

The NTD SC does not have new studies to report addressing this issue. It's an area of keen interest and there are some sites that are gearing up to look at this.

8. Implications of re-analysis of Miguel and Kremer study data and latest Cochrane review on STH (group)

Discussion

- Charles had a nice [blog posting](#) on the Impatient Optimists on this issue. The STH community came together to address the flurry of media attention and issued several [statements](#), both public and in the scientific journals.
- The COR-NTD meeting will have this topic as one of the breakout sessions, which David is organizing.
- The STH community must come to terms with both the strengths and the limitations of our data and with how we will address that.
- Judd Walson has been asked to put together an editorial on this topic for PLOS NTDs. Several other opinion pieces will be published in an issue of PLOS NTDs in the next few weeks.
- The STH community is motivated by concerns of equity and justice, hence the desire to move programs into the field. However, global health priorities are based on data and comparisons are made across diseases. The STH community needs to advocate for the importance of programs but also needs to be aware of how global health priorities are established and to conduct the research necessary to provide the most robust data possible in support of its programs.