Identifying Non-responsive Schistosomiasis and Soil-transmitted Helminthiasis Areas Following Treatment and Determining the Causes

Session Date: Saturday, October 27

Session Time: 1:00pm – 4:00pm

Session Location: Rex, 8th Floor

Session Description: Globally, treatment coverage against schistosomiasis and soil-transmitted helminthiasis is increasing, with many countries successfully reaching target populations. However, at a finer geographic scale, some areas do not respond well to treatment, even after multiple rounds. In these places high coverage is not sufficient to reduce levels of infection prevalence and intensity and related morbidity.

These non-responsive areas, also referred to as "persistent hot-spots", represent barriers to achieving the control of morbidity and elimination as a public health problem.

This session will discuss how programs can identify persistent hotspots following treatment and determine their causes.

The output of the session will be the identification of research studies to answer program-relevant questions:

- What is the definition of a non-responsive area? Does this vary by species, location, and programmatic goal?
- How can programs identify persistent hotspot areas? Which monitoring and sampling approaches should be used?
- How can programs determine the cause of sub-optimal response to treatment? What qualitative and quantitative tools are needed to identify the root causes of poor treatment response?

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KEY DISCUSSION POINTS

- **Schistosomiasis (SCH) –** While many endemic areas of Senegal have responded well to treatment, there is persistently high infection in some parts of the country, particularly along the Senegal River in the North and East. In some areas, prevalence is as high as 80-90% following 5-6 years of mass drug administration (MDA) at reasonably high treatment coverage. A number of possible causes were discussed. These included programmatic factors, such as varied treatment coverage (temporally and geographically) and the sampling strategy used in the assessment surveys. They also included non-programmatic reasons,

such as the effect of dams on the ecosystem, agro-pastoral developments, poor sanitation, and hybridization between human and animal schistosome species leading to lower praziquantel efficacy. A combination of factors is possible.

- **Soil-transmitted helminths (STH) –** Bangladesh has a long-standing STH control program. However, two districts were found to have over 20% prevalence of infection, and 7% and 25% of moderate/heavy intensity (MHI) infection of "any STH" following 21 consecutive annual rounds of MDA. These were driven primarily by *Ascaris* infections. Possible programmatic reasons include systematic noncompliance, poor program supervision, and variable treatment coverage (temporally and geographically). Possible non-programmatic reasons include poor WASH and environmental conditions, or low drug efficacy, and/or possible resistance.
- **Performance checklists –** Three checklists developed by the STH Coalition/Children Without Worms (CWW) are available to assess possible causes for persistent transmission. These aim to capture performance issues, and to identify drug efficacy issues and possible drug resistance (e.g., is it a treatment coverage or assessment of coverage issue?).
    - Treatment coverage issue – systematic non-compliance, treatment refusal
    - Failure of treatment – drug efficacy and possible drug resistance
    - Behavior – water-contact and/or sanitation behaviors that lead to repeated exposure/infection.
    - Assessment of coverage issue – are we getting accurate measures of coverage?
- **PSAC/SAC –** Where high prevalence is found in school-age children (SAC), it is important to also consider pre-school-age children (PSAC) as an at-risk group for both morbidity and continued transmission.
- **Granular data –** District or ecological zone measurements may no longer be at a sufficient level for impact assessment following multi-year interventions. This is because both infection and morbidity can be focally distributed. More granular data are required on both infection and treatment coverage, ideally at the site level, such as the community or village. The logistical and financial challenges of capturing granular data at-scale in a programmatic setting were acknowledged.

KNOWLEDGE GAPS IDENTIFIED

Three key knowledge gaps were identified:

1. What is the definition of a non-responsive area? Does this vary by species, location, and programmatic goal?
2. How can programs identify persistent hotspot areas? Which monitoring and sampling approaches could be used?
3. How can programs determine the cause of suboptimal response to treatment? What qualitative and quantitative tools are needed to identify the root causes of poor treatment response?

RECOMMENDED NEXT STEPS

The following discussions and operational research (OR) questions were generated in response to the three key questions:

1. **What is the definition of a non-responsive area? Does this vary by species, location, and programmatic goal?**

Discussion Points

- It was widely accepted that the definition of a non-responsive area would be context-specific and vary by species, location, culture, ethnic group, genetics, age, etc.
- The definition of a non-responsive areas would necessarily vary by programmatic goal. There are different expectations for a national program aiming for control of morbidity to one aiming for elimination of transmission (e.g., SCH in Zanzibar).
- The identification and use of as fine-scale, micro-data was recommended as far as possible, including for historical treatment coverage and transmission risk.
- It is important to first determine if it is a *programmatic hotspot* (due to non-compliance, low treatment coverage, or migratory populations) or a *biological hotspot* (due to drug efficacy, hybridization, high levels of transmission, or resistance).

OR Questions

- What "thresholds" can be tested to determine if a cluster of cases is a "hotspot" worth further investigation?
    - Using modelling and interrogation of available datasets
    - Comparison of fieldwork protocols
    - What is a reliable algorithm for determining non-responsive areas?
- Development and testing of standardized protocols to investigate non-responsive areas, that capture:
    - *Who to test* – identifying the appropriate sampling framework, to include number, ages, design of clusters, and geographical scale
    - *How often to test* – the interval after treatment, either immediately after treatment to determine treatment failure, or prior to next treatment round to capture reinfection. Ideally, sampling at both time points could be conducted. Also, the frequency of testing
    - *Diagnostic* – the choice of diagnostic will affect the definition of non-responsive area.
    - *End point* – What is the program target – control or elimination?
    - *Cross-NTDs* – Is there scope for including other neglected tropical diseases (NTDs) in the protocol?
- How does the starting prevalence (pre-treatment) affect the ability to reach the goal? How should this be considered when determining presence of non-responsive areas?
- What is the evidence base for the existing thresholds for MDA?
    - How does this differ between SCH and STH?
    - What data are available and what additional data are required?
    - Compare with MORBID study for SCH

2. How can programs identify persistent hotspot areas? Which monitoring and sampling approaches could be used?

Discussion Points

- The factors leading to hotspots are very likely to be situation-specific. However, there may be overlap in reasons between areas.
- We should be mindful that there will likely be more than one cause of non-responsiveness in any given area.
- Timing: to truly diagnose a hotspot, it would be beneficial to conduct surveys directly after MDA to measure the effectiveness of the treatment, and then right before the next MDA to measure transmission. Doing so would help to tease out the cause as programmatic or biological.
- Survey area: a broad survey area can mask what is happening at the site level which is of increasing importance as overall infection levels drop.
    - There was a call to move away from interpreting averaged, high-level data towards getting more granular, site-level data, and follow-up of individuals across time.
    - Such fine-scale data are needed for both infection prevalence and treatment coverage towards later stages of programs to parse out local areas of good and failed control.

OR Questions

- Development of a framework for the identification of non-responsive areas
    - Use of GIS to map co-variates (e.g., WASH, temperature, proximity to water, poverty, etc.) to rule out unlikely areas and determine where field work should be focused
    - Testing of that framework to predict location of future potential non-responsive areas
- What is the correct sampling approach to detect non-responsive areas? Based on Bangladesh (STH), an option is to stratify endemic areas according to transmission risk/intensity. Conduct more extensive sampling (e.g., community-based assessments in all ages) in higher risk areas and less intensive (e.g., school-based sampling) in lower risk areas.
    - Consider matching places with similar pre-control conditions and observing how they behave under treatment
- What is the correct scale to detect non-responsive areas?
    - What level of granularity is possible (technologically and financially)?
    - What level of granularity is programmatically useful? At what scale does/will the program make decisions?

3. How can programs determine the cause of sub-optimal response to treatment? What qualitative and quantitative tools are needed to identify the root causes of poor treatment response?

Discussion Points

- There is a need to look at coverage and compliance at the sub-district level given the focality of infection. The more fine-scale data available the better. This is true for SCH in particular but would also be useful for STH.
- Environmental factors should be examined, along with population migration, WASH, and behavior. These could be studied as potential co-factors for assisting persistent infection and as predictors of such areas to prioritize for sentinel surveillance.
- It may be useful to develop a checklist to identify hotspots for SCH by adapting the checklist developed for STH.
- There is an unspoken assumption that drugs perform well in suppressing infection. Is this true? There is some anecdotal evidence that drug efficacy is declining.

OR questions

- Do we have a coverage/compliance gap in SCH where infection levels remain high (such as Lake Victoria)? What lessons can we take from NTD programs in Asia where directly observed treatment is less common?
- Further testing of the STH Failure Checklist/s developed by STH Coalition
- Development and testing of a SCH Failure Checklist, bringing in questions on:
  - Programmatic performance (coverage, compliance, quality of social mobilization, and supervision)
  - External factors (population migration, WASH, and water contact behavior)
  - Incorporating anthropological/qualitative research (cultural/ethnic barriers to treatment, attitudes to health workforce/government, identifying key decision makers and connectors in populations)
- Development and testing of protocols to test drug efficacy
  - For SCH and three species of STH
  - In areas of varying endemicity
  - In areas of varying treatment histories