# Schistosomiasis in Africa: Defining the Program Targets

**Session Date:** Saturday, November 4

**Session Time:** 1:00pm – 4:00pm

**Session Location:** Harborview I

**Session Description:** The goal of this session is to assess emerging evidence and define new measurable targets to guide schistosomiasis control programs. The majority of the health burden of schistosomiasis is focused in Africa; thus, this discussion will primarily revolve around identifying control program targets for infections with *Schistosoma mansoni* or *S. haematobium*. If the currently available data are not adequate to define these targets, the qualities of the ideal target will be reviewed, and studies or analyses that can best lead to these answers will be explored.

**Session Chairs:** Evan Secor, U.S. Centers for Disease Control and Prevention
Fiona Fleming, Schistosomiasis Control Initiative

**Session Rapporteur:** Arminder Deol

**KEY DISCUSSION POINTS**

- Key findings raised by **M. French** presentation:

There is a need to refocus on morbidity control for schistosomiasis (SCH) in sub-Saharan Africa (SSA), which has been overshadowed by the push towards the ultimate goal of interruption of transmission. While elimination of transmission rightly remains the global aim, it is a long-term goal that has thus far only been achieved through significant socio-economic development and/or complementary health interventions, such as WASH or effective intermediate host snail control. Dr. French highlighted that WHO recommends aiming for interruption of transmission 'where appropriate' – where appropriate remains to be defined but most of SSA has focused on MDA with PZQ and thus, in the absence of significant investments in non-preventive chemotherapy (PCT) activities or economic development, the goal remains morbidity control and/or morbidity elimination.

- Key findings raised by **C. King** presentation:

With the shift to using antigen detection assays for diagnosis of *Schistosoma* infections, we will now have much more infection prevalence survey data without corresponding infection intensity data. Current WHO roadmap guidance for morbidity control is formulated only in terms of reducing the number of local heavy infections below a certain threshold. As yet, the guidelines do not address what target infection prevalence cut-offs should be to obtain morbidity control.

Based on prior work by van der Werf and de Vlas, it appears that population prevalence of egg-positive infections is a reasonable correlate of morbidity prevalence in untreated populations. However, the infection prevalence/morbidity links have not been well studied in low prevalence areas or in post-MDA communities. Prof King presented possible association curves for the links between different morbidities and SCH-KK or SCH-UF prevalence values. Some morbidities exhibit an upward sloping logistic curve, with lower prevalence communities having relatively minimal risk and higher prevalence

communities exhibiting increasingly higher rates of disease. The threshold above which disease risk starts to increase varies by schistosome species and by the type of morbidity studied. Such threshold infection prevalence values could be considered as possible targets for achieving morbidity control. For some morbidities, however, the infection prevalence effect is more linear and direct, suggesting there may be no 'safe' level of infection prevalence for those disease states. In addition, some morbidities, such as female genital schistosomiasis (FGS(, hydronephrosis, and hepatic fibrosis, emerge later in adult life after decades of cumulative exposure, so that local prevalence, typically measured only in school age children, is not a good proxy for community risk for these advanced forms of schistosomiasis.

- Key findings raised by **E. Muheki Tukahebwa** presentation

Despite MDA in Uganda since 2003, there are still areas of persistently high prevalence and high reinfection with related morbidity, including deaths. This is likely related to poor coverage, incomplete implementation of the PHASE[1] strategy (including inadequate WASH and no vector control strategy). Elimination or morbidity control requires long-term commitment, as the current strategy not enough.

- Key findings raised by **D. Evans** presentation

There are a number of challenges with the current WHO guidelines for schistosomiasis control and elimination because:

- The goal is based on population
- The treatment is based on age
- The outcome is based on intensity (<5%, <1% heavy intensity)
- The interventions are based on prevalence
- The global target is based on coverage (75% national, 100% geographical)
- **All based on expert opinion.**

The introduction of WHO 65.21 in 2012 complicated the situation as it changed the focus from control to elimination without first accomplishing control. Despite this change in focus or accomplishment, there was no change in treatment strategy.

**KNOWLEDGE GAPS IDENTIFIED**

- **M. French** knowledge gaps identified

How is morbidity control defined? The 1% and 5% heavy intensity targets originated in a different era – we can now develop evidence-based targets. Which age groups should we look at and what is the relationship between infection and morbidity? How is morbidity control achieved (who do we treat and how often)? And how can we demonstrate morbidity control (currently used diagnostics are insensitive, more robust M&E guidelines and framework – what are we aiming for and how do we know when we've got there?)?

- **C. King** knowledge gaps identified

POC-CCA is a better mapping tool than Kato-Katz for *S. mansoni*, but can prevalence data alone predict SCH related morbidity? Are estimated background levels valid for determining an adequate baseline, what are the comparable rates of a given morbidity in non-endemic areas? Is SCH morbidity really nil

[1] PHASE – Preventive chemotherapy, Health education, Access to clean water, Sanitation improvement, Environmental improvement. WHO-AFRO's Regional Strategic Plan for NTDs 2014-2020 http://www.afro.who.int/sites/default/files/sessions/documents/afr-rc63-10-add-en.pdf

when prevalence is below <10%? And what about PSAC – do these relationships still hold? There are data gaps for communities with <10% prevalence. Post-intervention correlation confounded by insensitive tests, missing impact of egg-negative or former infections amongst adults and SAC (e.g. FGS, MGS).

- **E. Muheki Tukahebwa** knowledge gaps identified

There is limited experience in the management of SCH severe morbidity by health systems. How can SCH severe morbidity be treated and managed more in-line with IDM NTDs and into existing health outreach systems? In persistent areas of high infection, what combination of additional interventions are required to prevent morbidity and interrupt transmission?

- D. Evans Presentation gaps identified

Programmatic challenges:

a. Confusing guidance
b. The 'elimination agenda' – no level of trust in current guidelines
c. POC-CCA results – how do they correlate with KK – it is clearly not a linear relationship
d. WASH indicator – huge spectrum of activities but no standardized metric – if increase WASH to X, then we can achieve elimination?
e. Molluscisiding approaches lacking
f. Programmability

**RECOMMENDED NEXT STEPS**

- **M. French** presentation

Refocus SCH control programs towards achievable targets and update evidence-based guidelines under leadership of WHO with SCH community support. Greater attention to defining morbidity, realistic targets. Interruption of transmission remains the ultimate long-term goal but in the (extended) meantime an effective strategy for morbidity control is required.

- **C. King** presentation

For *S. mansoni*, there are many different causes for the same morbidity. Need to construct infection/morbidity curves relating infection level and morbidity for post treatment setting as well as treatment naïve populations. Open to further discussions: ideally prevalence would replace intensity for morbidity control metric. Can we get more population-level data linking infection prevalence and morbidity prevalence? Can we obtain accurate SCH-related morbidity levels in low and very low prevalence areas to re-address the threshold question? What are the appropriate cut-offs to assure morbidity control using other diagnostic tools?

- **E. Muheki Tukahebwa** presentation

Many people do not like taking PZQ – evident early on in integration, due to fear of side effects. Solution is to increase community based sensitisation and mobilisation. Need to apply comprehensive PHASE strategy. Need to incorporate SCH morbidity management into health service delivery system.

- **D. Evans** presentation

What happens after the first 3-5 years when all districts reach 1 to 10% prevalence (on the WHO treatment guidelines (2011) Annex 10)?

To achieve a feasible framework for schistosomiasis, we need:

a. Clear measurable evidence-based objectives
b. Intervention strategies to address the objectives
c. Efficient plan for M&E that results in programme decisions (it does not currently)
d. Reasonable timeframe that can be budgeted and planned around
e. Ability to transition to elimination once a proven strategy is developed
f. It needs to be affordable

++++++++++++++++++++++++++++++

GROUP 1 (Nana Kwadwo Biritwum leading) *S. mansoni*

*You are country W, which has been implementing a SCH control program for 3 years with limited resources. Treatment with PZQ has been patchy - annual in some districts, biennial in others and no treatment in some endemic areas. You now have funds to map the country for Schistosoma mansoni with the POC- CCA test and then subsequently treat with PZQ annually for 5 years with the aim of reducing schistosomiasis infection to a level below which it is a public health problem.*

***1**. What might be your mapping strategy?*

***2**. What will your treatment strategy and monitoring strategy be for the next 5yrs /5 to 20yrs />20yrs?*

***3**. What are the main questions that you need answered by WHO and the schistosomiasis community to support your decision making?*

1) Mapping strategy – it may be worth investing in better mapping if you can then realize savings by more tailored treatments. Three-tiered approach:
   a. High level surveys of knowledge at district level to gauge first idea of endemic areas. Plus geospatial maps etc. Exclude likely non-endemic areas. (Dirk mentioned working in areas even where they were new foci with little historical knowledge)
   b. Countrywide mapping, using SAC, as per current WHO guidelines (but substituting CCA for KK)
   c. Plus more focal mapping, SAC, again using CCA. More schools, fewer children/school, higher resolution (evidence from Ghana of successfully achieving this)
      - Hospital records for historical high morbidity
      - Proximity to water bodies
      - Geospatial data
      - Local knowledge
      - Pooling samples?
      - Test and treat at community level?

2) Treatment: not a one size fits all, tailoring it to the focality.
   a. Aiming to treat fewer places, but at a community level, with more infected children and adults targeted, but fewer uninfected children (as often done by the current guidelines) – going to sub-district level. More targeted approach.
   b. Mapped at school level, but treat at community level
   c. First round, high coverage and potentially two rapid treatments, i.e. 6-8 wks apart – not universal support for this approach
   d. Then in low endemicity areas can transition to treatment every 2 years,

   e. Or, using results from SCORE studies – two years of CWT followed by two years of SBT to suppress infection
   f. Every year in high endemicity areas.
3) Monitoring
   a. Using sentinel sites, make sure they are guidelines for actually updating control strategies depending on results.
   b. Core mapping at baseline and 5 years. Using CCA, and also consider in a subset collecting intensity measurements with KK
4) Questions:
   a. Should be treating at a focal level but we do not currently map at that level: guidance required for focal mapping - Mapping strategy for focal hotspots? Options include Geospatial, concentric spatial circles from water bodies
   b. What level of POC CCA prevalence is a public health problem? What are the thresholds? WHO goals?
   c. Conversion of thresholds of KK into POC-CCA

Monitoring – community-wide monitoring is important. Reassess at 5 years. Sentinel site data are not often used to update strategy – needs to be discussed.
Need to decide: How many districts? Sub-districts? No. of children per school? More schools, fewer children? Are sentinel sites required if they don't change programme strategy?

GROUP 2 (Lynsey Blair leading) – *S. haematobium*
*You are country X, which has been implementing a SCH control program for 3 years with limited resources. Treatment with PZQ has been patchy - annual in some districts, biennial in others and no treatment in some endemic areas. You now have funds to map the country for Schistosoma haematobium using urine filtration or detection of microhaematuria and then subsequently treat with PZQ annually for 5 years with the aim of reducing schistosomiasis infection to a level below which it is a public health problem.*

***1**. What might be your mapping strategy?*
***2**. What will your treatment strategy and monitoring strategy be for the next 5yrs / 5 to 20yrs / >20yrs?*
***3**. What are the main questions that you need answered by WHO and the schistosomiasis community to support your decision making?*

1. Ecological zones are not appropriate as nobody knows what they are. Potentially a random cluster approach: 30 sites per districts, 50 SAC per school. Add in urine dipstick for hematuria. Local knowledge very important – ask local health leaders – add 3-5 purposive sample sites based on local knowledge. 'Piggy back' off other mapping programmes – random cluster sampling.

2. Treat SAC + WRA, reassessment every 5 years. Two consecutive years of community based treatments with above 80% coverage, door to door with directly-observed treatment. Switch to SBT +WRA after two years.

3. Key questions: How do you treat a highly heterogeneous area? How to operationalise sub-district information? What are the thresholds to make the switch from treating entire community to SAC/women of child bearing age? Q. how do you inform the treatment strategy when you have sub-district information problems? What is most effective attack phase followed by maintenance phase?

Questions: when you map and results are heterogeneous how do you operationalise that?
How do you switch from CWT to school-age and women of child bearing age?

GROUP 3 (Pauline Mwinzi leading) *S. mansoni*

*You are country Y, which has previously had high levels of morbidity associated with Schistosoma mansoni infections, including hepatosplenic disease. In recent years, mass drug administration has reduced the levels of severe pathology, although you know that morbidity affecting both children and adults remains. Design a study using the POC- CCA test to identify what level of infection (prevalence and/or intensity) you must achieve so that you find no substantial morbidity in subsequent years. How does the study design and outcome of interest differ for adults, school-age children, and pre-school age children?*

Selecting three age groups – pre-sac, SAC and adults. Review historical data to do power calculations to carry out a cross-sectional survey at: baseline, Y3, and Y5 and add multiple locations. Faecal occult blood, KK, POC-CCA and anaemia testing and malaria. Young adult – severe pathology to be assessed using ultrasound. Pre-sac PCR to get an idea of early infection. Evidence to feed into mathematical models to confirm cut-off points. Hospital records for hematemesis. Coverage survey to look at coverage and compliance.

Group 4 (Juerg Utzinger leading) *S. haematobium*

*You are country Z, which has previously had high levels of morbidity associated with Schistosoma haematobium infections, including fibrotic bladder disease. In recent years, mass drug administration has reduced the levels of severe pathology, although you know that morbidity affecting both children and adults remains. Design a study using urine filtration or detection of microhaematuria to identify what level of infection (prevalence and/or intensity) you must achieve so that you find no substantial morbidity in subsequent years. How does the study design and outcome of interest differ for adults, school-age children, and pre-school age children?*

Collect data for eligibility survey to identify village level prevalence (50 children, single urine filtration – rapid assessment). Villages with 4%, 4-10% and above 10%, with first initial cross-sectional assessment, 5 days filtration and 5 days reagent. Ultra-sonography, anaemia, haemacue, shuttle test, possible FGS – conduct host of morbidity measures. Come up with scatter plot of infection levels vs multiple morbidity measures, with the aim of obtaining a threshold. Treat everyone with a single dose of PZQ and a year later, repeat the exact same morbidity tests. Model outcomes of study beforehand and then layer in sensitive diagnostics as more results become available as more diagnostics come on line. Five days of urine of whole village and use model outcomes beforehand to determine sample size. We need a very sensitive test for *S. haematobium*.

| Breakout | Disease-Specific |
|---|---|
| 3I | Schistosomiasis |

**Knowledge Gaps**

*How is morbidity control defined?

*Which age groups should we look at and what is the relationship between infection and morbidity?

*How is morbidity control achieved (who do we treat and how often)?

*And how can we demonstrate morbidity control (currently used diagnostics are insensitive)

*POC-CCA is a better mapping tool than Kato-Katz for S. mansoni, but can prevalence data alone predict SCH related morbidity?

*Are estimated background levels valid for determining an adequate baseline, what are the comparable rates of a given morbidity in non-endemic areas?

*Is SCH morbidity really nil when prevalence is below <10%?

*And what about PSAC – do these relationships still hold?

*There are data gaps for communities with <10% prevalence.

*Programmatic challenges:

a. Confusing guidance

b. The 'elimination agenda' – no level of trust in current guidelines

c. POC-CCA results – how do they correlate with KK – it is clearly not a linear relationship

d. WASH indicator – huge spectrum of activities but no standardized metric – if increase WASH to X, then we can achieve elimination?

e. Molluscisiding approaches lacking

f. Programmability

* How can SCH severe morbidity be treated and managed more in-line with IDM NTDs and into existing health outreach systems?

*In persistent areas of high infection, what combination of additional interventions are required to prevent morbidity and interrupt transmission?

*Post-intervention correlation confounded by insensitive tests, missing impact of egg-negative or former infections amongst adults and SAC (e.g. FGS, MGS).

**Next Steps**

* Need to develop achievable evidence-based morbidity targets
* Develop robust M&E framework & guidelines based on what are we aiming for and estalishing how we know when we've got there
* For *S. mansoni* , there are many different causes for the same morbidity. Need to construct infection/morbidity curves relating infection level and morbidity for post treatment setting as well as treatment naïve populations. *Open to further discussions* : ideally prevalence would replace intensity for morbidity control metric.
*Use existing population-level data linking infection prevalence and morbidity prevalence for greater understanding of relationship
*Obtain accurate SCH-related morbidity levels in low and very low prevalence areas to re-address the threshold question
*Determine appropriate cut-offs to assure morbidity control using alternative diagnostic tools

* Increase community based sensitisation and mobilisation to reduce fear of side-effects and increase compliance
*Need to apply comprehensive PHASE strategy.
*Need to incorporate SCH morbidity management into health service delivery system.

Develop a feasible framework for schistosomiasis, with:

a. Clear measurable evidence-based objectives
b. Intervention strategies to address the objectives
c. Efficient plan for M&E that results in programme decisions (it does not currently)
d. Reasonable timeframe that can be budgeted and planned around
e. Ability to transition to elimination once a proven strategy is developed
f. It needs to be affordable