SCHISTOSOMIASIS CONTROL AND ELIMINATION: NEXT STEPS

Sunday the 5th November, Sheraton Inner Harbour Hotel, Baltimore, UK.

MEETING REPORT

1. WELCOME BY DAVID ROLLINSON, DIRECTOR OF THE GSA

Prof. David Rollinson started off the meeting by presenting the vision for the elimination of schistosomiasis as a public health problem and the GSA's five interconnected themes: implementation, research, advocacy, communications, strategy and policy. The GSA's goals for 2018 include, amongst others:

- To work with WHO/ESPEN to clarify goals for schistosomiasis control and elimination;
- Increase cooperation and support for endemic countries (e.g. Egypt and Ethiopia),
- Coordination of PZQ use,
- Development of PZQ inventory training module for NTD programme managers;
- Bringing together the implementation working group,
- Formation of new working groups: 'behavioural change and health education' and 'snail control'
- Research meetings to be held in Brazil and ICOPA (south Korea) 2018.

2. SESSION 1 DATA & MODELLING

a. *Jaspreet Toor, Imperial College, London: Making use of mathematical models to inform programmatic decisions.*

Dr. Jaspreet Toor highlighted current WHO goals for the control of schistosomiasis morbidity by 2020 and elimination as a public health problem by 2025, using treatment guidelines based on prevalence levels. She presented projected model outcomes of current WHO strategies:

- WHO goals will be achieved for control according to the models, for low prevalence settings (<10%).
- For moderate prevalence settings (10-50%), morbidity goals may be reached depending on starting levels, but less likely for 2025 targets of elimination as a public health problem.
- For high prevalence settings, unlikely to be achieved (either target).

- For overall prevalence: it is still high in School-aged children (SAC) even if the 2020 goals were achieved. Achieving or not achieving the goals depends on what prevalence setting you're in.

Recommendations:

I. For low baseline: goals likely to be achieved with current guidelines.
II. For moderate and high baseline: increase Preventative Chemotherapy (PC) to once a year or increase SAC 85% and adults 40% coverage. They recommend increasing coverage if given a choice.

Other findings:

- Benefits of school-based vs community wide (latter better), especially in high prevalence settings.
- Projected treatment coverage levels – if there is a high adult burden, we won't achieve eliminations by treating SAC only unless we treat adults. In general, goals reached faster if adults treated.
- Results vary depending on region (R0). Will depend on hotspots too, and the age-intensity profiles, e.g. showing regions where young adults also affected (outside SAC). More data needed to improve model projections.

Conclusion: WHO goals will be achieved in low settings, but need to increase coverage of treatment in moderate and high. Even when goal is achieved, the overall prevalence will still be high.

b. *Penelope Vounatsou, Swiss Tropical and Public Health Institute: Making use of mapping data to inform treatment needs*

Dr. Penelope Vounatsou presented on spatial & temporal changes in the distribution of schistosomiasis risk over the last 15 years, using combined historical and new mapping data and taking the focal nature of schistosomiasis into account. The geostatistical models included water, sanitation, infant mortality, climatic factors and population data.

The results presented by these models showed:

S. haematobium:

- The distribution of *S. haematobium* was shown to have declined from 11.4% in 2010 to 4.5% in 2017 (using population data for 2017).
- Country specific temporal trends showed significant risk reduction. Countries in West Africa showed a greater significant decline than countries in the East Africa

S. mansoni:

- The distribution of *S. mansoni* showed decline from 4.4% in 2010 to 3% in 2017 (population adjusted) and a high probability of risk reduction as with S h, Africa wide.
- Country specific temporal trends showed significant reduction.

There are countries that remain at moderate risk – some of these were countries where data was patchy or missing e.g. Angola, Mozambique and Sudan.

Preventative Chemotherapy coverage vs risk reduction plot showed that in some areas, low coverage (less than 40%) showed between 50-60% risk reduction (i.e. high-risk reduction despite low coverage).

Summary: In 2017 overall prevalence of schistosomiasis is estimated at 7.7%. Estimated treatment needs are 138 doses of PZQ for 341 million children over the age of 15.

Risk of schistosomiasis in sub-Saharan Africa has been reduced by 62% for *S. haematobium* and 37% for *S. mansoni* from 2010 – 2016. The countries with the highest prevalence levels (above 25%) in 2010 have the highest prevalence in 2017. Endemic countries with prevalence of 8.5% - 14.7% in 2010 reduced their prevalence to below 5% in 2017.

Discussion/questions:

Comment from Penelope: Bias based on the data availability, studies tend to take place when the prevalence is high.

Comment from Jaspreet: We are also looking into running simulations without the guideline constraints. For interruption of transmission, 100% coverage for close to a decade required.

Q: What would be the suggestion in terms of hotspots?

A: Could be the difference of compliance, adherence, and aggregation parameters.

Q for Penelope: Why is the decline in S. haematobium greater than for *S. mansoni*?

A: *S. haematobium* drops more dramatically after the first round of treatment whereas primary treatment for *S. mansoni* isn't as responsive.

Q for Penelope: Where was the data coming from?

A: They received the data in different formats, ranging from individual level, aggregated at district level (so couldn't geo-locate to lower than district level). NTD portal data is not included.

Q for Jaspreet: Have you compared your model to MDA data?

A: They have access to the data so will start.

Comment from group: Assumptions in the models may not be comparable to what has happened during the SCORE study – the reduction plateaus – so a lot to do to improve the models in this aspect.

Comment from group: Even in school-based treatment only, there was an impact on adults.

3. SESSION 2: WASH AND BEHAVIOUR

a. Mike Templeton, Imperial College, London: Links with the WASH sector

Dr. Mike Templeton provided a summary of his work in WASH and how he is now linking this to schistosomiasis control and elimination through a new project called WISER: Water Infrastructure for Schistosomiasis Endemic Regions.

There are several published papers on WASH impact on schistosomiasis and specific work has been focussed in Ethiopia. Systematic review and meta-analysis shows increasing access are important to reduce the odds of schistosomiasis infection.

However, what does WASH mean and what are the parameters? Mapping of Ethiopia in 2013-14 in 1645 school looked at WASH 'scores' to show the different aspects of WASH factors.

Results showed:

- Whilst *S. mansoni* was strongly associated with water contact, sanitation was not strong associated. This could indicate that there needs to be long term universal coverage of sanitation and hand hygiene.
- Schistosomiasis is unique in WASH needs compared to faecal-oral diseases. This needs emphasising.
- Reducing water contact is the most important aspect: all water needs, e.g. swimming and washing, any recreational, even in small pools, show risks.

Recommendations:

WASH specific:

I. Option 1: reduce water contact – look for protected bore holes or rainwater harvesting
II. Option 2: extract and treat contaminated surface water

- Needs to include occupational (i.e. boots and gloves for fisherman's) or recreational hazards (i.e. chlorinated swimming pools).

- Needs awareness raised on risks, uptake and maintenance through community ownership.

Link with WASH Sector:

- Find out the WASH NGO's and donors who are already in these areas and explain what schistosomiasis is and that it is not the same as other diseases in the transmission.
- Discuss schistosomiasis as a good indicator.

Water and SCH knowledge gaps:

- How to make water safer i.e. design a sand filter
- Water free from faecal oral pathogens – is the WHO standard enough to ensure SCH is not still remain in the water.
- Mapping
- How do we sustainably have community ownership with solutions that are fit for the context?

Discussion/questions:

Q. In the studies in the schools, are there specific methods for monitoring contact?

A. The scores that were discussed in the presentation (a range of scores which monitor different levels of access to sanitation units and the condition of the units etc.) were based on studies that were done in the school; the definitions came through the surveys.

Q. Tech could answer a lot of questions i.e. camera or chips to monitor usage. What do you think are the possibilities to expand the evidence base?

A. Is there a need? Already have the evidence so it is not a priority agenda.

Follow up remark: epidemiologically we would find it useful to know what the age-related specifics are.

b. *Uwem Ekpo, Federal University of Agriculture, Abeokuta, Nigeria: Developing new behavioural change interventions*

Dr Uwem Ekpo discussed how elimination of schistosomiasis will not be possible without human behaviour change. As Nigeria has over 29 million people infected with schistosomiasis it is important to utilise all tools available to reduce prevalence.

- Behavioural change interventions can come in a variety of ways, from building alternative safe water recreation sites for children, to developing educational material using multimedia platforms for children.

- Effective health education should ensure to cover transmission, transmission risks, signs and symptoms, when to seek treatment, deworming options either in school or community, and must be cheap, easy to use and user friendly.

When school based MDA is done, there is persistent prevalence, even after multiple rounds of MDA. This suggests that MDA alone will not eliminate schistosomiasis. Therefore, complimentary interventions must be used. These interventions must be relevant and effective though. Posters, bill boards, radio jingles are expensive and non-interactive.

The development of behaviour change interventions must answer key questions such as:

- what is the objective?
- who is the target audience?
- at what level will the intervention take place?
- what factors currently influence behaviour?
- what is the best strategy to create buy-in?
- how long does the intervention need to continue to achieve desired results?

Summary: The development of board games for health education has shown some success in changing behaviour after 3 months of play. Other local/traditional games can be adapted to support behaviour change. The interventions need to be tailored to local needs and context.

More research is needed to continue to develop behavioural change interventions.

4. SESSION 3: SCHISTOSOMIASIS MORBIDITY AND DIAGNOSIS

a. Dan Colley, University of Georgia: Egg negative/positive schistosomiasis

Prof. Dan Colley highlighted schistosomiasis diagnosis and that as we move forward we expect there will be better diagnostic tools. Newer assays are showing us there are more infections than we thought.

Overview of Schistosomiasis Consortium for Operational Research and Evaluation (SCORE) POC-CCA and UCP-CAA studies:

- Studies show that Kato Katz (KK) - CCA prevalence relationship shows that CCA doesn't come through from 0.
- From about 50% prevalence, both are saying the same thing.
- When moving down the scale, in terms of prevalence, you see much higher prevalence by CCA.

A Bayesian latent class analysis in moderate prevalence area showed that one CCA was good in both sensitivity and specificity, but with KK, sensitivity was low, but

specificity was high. Trace is likely to be positive individuals. CCA comes from the worms whereas KK use the eggs.

The question is should we worry about egg negative SCH?

Batch to batch variation has been observed in the level of sensitivity of POC-CCA. What are the possible prevalence thresholds for KK and POC-CCA? Depends on your goals:

- For morbidity control, gaining control threshold can be between 100-25% by KK or CCA >50%
- For morbidity control, sustaining control threshold can be between 24% - 6% by KK or CCA 20%-50%
- Elimination as a public health problem the threshold can be 5%-1% by KK or CCA 20%-5%
- Elimination defined as 0% transmission the threshold can be <1% - 0% by KK, CCA will show some positives

So modifying current thresholds for *S. mansoni* based on prevalence by POC CCA assay?

I. Gaining: 100% -30% prevalence
II. Sustaining goal: 29% - 16% prevalence
III. Elim as public health problem goal: 15% - 10% prevalence
IV. Elim 0% transmission goal: <10% - 0% prevalence

Conclusion: More sensitive assays find more schistosomiasis but need to determine if those with low intensity are risk of morbidity and contribute to continued transmission. We need to set thresholds in new guidelines for the new assays and they need to be set ASAP when new tools are available and proven useful, which should be realistic and achievable. We need to decide what goal is first and this should be based on using best tools available.

b. *Jutta Reinhard-Rupp, Global Health Institute, Merck: Measuring and treating schistosomiasis morbidity in pre-school age children and women at risk of FGS*

Dr Jutta Reinhard-Rupp highlighted the current issues with Female Genital schistosomiasis (FGS) and that there is no information on morbidity and mortality related to schistosomiasis of the genital tract, though the WHO website does contain info on "genital manifestations of schistosomiasis".

Mapping the publications of FGS between 1899 and 2015 showed that there have been over 100 years of publications on FGS over sub-Saharan Africa and parts of the Middle East and Brazil (publication: "Female genital schistosomiasis (FGS): from case reports to a call for concerted action against this neglected gynaecological

disease. Christinet V, Lazdins-Helds JK, Stothard JR, Reinhard-Rupp J. Int J Para. 2016, 46, 395-404). It's an under-represented disease and we need to raise the awareness of gynaecologists to its presence.

Currently it is hard to know what the burden of FGS is in women. It is estimated to potentially affect between 20-150 million women.

We know that schistosomiasis infections can occur under the age of 2 but generally morbidity information is scarce. The prevalence of FGS varies, from Madagascar 33% to Niger 75%.

So what are we doing at the moment?

- The clinical diagnosis is a gynaecologist examination; this excludes young girls and many women who won't take part in the process.
- Currently prevention is through regular Praziquantel (PZQ) treatment starting in early childhood, including preschool aged children (Pre-SAC).
- For a patient with FGS, there are no validated therapeutic options to treat/cure FGS. We largely don't know what to do, can FGS be reversed?

Summary: FGS must not be forgotten, but we need to understand the magnitude, impact, and pathology. We need to develop and improve diagnostic tools (no markers). Interventions are unclear (other than preventive) and need to be addressed. Finally we need to promote a cross disease approach including community, HIV workers, gynaecologists etc. The WHO got the ball rolling on the dialogue.

The Global Health Institute has created a new gynaecological ward in Cameroon and support the first-year salaries for the new team. This is to build local capacity and basis for potential clinical research on FGS. To develop this, the GHI is fostering partnerships with Centre International de Recherches, d'Enseignements et de Soins (CIRES), Medecin Sans Frontieres (MSF) and others.

Discussion/questions:

It is challenging to design a study, ethically, if we can't treat people. And especially diagnosing and checking children. At the moment, our best tool is treatment, particularly before and beyond the age of 15 in females, which would prevent genital lesions. We need to manage the morbidity associated with schistosomiasis due to chronic infections.

Egg-reduction rates go down a lot faster than cure rates, which means you'll still have some worms which will show positive with CCA (egg negative, worm positive).

c. ***Juerg Utzinger, Swiss Tropical and Public Health Institute & Rubina Imtiaz, Children Without Worms: Soil-transmitted helminth advisory committee update***

Prof. Juerg Utzinger and Dr Rubina Imtiaz presented the outcome of a meeting held on 1-2 Nov by the STH advisory committee. Key developments in the past year are:

- WHO guidelines for treating all at-risk populations;
- WHO inclusion of evidence-informed policy-making and expert advice from across the STH community;
- ESPEN ground-breaking work and country progress;
- Bellagio meeting on treating women of reproductive age (WRA) and ensuing recommendations;
- Inclusion of Ivermectin + Albendazole into the WHO model list of essential medicines.

Draft recommendations:

- Pressing need for a M&E framework tied to clearly defined end points.
- WHO provide further guidance on how to reach WRA and Pre-SAC;
- Need for diagnostics that are appropriate for reaching the decision goals.
- Additionally: use-cases for combination therapies to avoid resistance; align WASH sector for schistosomiasis and soil-transmitted helminths, and in partnership with the WHO draft a "beyond 2020" vision document.

5. SESSION 4: SCHISTOSOMIASIS CONTROL UPDATES

a. Maria Rebollo Polo, WHO AFRO: ESPEN update

Dr Maria Rebollo Polo presented on the Expanded Special Project for Elimination of NTDs (ESPEN) strategy for eliminating schistosomiasis morbidity in Africa. ESPEN has an expanded mandate to help countries to achieve the 2020 and 2025 goals. ESPEN has 4 priorities:

I. Scaling up treatment to 100% geographical coverage (overall in AFRO only 59%),
II. Scaling down (to stop treatment when validation of goals is confirmed),
III. Strengthening information systems,
IV. Improve the utilization of donated medicines (poor reporting and loss of tablets).

In the first year ESPEN supported 32 countries.

Globally only 54% (57% in SSA) of children are being reached for treatment for schistosomiasis and only 13.9% (11% in SSA) of adults at risk.

WHO v.s. ESPEN data system: data uploaded into the NTD portal. The WHO then only reports the national level rather than the regional information that ESPEN has.

The sixth RPRG recommendation on schistosomiasis in the African region highlighted that schistosomiasis is a focal disease but district level leaves out sections of the population.

Challenge: some countries are either not implementing MDA or not reporting.

ESPEN activities:

- Supporting countries to reach 100% geographical coverage;
- Site level data analyses to re-define disease prevalence;
- Refine mapping of schistosomiasis where needed to integrate with other mapping surveys like oncho;
- PZQ projection based on sub-district level endemicity;
- Building capacity of programme managers (PM) on new WHO PM guide on molluscicides to control morbidity in high prevalence areas;
- Impact assessments in countries that have conducted more than five round of MDA.

Other activities: Advocating for WASH and ensuring integration, accelerating at least 75% SAC, and extend treatment to children under 5 and out of school children and adults; coordinating a partners Matrix (where each partner is working).

NTD portal is an open access portal: ntd.afro.who.int

Discussion/questions:

Q. Have you thought of what scale you'd like these results on? How can you formulate a policy at the country level when you have so much heterogeneity?

A. For the epidemiological assessments that are shared through the Portal the countries provide the information they collect according to WHO guidelines on mapping and impact assessment, the methodology is not determined by ESPEN. For the coverage, the countries have site level information in every school and community but so far we are summarising the information by district in the portal.

b. *Lv Shan, Stanford University and NIPD China: China-Africa schistosomiasis collaboration*

Dr Lv Shan presented on the China-Africa schistosomiasis collaboration, an extension of inter-governmental collaboration. Established in 2000, with 51 countries in Africa and African Union and resulted in Beijing Declaration in 2013, which recommends schistosomiasis collaboration.

I. Research community: Network on China Africa Cooperation for schistosomiasis elimination (INCAS) meeting held in April 2015 in Malawi including WHO, China CDC, and Africa countries. This has established networks in nine countries:

- Cameroon,
- Malawi,
- Mali, Niger,
- Sudan,
- Zanzibar,
- Tanzania,
- Zambia,
- Zimbabwe

II. Progress: Malacology workshops through INCAS in Anglophone and Francophone Africa.

III. Case Study: In Zanzibar with Jiangus Institute. Distribution of helminth infections in Zanzibar. In 2014, China, Zanzibar and WHO signed an MOU for schistosomiasis control. The goal is to understand transmission pattern of schistosomiasis in Pemba and to implement control strategies to eliminate schistosomiasis. As well as provision of PZQ and niclosamide in early 2017 China supported the building of a new laboratory with new equipment. This includes a vector lab (for snails) and a testing lab (for diagnostics) and was launched in April 2017. Also includes study of *Bulinus* snails in the lab.

c. *Simon Brooker, Bill and Melinda Gates Foundation: Developing a schistosomiasis action plan*

Dr Simon Brooker highlighted that we need to know what to do after the 2020 goals. A summary of a high-level plan that has been drafted and a framework was presented.

Position of NTDs along a conceptual disease progression framework:

→ Socioeconomic progress & control interventions

→ Intervention capable of bending the curve and breaking transmission

→ End game – end of vertical intervention – disease only exists in small foci.

Schistosomiasis is furthest away from the goal compared to all the NTDs. We need to know how to scale up and push further. Morbidity control is feasible but a transformative intervention is needed to achieve global elimination.

Discussions identified the key actions:

I. Scaling up existing interventions for the max coverage and reach (ensuring full utilisation of donation, enhanced coverage and increased compliance).

II. Taking the existing tools we have and optimising them (revised diagnostics: how do these relate to thresholds and guidelines; optimised MDA: maybe introducing micro-targeting and broadening

MDA; sustain drug efficacy by identifying resistance; develop alternative to PZQ).

III. Introducing new tools (new diagnostics to verify infection, cheaper and safer snail control, develop vaccine). Each relates differently to different transmission settings. Do all of the scaling now – in low settings you can get to very low levels.

Discussion/questions:

Q; who will be doing this? What's the criteria for getting a check mark – is it dollars spent, time in field etc.?

Q. Maybe we need to include columns for major donors –DfID and USAID. Also we need to run with whatever donations we have been given by Merck.

A: You can have some settings we can define now as control others will look at elimination. How and what those implications are needs to be discussed.

A: Done this for each of the NTDs asides Guinea Worm, and where there are synergies, we need to pull those out. E.g. what do to when you stop the lymphatic filariasis programme?

Q. Seems like the vaccine is the solution you'd like to get to. We are down to 5 major vaccine companies. Who is going to determine this?

A: For the vaccines, we need to have very clear business plans. When we invest in a vaccine, we have an end point in sight, looking at modelling etc. developing an investment case.

Q. Elimination with current tools might be possible for japonicum.

A: This is mainly focussed on S. haematobium or S. mansoni due to the sub-Saharan Africa focus of the foundation.

Slides will be available on the GSA website shortly. Please find the meeting agenda below.

MEETING AGENDA

Schistosomiasis control and elimination: next steps

9am – 2pm 5th November 2017

Sheraton Inner Harbor Hotel, Baltimore, US

	Introduction and Group 1 Data & modelling. Chair David Rollinson	
8:30-9:00	Coffee	
9:00-9:10	David Rollinson (Director GSA)	Welcome
9:10-9:25	Jaspreet Toor (Imperial College, London)	Making use of mathematical models to inform programmatic decisions.
9:25-9:40	Penelope Vounatsou (Swiss TPH)	Making use of mapping data to inform treatment needs.
9:40-10:00	**Discussion**	
	Group 2 WASH and Behaviour. Chair David Rollinson	
10:00-10:15	Mike Templeton (Imperial College, London)	Linking with the WASH sector
10:15-10:30	Uwem Ekpo (Federal University of Agriculture, Abeokuta, Nigeria)	Developing new behavioural change interventions
10:30-10:50	**Discussion and Coffee Break**	
	Group 3 Schistosomiasis morbidity and diagnosis. Chair Mike French	
10:50-11:05	Dan Colley (University Georgia)	Egg negative/worm positive schistosomiasis
11:05-11:20	Jutta Reinhard-Rupp (Global Health Institute, Merck)	Measuring and treating schistosomiasis morbidity in pre-school age children and women at risk of FGS
11:20-11:35	**Discussion**	
11:35-11:40	STH Advisory Committee update by Juerg Utzinger and Rubina Imtiaz	
	Group 4 Schistosomiasis control updates. Chair Alan Fenwick	
11:40-11:55	Maria Rebollo Polo (WHO AFRO)	ESPEN update
11:55-12:10	Lv Shan (Stanford University and NIPD China)	China-Africa schistosomiasis collaboration
12:10-12:25	Simon Brooker (Bill & Melinda Gates Foundation)	Developing a schistosomiasis action plan
12:25-12:45	**Discussion**	
12:45-14:00	**Networking & Lunch courtesy of the GSA**	