COR-NTD 2019 Meeting Outputs

Knowledge gaps and recommended next steps identified at the annual meeting of the Coalition for Operational Research on Neglected Tropical Diseases (COR-NTD), which took place in National Harbor, MD, on November 18 and 19, 2019.

Contents

Click on a title to access content directly.

COR-NTD 2019 Meeting Outputs

COR-NTD 2019 Meeting Outputs

Glossary of Commonly Used Terms

Acronyms are defined here for easy reference.

Ab	*Antibody*
Ag	*Antigen*
CCA	*Circulating Cathodic Antigen*
CDC	*U.S. Centers for Disease Control and Prevention*
CDD	*Community Drug Distributor*
CF	*Complement Fixation*
CFA	*Circulating Filarial Antigen*
CHW	*Community Health Worker*
DA	*Diethylcarbamazine and Albendazole*
DBS	*Dried Blood Spots*
EDC	*Electronic Data Capture*
EMCT+	*Eliminating Mother-to-Child Transmission Initiative*
ESPEN	*Expanded Special Project for the Elimination of Neglected Tropical Diseases (WHO)*
EoT	*Elimination of Transmission*
EQA	*External Quality Assessment*
EU	*Evaluation Unit*
FGS	*Female Genital Schistosomiasis*
FTS	*Filarial Test Strip*
GDP	*Gross Domestic Product*
gHAT	*Gambian Human African Trypanosomiasis*
HAT	*Human African Trypanosomiasis*
HCW	*Health Care Worker*
HIV	*Human Immunodeficiency Virus*
HQ	*Headquarters*
IA	*Ivermectin and Albendazole*
IDA	*Ivermectin, Diethylcarbamazine and Albendazole*
IDM	*Innovative and Intensified Disease Management*
IU	*Implementation Unit*
IVM	*Ivermectin*
LF	*Lymphatic Filariasis*
M&E	*Monitoring & Evaluation*
MDA	*Mass Drug Administration*
Mf	*Microfilaria*
MoH	*Ministry of Health*
MX	*Molecular Xenomonitoring*
NGO	*Non-governmental Organization*
NTD	*Neglected Tropical Disease*
OEM	*Onchocerciasis Elimination Mapping*
Oncho	*Onchocerciasis*
OR	*Operational Research*
PAHO	*Pan American Health Organization*
PC	*Preventive Chemotherapy*
PEP	*Post-exposure Prophylaxis*
PKDL	*Post Kala Azar Dermal Leishmaniasis*

PCR	*Polymerase Chain Reaction*
POC	*Point of care*
PNG	*Papua New Guinea*
PVS	*Post-validation surveillance*
QA	*Quality Assurance*
QC	*Quality Control*
RANAS	*Risks, Attitudes, Norms, Abilities and Self-regulation*
RDT	*Rapid Diagnostic Test*
ROI	*Return on Investment*
RUSTA	*Rapid Urban Schistosomiasis and Trachoma Assessment*
SAE	*Severe Adverse Event*
SAFE	*Surgery, Antibiotics, Facial Cleanliness and Environment*
SCORE	*Schistosomiasis Consortium for Operational Research and Evaluation*
SES	*Socio-economic*
STH	*Soil-transmitted Helminthiasis*
STI	*Sexually Transmitted Infection*
SWIFT	*Sanitation, Water and Instruction on Face-washing*
TANT	*Test and Not Treat*
TF	*Trachomatous Inflammation – Follicular*
TAS	*Transmission Assessment Survey*
TB	*Tuberculosis*
TIS	*Trachoma Impact Survey*
TPP	*Target Product Profile*
TSS	*Trachoma Surveillance Survey*
TT	*Trachomatous Trichiasis*
UHC	*Universal Health Coverage*
USAID	*U.S. Agency for International Development*
VL	*Visceral Leishmaniasis*
WASH	*Water, Sanitation and Hygiene*
WHO	*World Health Organization*

COR-NTD 2019 Meeting Outputs

Lymphatic Filariasis

Accelerating the elimination of lymphatic filariasis using Ivermectin, DEC and Albendazole (IDA): applying lessons learnt from 5 early adopter countries

Knowledge Gaps

Attendees gathered in small groups to identify research gaps listed below around the underlined thematic areas.

Low Coverage and failed-TAS settings

- What are the best practices in DA/IA MDA areas (and IDA areas with data) and which are most cost-effective?
    - What framework can help us identify best approaches to implementing MDA (regardless of regimen) and achieving high coverage?
- What are the messages about ivermectin that spread most effectively throughout communities?
- How to address obvious systematic non-compliers (e.g., higher SES populations), what different approaches are needed to reach them?
- What are motivating factors for people taking DA that can increase coverage for IDA and DA in other areas?
- How can tools be revised to better measure coverage in urban areas or areas where the total population isn't known?
- In Brugia areas, is there something biologically happening to cause TAS failures?

MDA with IDA after persistent/hotspot infection

- Are there differences in response to IDA among worms or among humans? (i.e. variable drug sensitivities and what are the factors associated with the observation)
- Are remaining infections post-IDA persistent infections, re-infections or non-compliance?
- Can a focalized systematic non-compliant population sustain transmission in hotspots?
- Is there any way to strengthen coverage surveys to assess true ingestion of medicines in addition to self-reporting?

Hard-to-Reach Populations

- How do we define hard-to-reach? Are these the same as systematic non-compliers or just those that are hard-to-reach operationally? This is an important distinction, as it will influence the intervention used.
- How do we know who we are not reaching? It is hard to know who is being missed and why they are being missed.
- If there is inadequate census/demographic data, it is difficult to ascertain whether we are reaching individuals who may be contributing to the disease burden or who are vulnerable to infection.
- What extent of the total disease burden is carried by these hard-to-reach populations?
- What are the best approaches for reaching these populations? These will likely have to be tailored/targeted based on the population and why they are hard-to-reach.

- Are there incentives we can use to identify and encourage hard-to-reach populations to accept and consume medicines during MDA?
- Are there national or local systems that successfully identify and reach hard-to-reach populations that could be a useful platform to use with MDA?

End Points, When Can You Stop?

- More longitudinal cohort studies of persons who cleared Mf and/or from areas where IDA MDA was performed would provide useful insights for stopping MDA
- Need to better understand the relationships between Mf, CFA, and antibody prevalence post-IDA and the thresholds necessary for stopping MDA
- What new biomarkers would improve the probability of making the correct stop IDA decision?
- What are the differences in effectiveness between test & treat versus a round of MDA? Do differences change depending on the setting? Could one strategy be more effective in hot-spot/hard-to-reach areas versus the strategy that is most effective in the general population?

Recommended Next Steps

- In populations that have participated in IDA rounds, explore perceptions of an enhanced MDA and the added value of including ivermectin as compared to the standard two drug regimen. Identify the best practices that could be implemented in other localities using IDA MDA.
- Identify health care delivery platforms that have high population coverage to traditionally hard to reach individuals and explore these platforms as potential avenues to provide awareness about and/or to conduct MDA.
- In populations that are hard to reach, conduct research to understand prevalence of systematic non-compliance, health care seeking behavior as well as assess for risk of infection based on exposure to vector.
- Costing studies on the comparative savings (or not) of using IDA in an enhanced high-quality MDA with fewer rounds rather than a longer timeline with standard MDA using DA.
- Two types of cohort studies could provide additional insight related to stopping MDA:
    - A longitudinal cohort study that would follow persons who cleared Mf without clearing CFA after IDA treatment. Ideally people would be followed for at least 2 years following treatment (without retreatment) to determine the frequency of Mf recurrence. The study should be powered to show the rate of recurrence is less than 2% over two years with 95% confidence.
    - A cohort study performed in an area where two rounds of IDA have reduced Mf prevalence so that the upper 95% confidence interval for the estimate is no higher than 2%. Young school-aged children (ages 6-8) who are FTS negative would then be followed for two years to assess incidence rates for FTS and anti-filarial antibodies. The study should be powered to show the rate of seroconversion is less than 2% over two years with 95% confidence.
- Modeling studies to examine relationships between Mf, CFA, and antibody prevalence or clearance post-IDA for identifying a threshold that could indicate interruption of transmission.
- For areas with persistent LF despite seemingly adequate MDA and success in most parts of an EU, it would be interesting to compare the impact of 3 different interventions for managing the

"hotspot" (e.g. one additional round of MDA vs. one round of targeted MDA to subgroups in the EU with higher CFA and Mf rates (often adult males) vs. a test and treat program focused on high risk subgroups.

- Studies to assess the impact of IDA on parasite DNA rates in mosquitoes, particularly in areas with Brugian filariasis. Currently supported studies are all in areas with bancroftian filariasis.

Alternative surveillance and response strategies for lymphatic filariasis elimination: lessons learnt from the Pacific

Knowledge Gaps & Recommended Next Steps

Knowledge/implementation gap	**Priority next steps/research questions**
Detection, definition, and importance of hotspots	
<u>Definition of hotspots and 'hot populations'</u> - Hotspots can be defined in terms of geography, demography, thresholds for prevalence in vectors vs people (and depending on what marker of infection in people) - Which monitoring tools are most relevant for the detection of hotspots? - What level of prevalence is important for transmission/resurgence at the local level and at a programmatic 'public health problem' level? - At what geographic scale should hotspots be defined? E.g. household level vs village level. - What is the appropriate geographical scale for response to hotspots?	<u>Definition of hotspots and 'hot populations'</u> - Work to develop a geographic element (perhaps varying by context) in the definition of a hotspot - Consider a demographic element to a definition of a hotspot - Consider whether hotspot definition should be based on MX, CFA, Mf, and/or Ab, and if so, at what levels of infection indicators? - Develop definitions of 'hot populations' that are useful for the context – and identify whether these vary across settings. This may be very helpful as a first step in describing and informing appropriate response strategies - Investigate the characteristics of a hot population: low participation in MDA, efficient vector, and/or increased likelihood of exposure?
<u>Understanding importance of hotspots in terms of ongoing transmission and resurgence</u> - When is a hotspot is a public health problem or at risk of leading to resurgence which would become a public health problem?	<u>Understanding importance of hotspots in terms of ongoing transmission and resurgence</u> - Model how the presence and attributes of a hotspot relate to its risk for ongoing transmission and risk of resurgence, and test the predictions over time where empirical data are available
<u>Understanding why a hotspot is a hotspot</u> - In terms of environmental, vector, demographic, compliance, geographic factors. This will help identify and predict hotspots	<u>Understanding why a hotspot is a hotspot</u> - Conduct multivariate spatial and risk factor analyses to determine the environmental, vector, demographic, compliance and geographic factors (and their combinations associated with hotspots, for

- How can we predict hotspots in areas that have not been sampled, and assess the role of unidentified hotspots?

regions/countries where these data are available, and examine novel modelling methods for doing so
- Conduct retrospective follow-up of individuals previously identified as antigen positive (or negative) to assist in identifying risk factors for infection and identifying hotspots (or what is not a hotspot)
    - Include areas not previously sampled to identify other potential hotspots, especially but not limited to situations where hotspots have already been found.

Determine if there are proxies or predictors that could help identify such previously unidentified hotspots or those in areas not sampled.

Molecular xenomonitoring

More information is needed regarding the role of xenomonitoring (MX) during TAS and PVS and how to best conduct MX:

<u>Interpretation of MX findings (and informing sample size requirements)</u>

- What further evidence is needed for a combined TAS/xenomonitoring?
- Does an infectious vector always mean that transmission is ongoing?
- What is the efficiency of the vector to become infected with LF parasite? Does this vary by species? This is important to determine the sample size necessary for mosquito collections and may assist in interpreting how positive MX results relate to human infection
- What thresholds should be used to define ongoing transmission? Should this vary by vector and parasite species?
- More comparison between human and xenomonitoring surveys is needed.
- Gaps in understanding the relationship between MX, results and CFA, Ab and Mf results in humans.
- Does vector biomass have an important role in transmission?

<u>Interpretation of MX findings (and informing sample size requirements)</u>

- In areas where side by side human /MX surveys have been done, compare and analyse the relationship between mosquito and human infection. (also see ‘alternative surveillance strategies)
- Conduct more combined studies of TAS/community human studies and MX together.
- Review literature and conduct studies to determine the efficiency of different vectors to become infected with LF parasite.

COR-NTD 2019 Meeting Outputs

Mosquito collection methods - What types of traps are best for each species? - When is the best time to collect mosquitoes? Should this be based on season, timing of IRS, etc?	Mosquito collection methods - Compare existing data and/or data on mosquitoes collected for different purposes or programs, and/or undertake mosquito collection at different times to determine best times to collect mosquitoes. - Use existing data/evidence and/or conduct trials of different collection methods in settings with different vectors to determine most efficient methods of collection for different vectors.
Mosquito processing issues, efficiency and cost effectiveness - When is speciation necessary? This is important because it may be more efficient in terms of human resources and expertise not to speciate and may increase the feasibility of MX - How does the cost effectiveness of speciating vs not speciating compare?	Mosquito processing issues, efficiency and cost effectiveness - From available studies, compare results obtained when combining all mosquito genera (e.g. all *Anopheles* in PNG and all *Aedes* in the Samoas) or distinguishing by species. Does this vary by setting depending upon the species present? - Develop and test simplified PCR processing to make it more accessible and less requiring of specialist expertise - Form regional agreements to increase number of PCR facilities that may be more accessible to countries with LF

Alternative response strategies (i.e. how to respond to CFA-positive people identified in surveys, hotspots, recrudescence)

Reaching hot populations - These populations have high prevalence and/or low participation in MDA, so may provide a reservoir of infection enabling ongoing transmission and resurgence	Reaching hot populations - Investigate and compare (by modeling and testing on the ground) ways to reach and engage 'hot populations' in MDA uptake to determine which are most effective and efficient
Response to identified hotspots - Once a hotspot has been identified, there are currently knowledge gaps about the response required in order to prevent ongoing transmission and elimination of LF as a public health problem - The programmatic feasibility of different response strategies	Response to identified hotspots - Once identified, what should be the programmatic response to hotspots? Is a response always required or is it dependent upon the scale (i.e. household/cluster of households/village-level/region)? E.g. further testing and individual treatment of individuals/ localized MDA? What further surveillance should occur following identification of a hotspot?

COR-NTD 2019 Meeting Outputs

	- What response is programmatically feasible at a hotspot (are there resources to undertake individual test and treat or MDA of a whole village? Which response would be more feasible, effective and cost effective?)
<u>Impact of positive people and ineligible populations (e.g. pregnant women) on ongoing transmission</u> - Antigen positive people and groups ineligible for MDA may serve as important sources for ongoing transmission, but the extent of this is unknown	<u>Impact of positive people and ineligible populations</u> - Those ineligible for MDA should be included in surveillance - Is it important to treat CFA (and Mf) positive people, but also investigate local test and treat responses to limit potential for ongoing transmission? This includes testing how broad the test and treat response should be i.e. the household of the CFA and/or Mf positive person? Surrounding households?
<u>Response strategies tailored for different settings</u> - It is not known if different response strategies are required for different settings.	<u>Response strategies tailored for different settings</u> - Model the best response strategy for a setting to determine whether this varies by setting and if so, what criteria/spatial factors are important in identifying best response strategy
<u>Learning from other disease control programs</u> - There may be opportunities to learn from other public health disease control programs on ways to eliminate LF, especially once prevalence becomes low and heterogenous	<u>Learning from other disease control programs</u> - Review other disease control programs to determine lessons that can be learned and/or potentially trialed or applied to LF elimination.
<u>Surveillance activities following different response strategies</u> - It is not known if the type of surveillance should vary depending upon what response strategy has been used to limit ongoing transmission	<u>Surveillance activities following different response strategies</u> - Link surveillance strategies to the type of response strategy used. E.g. following identification and response to a hotspot, investigate what surveillance should be prospectively undertaken and whether this should vary from the standard surveillance
<u>Cross-border transmission</u> - It is not known whether there may need for tailored response strategies if there is suspected or potential cross-border transmission	<u>Cross-border transmission</u> - Review data from neighboring areas where there is potential or suspected cross-border transmission and data available from both sides, to investigate what combined

surveillance and response strategies are indicated.

Decision-making process

- It is unclear what process should be undertaken to make decisions (i.e. recommendations) on key programmatic actions, e.g. surveillance and response under situations of uncertainty and imperfect evidence. It is unclear how new evidence (e.g. those presented in this session) and expert opinion (e.g. when there is no or limited evidence) should be considered and acted upon, and taken into account when updating recommendations.

Decision-making process

- Develop explicit and transparent decision-making process to decide upon response and surveillance strategies tailored for different scenarios with varying levels of uncertainty, with a decision-making tool/framework to assist in thorough consideration of important elements. The process should take into account risks, potential impact of action/inaction, missed opportunities, and be able to adapt to new information as it becomes available. Other considerations include the precautionary principle, benefits vs harms, resource use, values and preferences, acceptability, and feasibility.
- Ideally, action should be evidence-based, but what do we do if there is no robust evidence? Or if there is high uncertainty about available evidence? Whilst waiting for evidence to be generated, how do we best incorporate expert opinion into decision-making? How do we prioritise what evidence is most urgently needed?
- Do we need operational research on decision making under uncertainty? What are the barriers to decision making? What type of support would decision makers find most useful? How do we best deal with setbacks, and how do we use them as opportunities to learn and improve?

Turning lymphatic filariasis survey failures into success

Knowledge Gaps

Small groups discussed the identified the following additional methods that could be explored for use after pre-TAS or TAS failure.

- Geo-narratives which work with community members to conduct geographic storytelling
- Community based participatory research
- Photo voice and pictorial diaries
- Clinical history - creating a history of the individuals testing positive, including information on social norms

- Collect simple and rapid qualitative feedback from colleagues working in other NGOs outside the NTD space
- Add qualitative questions to the supervisor's coverage tool (used during MDAs) and to coverage evaluation surveys (conducted after MDAs).
- Add 1 or 2 questions to pre-TAS surveys
- Conduct targeted educational follow up *(learnings from malaria programs: persons refusing indoor residual spraying are identified and teams follow up with targeted information on the spraying)*

Recommended Next Steps

Next steps should include a systematic review of these methods and based on that a preparation of tools and approaches for large-scale dissemination for use by global programs on NTDs.

COR-NTD 2019 Meeting Outputs

Onchocerciasis

Entomology for Onchocerciasis: Current Guidelines and Gaps

Knowledge Gaps & Recommended Next Steps

- How many vector collection sites are needed to determine that a transmission area can stop MDA? How do programs determine the size of the transmission areas represented by each breeding site? Should vector collection sites be dispersed across the entire area or only in first-line communities? Operational research is needed.
- What are strategies or best practices to prevent, detect, and treat recrudescence? How can we differentiate recrudescence of transmission from imported infection, especially when migration may play a role in recrudescence? Operational research to determine thresholds for restarting treatment after cessation of MDA is needed.
- Hot spots will be a challenge for programs.
    - It may be unwise to stop MDA in only a portion of a transmission zone when transmission is occurring within close proximity to the area, but distant breeding sites are unlikely to have fly populations that intermingle. It may be an option to stop MDA when an area is surrounded by a buffer zone) in which transmission is not occurring or has been interrupted. For example, if there is a zone that is equal to 2 times the average flight distance of the local vector where treatment is continue but where evaluation indication lack of transmission. Operational research to determine how program could establish buffer zones would allow programs to stop in some areas and focus resources those areas with continued transmission.
    - Intensive study of the hotspot in Ethiopia, including entomologicial indicators, could provide value information to the many other programs considering a similar approach to stopping MDA.
    - Hotspots may also provide an opportunity to examine the role of systematic non-compliance in maintaining transmission.
    - An alternative strategy for hotspots would be a test and treat strategy, but that would require an individual diagnostic for patent infections that is sensitive in populations treated with ivermectin (e.g. detection of adult worms).
- More work on identification of breeding sites in hypoendemic areas is needed. These breeding sites are not well-mapped and may be more challenging to identify because they are often small and/or only exist seasonally. What are the environmental characteristics that are conducive to these sites? Can satellite imagery be used to assist in identifying these sites?

Ethics & algorithms: the way forward for onchocerciasis elimination in *Loa loa*-endemic areas

Knowledge Gaps & Recommended Next Steps

The breakout session split into two groups. The first discussed what OR questions need to be answered to ensure that TaNT can be applied in a programmatic setting, and the second discussed how we shrink the map to determine where TaNT needs to be performed. OR questions which need to be answered to ensure that TaNT can be applied programmatically:

COR-NTD 2019 Meeting Outputs

- What is the best approach to identify people in need of testing year after year?
    - Options suggested: Tablet-based, paper-based, biometrics
- Effect of forecasting LoaScopes on the efficency of TaNT
    - What is the ideal number of LoaScopes?
    - What is the impact of incoming children, migration and systematic non-compliers?
    - When deploying Loa TaNT, should oncho also be tested for using the RDT (or DBS), and could community teams do this, so that patients negative for onchocerciasis are not treated?
    - Is there a need to re-map in districts that are partially treated?
- Coverage and Compliance
    - What is the impact of previous SAEs on coverage in a district?
    - How does the LoaScope allow for increased coverage?
    - How do we optimize coverage in hypo-endemic areas?
        - What is the impact of social mobilization?
        - Does integration with other diseases/programs increase coverage?
    - What are the current barriers to high coverage in co-endemic areas and how can we increase acceptance?
    - How does TaNT affect compliance in areas which are highly endemic for *Loa loa*?
    - What is the desired coverage of TaNT to hit desired elimination goals?
- Cost:
    - What are the costs of TaNT s and how would they change over time?
    - What is the cost/benefit to the overall oncho elimination program of not doing TANT?
        - Do hypo-endemic oncho areas go away?
        - Do they worsen (become meso-endemic)?
        - Do they re-infect neighboring meso-endemic areas?
    - What adjunctive strategies could be used and what are their costs (ie doxy)?

The proposed strategy for "shrinking the map" is to combine existing knowledge, geostatistical inference, adaptive mapping, and new sampling using the LoaScope and Loa RDT to exclude areas where Loa loa is not endemic and therefore TaNT is not needed and IVM MDA can be performed. The key OR questions which this approach seeks to address are:

- What is the relationship between Loa RDT village-level prevalence and the presence of high mf individuals in those communities as measured by the LoaScope?
- How can we combine information from the RDT and LoaScope to find a cost- and resource-efficient way to map for loiasis non-endemic areas where people feel comfortable treating?

The exclusionary mapping strategy proposed is, for a country with *Loa loa*:

1. Exclude areas where *Loa loa* transmission is not possible:
    a. Map the vector (*Chrysops*) to determine which areas could not have *Loa loa* based on environmental covariates and can therefore be excluded
2. Exclude areas where *Loa loa* is not endemic:
    a. Utilize existing data from across diagnostics to create a map that determines in which areas IVM MDA would be safe, unsafe and of unknown safety
    b. Adaptively sample in areas of unknown safety: Sample using 200 villages in a country and test all of them with RDT, as well as testing a subset of those with LoaScopes (at a rate limited by their availability)

3. Exclude areas where oncho is not endemic:
    a. Include ongoing data from OEM
    b. Potentially add an oncho testing component to determine if oncho is truly endemic in the areas thought to be hypo-endemic and therefore being targeted.

Note: Selection of the country in which to test this strategy should keep in mind that as an exclusionary strategy, it needs to have non- and low- endemic areas

COR-NTD 2019 Meeting Outputs

Schistosomiasis

Optimizing focal interventions for schistosomiasis

Knowledge Gaps

- How are the WHO protocols taking diagnostics with varying sensitivity into account?
  This has been discussed by the group. We are open for a rapid diagnostic test to come which can be used.

- For the ESPEN approach, as sampling strategies involve some error, have calculations been done to see if subdistrict errors are smaller than district level errors?
  Sampling 5 sites per district. They are looking at how representative this is for the site to see how confident they can be in making the next steps.

- Will vector mapping be incorporated as there is currently an absence of snail mapping that has been mentioned?
  Countries that have snail mapping data were able to exclude areas that they had not seen the disease in.

Recommended Next Steps

Two groups were formed to discuss the WHO protocols and the WHO ESPEN data approach.

<u>Actions and gaps identified in the WHO group:</u>

- Can we re-assess the treatment strategy before waiting 5-6 years?

a) There is evidence from recent SCORE studies that the treatment strategy can be re-assessed sooner than the WHO recommendation of 5-6 years (for example, using year 3 prevalence).
b) NTD Modelling Consortium work has shown that not all settings (particularly lower prevalence settings) need 5-6 years annual treatment before reaching morbidity control/elimination as a public health problem if there has been good coverage and adherence so re-evaluation could be done earlier in such settings.

- How is non-endemic defined?

There needs to be a clear definition of non-endemic so we know how to classify these areas.

- We need to ensure that we are not always sampling the same areas and that we are not excluding non-endemic areas completely.

There are concerns around only surveying endemic communities.

- How will old Kato-Katz data be compared to new CCA data?

- The WHO working groups for the protocols still have work to do and the protocols need further clarification before they can be implemented in the field.

COR-NTD 2019 Meeting Outputs

Actions and gaps identified in the WHO ESPEN group:

- In terms of refining data, when is in depth mapping required? Is it more cost-effective to use current data or collect new data?

a) *Defining areas where there is a benefit to collecting more data through midterm assessment, for example IUs with poor quality data or high starting prevalence.*
b) *When is it appropriate to use the dataflow strategy to assign treatment and when is more in-depth mapping required?*
c) *When is it more cost effective to use the data flow map or to collect new data?*

- It is costly to collect data. What is the best way to compile local knowledge?

- How accurate is local knowledge? Can the relationship between qualitative local knowledge and survey prevalence be modelled to validate?

- Is it possible to integrate data from frontline health services to the dataflow strategy?

- Is it possible to follow the suggested dataflow when there are no shapefiles for a country's subdistricts?

COR-NTD 2019 Meeting Outputs

Schistosomiasis & Trachoma

Re-assessment of the distribution of schistosomiasis and trachoma in urban areas in order to improve interventions targeting both disease in sub-Saharan Africa

Knowledge Gaps

- Urban vs. peri-urban: need a clear definition of each and how they are different. This definition will likely be different in different contexts. Experts have suggested that there is not a global definition so this also needs to be considered.
- Are there common approaches being taken to collect data in urban environments?
- In order to map in urban areas, we need to know:
  a. Evidence of endemicity from rural areas
  b. Connectivity to endemic rural areas
  c. Other evidence suggestive of urban endemicity (e.g. desk review, hospital records)
  d. Level of migration
  e. Where to sample – schools or households?
  f. Proximity to freshwater bodies that might harbor intermediate snail hosts
  g. How can geospatial predictions and/or satellite imagery help inform sampling strategies?
  h. How to measure migration and connectivity?
  i. What urban data are available through other programs (Ebola, malaria)?
  j. What will be the unit of sampling and implementation for each disease?
  k. WASH questions related to both diseases?
- Are there common approaches to set up urban intervention structures and/or reach urban populations?
- Identification of areas at risk for both diseases: distance to water bodies, water used for various activities, and movement of people between rural areas and cities

Recommended Next Steps

- The factors maintaining the prevalence of schistosomiasis in urban environments need to be resolved. How is schistosomiasis introduced into urban areas, how does transmission vary in different settings and how likely is reinfection? What lessons can be learnt from LF and other NTDs?
- Knowledge on trachoma urban endemicity is limited and variable. Further work on determining whether trachoma (TF and TT) is a public health problem in urban settings is needed, including identifying routine data sources available to support health ministries identify that trachoma may be a public health problem (e.g. hospital reports of TT surgery). If trachoma is a public health problem, factors maintaining the prevalence of trachoma in urban environments need to be resolved.
- What control interventions, in addition to preventive chemotherapy, can be used in the urban setting, what would be the role of behavioral change, WASH and for schistosomiasis - snail control? In addition, what morbidity management interventions can be used in urban settings – e.g. organization of TT surgery for trachoma.
- If urban health centers were to play a key role in diagnosis and treatment, what extra training and capacity building might be required? Is there a process to ensure praziquantel/azithromycin are available in urban health centers?

- It was concluded that it was best to optimize the assessment for each disease separately and then assess the feasibility of combining the two assessments into a RUSTA. Test in nominated cities whether the proposed RUSTA method to assess the distribution of schistosomiasis and trachoma is feasible and whether integration provides benefits.

COR-NTD 2019 Meeting Outputs

Trachoma

Alternative strategies to reach WHO elimination of trachomatous trichiasis as a public health problem

Knowledge Gaps

- How should geostatistical approaches be used to generate more precise TT prevalence estimates (or similarly precise estimates at lower cost)?
- How do you organize and execute the case finding in a cost-effective, efficient and consistent way that will also ensure that the MoH (and WHO) is confident that elimination as a public health problem has been achieved?
- How to document full geographical coverage for purposes of demonstrating elimination?
- How do we move from good case finding to ensuring that the potential cases get a service?

Recommended Next Steps

Geostatistical Approaches

- Examine the spatial correlation distance of cluster-level TT data at different time-points, and in different countries, using data collected using standardized approaches by the Global Trachoma Mapping Project and Tropical Data. Data from Mozambique and Nigeria present particular opportunities.
- Convene a policy dialogue to determine (a) how confident we should be that TT prevalence is below the 0.2% elimination threshold for validation of elimination of trachoma as a public health problem; and (b) for what population size range we should allow TT prevalence estimates to be generated.
- Determine whether geostatistical approaches can be used to guide sampling locations for surveys in real time. (NGO partners supporting programmes in Amhara and Oromia, Ethiopia, both expressed interest in participating in a trial.)
- Undertake similar analyses for TF and anti-Chlamydia trachomatis seropositivity, expecting that the spatial correlation distance would be considerably smaller.
- Consider whether the geostatistical approach could also be applied to post-validation surveillance.

Case Finding

- Compare different models of case finding and surgical camps in order to understand the cost drivers, the effectiveness and completion of geographical coverage and patient loss to follow-up. With the wealth of data available this may start with a desk review.
- Consider confidence in available data. How can we validate case finder documentation? What needs to be understood if a program reports 100% geographical coverage but a survey shows a district to still be above elimination threshold? There is an ongoing study to understand the 'mismatch' i.e. the discrepancy between survey findings and program or interview findings.
- Are there electronic means to better manage data and understand where to target/follow-up patients?

Documenting full geographic coverage

- Examine difference between CF coverage and surveys.

- What minimum coverage is needed of households for TT elimination thresholds? For example, to be below 0.2%, how many houses don't have to be seen?
- What triggers repeated case finding? What time frame is needed before the dossier? And what are the geographical areas?
- Best practices for documentation are based on country-specific examples, which come from country representatives (not just HQ staff).

From case finding to service delivery

- Short intervals are needed between case detection and management.
- Complete documentation linking case identification to services.
- Where possible, use electronic data capture with a build-in alert.
- CF role must include reminding detected cases to attend the service on the day when the TT surgical camp is conducted.
- Bring services closer to the community where the intervention is needed.
- Need an effective plan from case detection to case confirmation and management
- Ensure quality service delivery as a preferred practice. This includes proper outreach, planning, effective health education, and proper counselling.

Workflow analysis of TT case management during service delivery may minimize number of people dropping out.

Eradicating trachoma by 2030?

Knowledge Gaps

- How do we reach targets and targeted populations amidst insecurity, migration? How do we ensure we are getting consistent coverage and surveys are accurately determining prevalence?
- What existing or new tests of infection would be needed if we moved to eradication of trachoma as the global goal? What are the required target product profiles of tests to support monitoring of progress towards and attainment of interruption of transmission?
- How do we better understand communities that remain hyperendemic? Do we need to look into other social determinants of health, co-morbidities and their impact on SAFE effectiveness?
- What new strategies or targeted interventions might be required for districts with persistent TF prevalence above 5%?
- How can we better inform decision-making around districts that stop treatment and are around 4.99%? Or those neighboring areas of high infection?
- What does eradication look like as not everyone has symptoms or signs? How will we know it is truly gone?
- Are there alternative indicators that should be incorporated into surveys?
- How do we better understand countries where progress is slow and protracted?
- Would an eradication goal require changes to the SAFE strategy?
- Would an eradication goal require a vaccine effective against *C. trachomatis* infection?
- What messaging would be required to donors and global partners to convey the change in targets?

COR-NTD 2019 Meeting Outputs

Recommended Next Steps

- Identify learnings from the Stronger SAFE and SWIFT trials around WASH interventions and adherents to WASH
- Conduct operational research on districts-in-waiting – those that have passed impact surveys but are near districts that still require interventions. What's the risk of re-introduction of infection with subsequent recrudescence of disease?
- Conduct operational research on routes of transmission
- Conduct cost modelling for eradication, what would it take to move from control to eradication financially?
- Conduct OR on hot spots or "islands of supercriticality" – areas of high disease prevalence where trachoma appears to be refractory to interventions
- Support efforts to develop a vaccine effective against *C. trachomatis* infection

Trachoma surveillance: are countries prepared to sustain elimination goals?

Knowledge Gaps & Recommended Next Steps

- The 2018 WHO serology meeting concluded that there is a need for further study before serology is used for post-validation surveillance.
    - Collection of data in the following settings should be prioritized:
        - Moderate to high TF prevalence pre-intervention
        - Settings where individuals and populations can be followed longitudinally
        - Settings with unexpected discrepancies between TF, infection, and serology (excluding Melanesia)
    - Populations with high likelihood of recrudescence should be sampled first.
    - Studies should be conducted on the potential contribution from urogenital chlamydia and how to interpret serology in such areas.
- Further research is needed to inform recommendations for PVS systems.
    - Is it necessary to conduct PVS in all districts?
    - Should districts be targeted based on empirical evidence (e.g. previous TIS or TSS with TF ≥5%, low uptake of F and E) and/or modeling?
    - We can compare alternate sampling methods with repeat TSS surveys conducted after validations. Alternate surveillance methods should be at least as sensitive as TSS and no more resource intensive.
    - Is it appropriate to conduct surveillance on the EU level or are there other options? Is it useful to consider surveillance on a sub-district level?
- There is a need for operational research on recrudescence.
    - How do we define recrudescence? How can we detect a real signal versus noise?
    - What is an acceptable interval of uncertainty for measuring recrudescence?
    - What should the threshold be for restarting MDA after validation of elimination?
    - How long must PVS/monitoring for recrudescence continue?
    - Which metrics should be used to determine whether recrudescence has occurred?
    - Can F and E metrics predict recrudescence?

  - Whenever possible, multiple indicators (serology, TF, infection) should be included in OR studies.
  - How should non-endemic areas surrounding endemic districts be considered in assessment of recrudescence?
  - It is important to consider nomadic populations or other special populations when monitoring for recrudescence.
- Further work on the 5% TF threshold is needed.
  - Does TF ≥ 5% indicate recrudescence in a post-MDA setting?
    - Operational research studies can monitor villages with small increases in TF prevalence to determine whether this indicates recrudescence.
  - Does TF < 5% mean that transmission has been interrupted?
    - A systemic review of existing data could suggest whether this is an appropriate threshold.
  - Does interpretation of TF prevalence vary by how well F and E have been implemented in the area in question?
  - Should there be a minimum threshold for F and E implementation? If so, how should we monitor behavior change?
- Further modeling work is needed for serology data.
  - There is a need to enhance the existing model for predicting serologic outcomes.
    - This can be done initially with existing data. Will this model be able to predict recrudescence?
    - Data to add to the model:
      - Data from different program stages
      - Longitudinal data in kids
      - Community-level prevalence indicators over time
  - How can modeling help us target opportunities to measure recrudescence/understand the length of time that monitoring needs to continue?
- More evidence is needed before serology can be implemented programmatically.

COR-NTD 2019 Meeting Outputs

Other NTDs

Enhanced case detection and skin NTDs

Knowledge Gaps

- ***'Basic pictorial tool / algorithm'*** for screening and diagnosing skin NTDs and common skin diseases (guide and simple training module), and 'red flag' signs. Possible use of digital health/teledermatology.
- ***'Essential care package'*** would be needed with simple definitions and characteristics of the relevant disabilities and complications, tools for assessment and guidance on management/treatment. Treatment cost of skin diseases need to be assessed.
- ***'Traditional and novel diagnostic tools'*** both would be needed. For skin NTDs amenable to MDA, diagnostic tools with wider margins of sensitivity or specificity will be generally acceptable – International Alliance for the Control of Scabies (IASC) criteria for scabies provide a good example.

Recommended Next Steps

Operational research will include:

- How best to validate different training materials/strategies and their impact on case detection and/or management?
- How to optimize the use of CHWs to improve early case detection of skin NTDs to achieve the best results?
- Which algorithm combining existing methods work best in diagnosing skin NTDs?

There is an urgent need to take an inventory of available guides/aids/tools on skin diseases to allow the development of a consolidated training document/tools that can be universally used or adapted regionally to support the work of CHWs, HCWs, lab technicians, etc. Logical integration, health promotion on skin health, and access to treatment for all skin diseases are essential for success in enhanced case detection and management of skin NTDs.

Innovative, integrated and standardized approaches in mapping IDM diseases

Knowledge Gaps

- We need better understanding about where models have been applied effectively and how to improve integration between models and data collection on ground.
- Quality of data and predictions
- Challenges of communicating academic-oriented results to programs and engaging programs in process of model development
- Unrealistic expectations of what models can provide
- Need for further ground validation data to improve models and understand limitations
- What are the barriers/facilitators to health-seeking behavior?
- Are diagnostic tools and visual inspections only sufficient?
- There is a need to come up with a framework to operationalize integration.

Recommended Next Steps

- Models should be used to direct data collection and data should be used to improve model prediction.
- Models should not be used on their own in the absence of data.
- Develop feedback and communication between field activities and models to ensure models are data-driven and field activities use model data appropriately
- Improved evaluation of the predictive power of models
- Identification of new sources of data to fit and validate models iteratively
- Identification of the uses and objectives of models at different phases of understanding transmission and steps between control and elimination
- Further research on where and how models have been applied most effectively
- Research on integration and applications across diseases
- Need to develop capacity locally to support model development as well as interpretation of results
- Validate models
- Integration of the health system at the community level
- Validation of the mapping vs. actual survey results and what are the ways to do so?
- Overlay the healthcare capacity (access to care, healthcare worker per population, training, community education, etc.) vs. the disease and understand how/how much the healthcare capacity has impact on prevalence of disease(s).
- What are the ways to understand the infection dynamics?
- What are the ways to understand the burden estimate?

Maintaining the drive towards 2030 goals for HAT and VL: accelerating progress and indicators of continued success

Knowledge Gaps

There remain gaps regarding the undocumented burden of disease for gHAT, the diagnostics to address transmission in the last pockets for both diseases, and the treatment of gHAT in extremely remote areas.

- **Undocumented burden of gHAT.** It is unclear how many gHAT deaths occur outside of care, a metric indicative not only of the existing prevalence (cases infected in the past) but that would help validate current models of the ongoing transmission of disease (cases yet to be infected). Such a metric would also bolster advocacy efforts surrounding the value-for-money proposition of the increasingly more difficult control and elimination efforts. Generally speaking, symptoms of gHAT are not recorded in aggregated case reporting, whilst they are for VL. This additional data type could be valuable for modelling or other evaluations, especially with the anticipated removal of staging data with the introduction of the new drug.
- **Diagnostics.** There are a range of reasonable diagnostic tools (including POC) for both diseases, although there are gaps in the diagnostic portfolio which, if filled, could help to reach elimination goals. In order to reach EoT of gHAT, it is unclear how existing diagnostics might be able to prove cure in the more remote locations where gHAT remains. Whereas for VL, the biggest diagnostic gap identified is monitoring VL treatment and identifying PKDL patients (both gold standard and field tools are still lacking), as well as implementation schemes to screen individuals for PKDL. Due to the mild symptoms of PKDL, individuals might refrain from seeking care, thereby serving as lingering reservoirs of *L. donovani* in the community.

- **Learning from MDA diseases.** A limitation of interventions for these two IDM diseases is the inability to perform MDA, because both require case confirmation before treatment. Discussions ensued around the need for a single-dose medication effective against both stages of gHAT but posing fewer side-effects than existing medications. Such a drug is of special interest primarily to treat gHAT suspects in locations too remote for existing confirmation tools and treatment. This would present an opportunity to go to extremely remote villages on motorcycles and treat gHAT serological suspects. This would increase the coverage of treatment (current algorithms can miss false negatives) although it would inevitably overtreat non-infected people. Even the new (fexinidazole) treatment, which can be administered in the community under some conditions, is too toxic to give to gHAT suspects without confirmation. Treatment of those serologically positive for VL is not currently possible without corresponding symptoms, unless more specific tests were to be made available that could confirm serological suspects, or unless a treatment for all suspects could be delivered.

Recommended Next Steps

- **Burden**. For both diseases, it is imperative to identify further metrics of the success of elimination goals by 2030, including metrics for unattended mortality in the community. In order to infer on gHAT deaths in the community, verbal autopsies were suggested.

- **Intermediate goals.** Neither the gHAT or VL communities have set specific goals between 2020 and 2030. The group identified that creating a "2025" target could help make sure that we are on track for 2030. It would be desirable to investigate what the individual goals would need to be if the subsequent 2030 goal is to be successful (e.g. what reduction in gHAT cases would we hope to see by 2025, how many countries should have been validated for elimination as a public health problem? What should the spatial clustering of remaining VL cases look like? Do we need a shrinking geographic area?)

- **Diagnostics.** During discussion the central importance of diagnostics was emphasized. There does not exist a market commitment from companies of existing diagnostics of either disease to produce and provide diagnostics at the levels necessary to reach control and elimination goals. In addition, better, novel diagnostics are necessary for the endgame: for the cure of gHAT and a diagnostic that can show the right trade-off between suitability for POC and accuracy for VL, follow-up and PKDL. Furthermore, an area of development that has received concerningly little attention is the possibility to add HAT and/or VL to multiplexed diagnostic platforms, since passive or clinic-based surveillance will become more important towards the endgame. This is especially important for PKDL, where dermatologist might be the primary health system contact for patients. Moreover, manufacturing of diagnostics is likely to become harder under new EU legislation.

- **Single-dose treatment of gHAT.** There was a discussion surrounding the possibility to treat gHAT suspects rather than only confirmed HAT cases if a single-dose treatment with a safer profile than existing treatments materializes. Such an approach would address the last geographic pockets of transmission, some of which are suspected to be too remote for current logistical approaches of intensifies case detection. It was suggested that economic evaluation modeling could help underpin futures discussions around the costs, benefits, and risks of possible approaches.

COR-NTD 2019 Meeting Outputs

Preventing mother-to-child transmission: scaling up access to eliminate Chagas disease

Knowledge Gaps

- Which groups should be prioritized for screening to prevent mother-to-child transmission?
- How can interruption of congenital transmission serve as an entry point to expanding coverage for all people affected by Chagas disease?
- What is the best point within people's healthcare interactions to implement screening for Chagas disease?
- How can diagnosis of congenital infection be simplified, eliminating the 10-month gap between screening of neonates and confirmatory diagnosis?
- What is the current capacity in countries; how can laboratory and information systems be strengthened?
- How to increase collaboration between public and private health facilities? Most patients are treated within the public sector, but many initiatives are taking place in the private sector.
- How is GDP impacted by Chagas disease and prevention efforts?
- What are the costs and benefits of elimination of mother-to-child transmission?
- What are the socioeconomic benefits of achieving EMTCT+ targets for Chagas disease?
- What are the costs of implementing EMTCT+ at the country level?
- How can universal screening/treatment programs be adapted to local contexts?

Recommended Next Steps

- New diagnostic technologies capable of confirming congenital infection at birth.
- Ascertaining whether new/shorter drug regimens are effective at eliminating congenital transmission.
- Promote compulsory reporting of Chagas disease while strengthening in-country data collection and reporting to track progress toward EMTCT+ goals.
- Encourage local pilots to gather data regardless of national system maturity level (strengthen data collection from the bottom up).
- Develop an economic valuation of elimination of congenital transmission which considers the full range of social and economic impacts of the disease.
- As a first step, consider feasibility of screening girls at school or in tandem with vaccination programs to promote wide coverage, using a rapid test.
- Compare potential impact of different screening strategies (via schools, vaccinations, antenatal care, all women) in different settings.
- Develop laboratory capacity in all affected countries, taking into account geographic differences in the performance of tests.
- Consider the use of health economics tools such as cost- effectiveness analysis, modeling and budget impact to leverage EMTCT (+) adoption.
- Learn from other initiatives (e.g. Global Cancer Observatory) to improve systematic data collection.

COR-NTD 2019 Meeting Outputs

Preventive chemotherapy against leprosy: results to date, challenges and solutions

Knowledge Gaps

- How can PEP interventions be expanded to prevent the 70% of cases that arise from individuals with no known contact with index cases?
    - Can a blanket approach be used to target the 70%? In which programmatic settings is the blanket approach appropriate and feasible?
- Is it possible to identify and address "super spreaders" that may pose an increased risk of transmission?
- How can PEP interventions be tailored to overcome the need for disclosure?
- How can contact-based case finding through PEP interventions complement other active case finding efforts and vice versa?
- What is the most effective and efficient active case finding methodology to identify new cases, especially in non-contact populations?
    - Evidence base needed in order to provide guidance and recommendations on methodology tailored to each programmatic setting
- Need to understand where to implement PEP interventions. Can criteria from existing data be developed to guide decision making? Can alternative strategies such as sero-surveillance be used to decide on the need for PEP?

Recommended Next Steps

- Design a study to develop and explore an alternative approach to PEP in which active screening of contacts with provision of PEP is reinforced with blanket PEP distribution among those who are not direct contacts but do belong to the same high incidence communities
- Conduct modelling, costing and other analyses of existing data to provide programs with a decision-making tool for PEP implementation.
- Conduct follow-up studies in areas where PEP implementation did not go well to understand what went wrong and what can be improved for better results
- Develop and test alternative implementation strategies that avoid the risk of disclosure when targeting neighbor and social contacts.
- Explore feasibility of sero-surveys as a surveillance tool for leprosy, preferably combined with other NTDs.

COR-NTD 2019 Meeting Outputs

Cross-Cutting

Approaches to maximizing the influence of implementation research on NTD policy and programming

Knowledge Gaps

- Conceptual: how can program managers and teams be supported to identify knowledge gaps?
    - Need for a simple, cheap and useful tool for diagnosis of FGS to prevent misdiagnosis in girls/women as a STI, in addition to comprehensive diagnosis/treatment guidelines.
    - Should morbidity be managed on a case by case basis or on a large-scale level (i.e. MDA)?
    - Lack of communication strategy for behavioral awareness to reduce the stigma attached to FGS
- Instrumental: how can innovative research and program methodologies be used to support service beneficiaries to make program change?
    - Need for mapping levels of bureaucracy in implementation of programs to understand how NTD programs interact with the health system at a country level
    - Missing links in understanding the barriers to MDA that could be bridged through training community members to do ethnographic surveys
- Capacity building: how can program managers and teams be best supported to demand and use research evidence to make program change?
    - How can partnerships be evaluated (cost/benefit) to different stakeholders?
    - A disconnect exists between academic findings and outputs and program managers; can the impact of these findings be measured, starting with if the research was requested by a program team (by who and when) and if the findings were subsequently relayed and used?
    - Develop strategies to evaluate whether a training has been successful and if it has been implemented in a sustainable way (i.e. knowledge cascade to ensure national sustainability)
    - How to best set priorities for programs and can this ability be developed all levels in a country, where these priorities can then be relayed back to funders
- Enduring connectivity: what strategies can be used in research programs to ensure sustained engagement of implementers and communities?
    - It is a challenge to get all partners to invest their time, for example government partners should be involved from the beginning of a project and capacity to sustain programs developed
    - Training for skills development takes time (2+ years), but there are intermediate steps (e.g. abstract writing, questionnaire design) and would resources such as these work to develop capacity?

COR-NTD 2019 Meeting Outputs

Recommended Next Steps

- Need for further training tools and guidelines to easily screen and diagnose FGS at point-of-care, as well as ensuring the availability of drugs in communities after an MDA so access exists outside of scheduled distribution.
- Determine if the use of innovative technologies allow for better understanding of barriers to treatment/services, such as through photos or voice recordings, to understand the daily challenges that community members face. Further, use geo-tagged photos to outline potential transmission sites (e.g. schistosomiasis).
- Strengthen communication pathways between program teams and academic institutions to determine research questions of interest from a field/program setting, facilitate the feedback of the findings, and the measure the subsequent impact on/uptake by programs.

Diagnostic needs for meeting the new WHO NTD Roadmap goals for 2030

Knowledge Gaps

- A lack of understanding across all NTDs as to what was being discovered, what had been developed and how that might impact the formation of a diagnostic.
- The group felt that the process of diagnostic development was potentially very long and fragmented and although people felt WHO's move around diagnostics was positive it was still unknown how it would work.
- The market for diagnostics is very unknown and also the economic impact of having diagnostics to support the business case.

Recommended Next Steps

- A more comprehensive landscape exercise on what is being developed should be carried out to give a full picture.
- The development pathway should be mapped out and ways to fastrack it – TPP through to field trials and how many trials would be needed
- Comprehensive work on the diagnostic market so that economic understanding and modelling can be achieved to strengthen a business case.
- Comprehensive understanding of the use cases and where in the health system the diagnostic will be used so that the end product is fit for purpose.

Digital Tools for Morbidity Management and Disability Prevention

Knowledge Gaps & Recommended Next Steps

- One thing that would be helpful apart from having a congruent data platform is considering the actual tools that are used– are the tools that are being used in the field similar or congruent?
- Morbidity is a big umbrella term. How are we measuring it?
- Underreporting is dependent on tools used to measure and the very type of disease.
- Is our data dynamic enough? Should we continue including people in our data that have received treatment?
- How do we capture sub-national level data?

- There is underreporting, when you go house to house and look for cases you find them, but that real data doesn't trickle up to the national government. How do we deal with unreliable information? How do we get more accurate primary information?
    - Incentives could be a solution, using smaller studies to verify larger data could help
- Could we use mobile technology to help administer care for or information about these diseases, in addition to using it to finding cases?
- Leprosy tends to have better registration than other NTDs, but after treatment people stop engaging with the health system, so district level health personnel often don't know how many people impacted by leprosy disability may be in their catchment area.
- You don't need to do national burden estimates every year, probably every 5-10 years. In the interim you'd need a tracker to follow treatment for NTDs. How many people have had surgery to treat an NTD, or other kinds of treatment?
- The more cases the government finds, the more resources they are obligated to designate for morbidity management. There's a disincentive to find more cases. How do program managers deal with that conflict?
    - Accurate numbers can help to compete for resources and demonstrate what priorities should be, based on burden of disease.
    - If we look at this from a rights-based perspective it might be easier to align incentives. Everyone has a right to care.
- Where is information about the quality of facilities in addition to data about the availability of services? Could this be digitized?
    - WHO has surveys that could be collected using standardized data systems, but then, how do we make that available? How do we embed it into the routine system? There's a lot of data available, but it's not put together.

Exploring the potential of integrated serological surveillance platforms in elimination settings

Knowledge Gaps

- More sensitive and specific assays are needed for some diseases
- Commercially available and well characterized tests are needed for multiplex platforms
- Reference sera are often not available
- International standards including QA do not yet exist
- Surveys currently conducted for specific diseases often target specific age groups or seasons which may not be relevant to across all diseases, limiting the value of integrated surveillance based on those surveys
- Nationally representative samples may not have sufficient geographic resolution to identify the remaining foci of infection
- Some powerful analytic tools require longitudinal data or data with multiple age cross sections which are not routinely collected in existing surveys
- Growing need for analytic capacity and tools to translate antibody data into actionable information
- Measurement and modeling of low levels of transmission is a challenge across diseases
- Using only binary data in low prevalence settings may introduce artificial information loss
- Spatial models and transmission modeling are powerful tools for analyzing serological data but are not in widespread use

- Most country programs do not yet have the laboratory, analytical, and human resources capacity to conduct integrated sero-surveillance
- There is currently no established framework for how NTD multiplex data should be analyzed and how that will result in programmatic response
- Integrated surveillance will require coordination between disease programs within ministries
- Blood collection can be culturally sensitive, especially repeated collections
- Specimens are often collected for a single disease survey but may retrospectively be assessed for multiple diseases
- Integrated surveillance methods are not currently included in guidelines for disease control
- There are not currently clear use-cases for these platforms and serology in general
- Financing and business cases are not clear
- Implementing integrated surveillance in country programs will not be without cost, especially when the broad scope of assays, laboratory equipment, consumables, maintenance and analysis is considered.
- There is currently a lack of coordinated financing across global health groups
- Ministries of Finance are important partners in ensuring the longevity of programs but may not be engaged

Recommended Next Steps

- Centralize sources of purified antigens for coupling to beads or printing on arrays
- Archive global reference sera or antibodies to standardize across labs and surveys
- Learn lessons from:
  - Other diseases with established reference sera including HIV and TB or Vaccine Preventable Diseases
  - Other initiatives such as PAHO: Destination Elimination and the Finland biodata program
- Design new adaptations to existing surveys to ensure that data collected can be relevant to multiple diseases.
- Target specific subsets of diseases for which combined surveillance could provide gains
- Follow-up nationally representative sampling with spatially adaptive sampling
- Build capacity and develop networks across disciplines to ensure that the most robust tools can be utilized widely
- Consider continuous analysis of output from multiplex sero-surveillance, especially in low prevalence settings
- Investigate creative modeling approaches, such as modeling multiple diseases with similar transmission dynamics or using multiple antigens
- Develop and refine spatial modelling to allow for wealth of data on ecology and environmental change
- Integrate programs into the health system to ensure the longevity of projects and strengthen the health system
- Establish antibody-based benchmarks for monitoring goals to drive program action
- Build HR capacity in programs and local partner institutions
- Harmonization of train laboratory and analysis techniques within and between areas
- Transfer technology and QC to endemic countries/regions
- Assess sensitivities around blood collection or other potentially difficult issues
- Emphasize working with communities and getting buy-in for the work from those communities
- Develop language that allows future analysis of bio-banked samples

- Develop international standards
- Define use-case scenarios for integrated surveillance and their relative benefit over and relationship with other approaches
- Undertake research on standards
- Conduct policy dialogues
- Review possible financing mechanisms
- Undertake health economics studies for field, lab, analytical and intervention elements to show ROI. Particularly in countries where centralized serological surveillance is proposed
- Undertake studies of the cost effectiveness of multi-disease surveys to show the value of integrated surveillance
- Undertake advocacy to generate buy-in from technical and non-technical people to encourage investment
- Develop a cost effectiveness analysis method
- Establish projects with longevity and broad remit so that human capital is not lost due to funding reductions

Neglected tropical diseases and mobile populations: challenges and gaps*

Knowledge Gaps

- There is a lack of fundamental knowledge in how movement of populations are tracked.
- What is the role of movement with transmission? What are the transmission dynamics?
- How to figure out organizational priorities; what is the leverage with partners who have access with these populations and how to convince or buy in?
- How to ensure access to healthcare in war-torn areas and how to predict the disease burden and potential outbreaks

Recommended Next Steps

**Outputs from this session have not been finalized.*

New diagnostics for NTDs: harnessing advancements to support surveillance and elimination goals

Knowledge Gaps

This session focused on the knowledge gaps identified from the point where new diagnostics have been developed, and now need to be implemented.

- **Disease Requirements:** The laboratory needs will be different for each disease due to the fact that the diagnostic needs and target product profiles (TPPs) are different for each disease. For example, a mobile diagnostic clinic for Trachoma is much more feasible than that needed for molecular diagnostics for STH, mainly due to the DNA extraction requirement. Therefore, the laboratory and technology needs should be tailored to the disease and what the operational research question is: For example, for monitoring control interventions of schistosomiasis basic microscopy is sufficient and no technology transfer maybe needed but, for the elimination of schistosomiasis highly sensitive diagnostics are needed and the more advanced methodologies need to be transferred.
    - **The diagnostic and technology will be different for different diseases:** For example, for STH, presence absence in the general community maybe sufficient but for

schistosomiasis each individual infected needs to be identified and treated. This relates to the biology of the pathogens, and this should not be over-simplified.

- **Engagement with Policy**
  - The diagnostics that are currently being developed are frequently more sensitive due to the need to detect low level infection in an elimination setting.
  - This needs to be taken into account when determining thresholds for elimination. Will these need to be changed to take into account the rise in infection once new tests introduced. This could affect drug donations, and national targets.
- **Lack of standards for commercially developed tests:**
  - Both commercial companies that have developed the LF antigen test and POC-CCA, do not want to produce a quality control test. This should be a part of test development and needs to be included in Target Product Profiles to include standards. In this case, two academic groups have independently developed a control. For LF this standard is provided to WHO, who then provide this to endemic countries. For POC-CCA the standard is provided to those who ask. It is unclear if this mechanism is widely used.
- **Evaluation of diagnostics is difficult for commercial companies:**
  - Companies cannot access clinical samples and data, and there is currently no central source or repository of samples. This may not be possible centrally due to restrictions in sample movement. However, a virtual biobank or list of resources, where ethics are in place to use samples is worthwhile. Groups storing samples should be incentivized or recompensed in some way for provision, storage, expertise and reference test results. Further involving groups by knowledge transfer or capacity building would be best.
- **Training gaps:**
  - The ESPEN Onchocerciasis lab was mentioned as a good example where technology transfer and knowledge exchange are successfully being implemented. This is a high-level reference lab, and we need to think about the implementation of diagnostics at all levels in the system:
    - Very basic (very little or no infrastructure) – no trained staff available
    - Basic laboratories (infrastructure in place but needs development)– capacity for training staff
    - Working laboratories (currently working but will need continued support and training) – staff members available but need training
    - Advanced laboratories (up and running and well maintained - trained staff available

Recommended Next Steps

Standardization and EQA: Need to develop standards for quality assurance and build capacity in laboratories for implementation.

- Requires an expert team to come up with standardized protocols for collection and storage of samples

Incorporating ethical considerations for long term storage and use in initial ethics applications

- Need to combine a number of laboratories in Africa (ESPEN has started this process) and beyond.
- POC-CCA are now undergoing quality control by industrial partners. Proficiency testing kits need to be developed for countries that re-package the test kits such as Brazil.

Virtual Biobank: Equivalent Open Access for data in papers.

- Requires a team to decide what information would need to be stored
- How to incentivize groups to contribute, especially considering that many countries will not allow samples to be sent out.
- How to ensure that these samples are good quality, and standardize data collection processes.

Reference Laboratory(ies):

- ESPEN Oncho lab has been developed (funded by USAID) whereby a subset of the samples is quality control checked. As the network is created LF antigen test and POC-CCA, both commercial companies that make this test do not want to produce a quality control test. However, two academic groups have independently developed a control. For LF this standard is provided to WHO, who then provide this to endemic countries. For POC-CCA the standard is provided to those who ask.

Training Gaps:

- The example of microscopy detecting eggs was brought up and how quality control has shown that training is needed to maintain high standards. i.e. it is not only new diagnostics that need access to standards, but also we must maintain expertise in traditional areas of diagnostics.
- Can we produce training materials for all levels of laboratory and staff in order that we retain knowledge and importantly quality of testing.

Funding: Who will fund these activities?

- Ideally for sustainability multiple funding sources such as USAID, CDC. Walter Reed already run reference laboratories around the world, perhaps they could be asked to help either contribute knowledge and know-how.
- If labs can put budgets and requests together then funders will be interested in this. ESPEN is currently setting up this laboratory network for this standardization purpose.

Supporting countries to develop high-quality NTD prevalence data

Knowledge Gaps

- Gap in engaging local stakeholders to design participation and trainings
- Design issues for special populations (especially migratory and displaced individuals living in camps)
- Appropriate sample size attainment (the number of households needed to achieve the correct number of age-appropriate individuals)
- No standardized process for protocol reviews.

- WHO guidance on survey methodology/protocol for Schistosomiasis and Soil-transmitted Helminthiasis are not as developed as other diseases
- Gaps in knowledge on WHO guidance and the underpinning survey methodology, so knowledge of what to do when it deviates from the protocol in the field
- Some countries are not ready for EDC, can they still generate high-quality prevalence data?
- Monitoring the fieldwork - are teams working in the correct locations?
- Standardized forms are not available for each disease
- Need training based on common field errors
- Sharing analysis code on Github
- Non-ESPEN countries need to use a standardized reporting format for programmatic decision making and reporting as part of the database
- Anonymize participant and household identifications for stored surveys
- What are the standards for "secure" data storage?
- Trainings often focus on data collection, but there needs to be training for data management and analysis as well
- Lack of support for reporting to the scientific community (e.g. – publications)

Recommended Next Steps

- Look at the output and see how these principles can be used in each NTD program to help provide guidance to conducting high-quality prevalence surveys.
- Continue to improve existing programs collecting high-quality prevalence data for NTDs through solutions and recommendations provided above
- Collaborate between disease programs to share new solutions and insights building on current practices.

The road to 2030: country perspectives on the role of drug donations beyond 2020

Knowledge Gaps

- **Situational assessments** in country will be key. **Drug needs, impact data**, **partner mapping** and **cost analysis** will all help with decision making.
- **Country specific guidelines and procedures** and **defined roles and responsibilities** will be required moving forward**.** Guidelines will be needed for disease programs as well as procurement and supply chains.

Recommended Next Steps

- **Political commitment/will** on **policies, budget and UHC** is needed from countries
- Collaboration will be needed to ensure the **availability of quality affordable medicines**, delivered through **effective procurement, supply chains & UHC programs**. Protocol for leftover drugs should be considered.
- Further bespoke country **capacity building and training,** will be required (including M&E)
- Continued **advocacy for internal or external financing and resources** will support programs
- Donors will need to be **consistent and aligned in support and expectations** in country.

COR-NTD 2019 Meeting Outputs

Using a systems approach to improve effectiveness of MDA with PC-NTDs

Knowledge Gaps

Efficacy Decay Framework

- How can we use systems thinking to support the determination of MDA adherence?
- How can we use the framework to determine when and where MDA is appropriate?
- How can we use this approach to contextualize MDA strategies?

Access

- What are the best context specific platforms for reaching hard-to-reach (mobile, migratory) groups?
- How can we address measurement challenges, including baselines and changing population sizes?
- How can we prepare for and manage the transition from campaigns to integration within the health system, and ultimately in Universal Health Coverage?

Provider Compliance

- What are the means to give agency to CDDs that they can apply to their work (motivation, empowerment, adult learning principles in training, flexibility of scheduling)? Will this have positive outcomes on the program overall?
- How can we measure quality in MDA coverage beyond drugs distributed?
- What are the providers' perspectives on how to tackle areas of prevalence <5%?

Participant Compliance

- What motivates compliance over time?
- How can we measure compliance without reliable denominators (changes due to political events, migration, displacement, etc.)?
- What role can incentives play in increasing level of compliance?

Recommended Next Steps

- The Efficacy Decay Framework should be used to identify MDA efficacy challenges and inform solutions from a systems approach, especially in "hotspot" areas of persistent transmission. Lessons learned from these experiences should be documented and shared.
- Access among hard-to-reach groups, should be studied and innovative ways to measure and plan for improved access among these groups should be piloted and shared.
- PC-NTD partners should begin planning for how to best transition from campaigns to integration of PC into the health system, including advocacy for inclusion in UHC packages.
- WHO guidelines for PC-NTD treatment, including eligibility criteria, should be reviewed annually with both new and established program staff. Community leaders should be well informed about eligibility criteria and the purpose they serve for the program.
- Training guidelines for CDDs should be revisited and made more adaptive, incorporating interpersonal communication training, role play, and space for CDDs to share challenges with one another. Attention should be paid to the profiles of CDD volunteers in training, considering incentives and providing support.
- Communities should be engaged in describing challenges facing PC-NTD programs and developing appropriate solutions. Having communities co-develop strategies will help to ensure they are appropriate and acceptable, and increase motivation.
- Research is needed to identify the extent to which behaviors, socio-cultural factors, program delivery, and other contextual aspects influence MDA compliance, and what works in addressing them.

- The effectiveness of the RANAS technique should be studied further in different contexts and at different scales, and other behavior change tools should be tested and/or adapted to identify and understand key influential behaviors for participant compliance in MDA.