BILL & MELINDA GATES foundation

NEGLECTED TROPICAL DISEASES SUPPORT CENTER

USAID FROM THE AMERICAN PEOPLE

Table of Outputs from COR-NTD 2016

LF	OV	LF/OV	SCH	STH	SCH/STH	TRA	IDM	CROSS

Breakout	Disease-Specific	Knowledge Gaps	Next Steps
The Potential Value of a Triple Drug Regimen (IDA) to Accelerate Elimination of Lymphatic Filariasis	Lymphatic Filariasis	• Where will IDA make the greatest impact? • How might IDA improve coverage? • What would be the cost for increasing coverage? • Can IDA be used for onchoceriasis (depending on ocular Mf counts)? • What other strategies besides IDA should be considered for onchocerciasis?	• Assess changes in gains when comparing IDA to once- or twice-annual strategies with conventional IDA • Pilot strategies to increase coverage, including messaging the additional health benefits of ivermectin to communities • Involve donors in discussions on new strategies, including points on cost savings and additional improvements to programs beyond the new IDA strategy
Ov16 Serology in Africa	Onchocerciasis	• Is the low sensitivity seen in the initial field use of the Ov16 RDT indicative of a problem with the test, or a problem with field implementation of the test? • How do we use the new tools to map infection and transmission in low prevalence settings? • What are the appropriate serologic thresholds and age groups to look at when evaluating the status of transmission? • What is the minimum sensitivity and specificity needed for the RDT? • How should a “pre-TAS” for Oncho be developed?	• Evaluate the Ov16 RDT using the harmonized ELISA under development • Determine which “pre-TAS” strategies being tried by country programs work best • Determine the critical seroprevalence threshold for stopping MDA, adjusted by baseline endemicity across areas • Delineate hypoendemic regions on onchocerciasis via mapping • Integrate mapping with other filariasis mapping and TAS surveys, when feasible

		• What are the other use cases for the RDT? • What information is needed to validate the simulation models?	
Programmatic Decisions in Loa-Endemic Areas	Lymphatic Filariasis and Onchocerciasis	• Is individual examination of every patient needed in all areas with hypo-endemic oncho and loa? Or, are there some epidemiologic cut-offs that can be used to mark a community as safe for treatment with ivermectin? • How can we translate the TNT strategy into a viable MDA strategy that can be implemented by the national NTD programs? • When it comes to treatment of Oncho, do we need to test patients for Loa loa every year? • What kind of coverage can be reached in areas with loiasis co-endemicity? • What is the cost of the additional efforts for programmatic implementation? • What are the numbers of people with high levels of Loa loa that would be excluded?	• Evaluate epidemiologic cut-offs that could potentially be used to mark a community as safe for treatment with ivermectin • Conduct cost-appropriate operational studies (planned for 2017 in Cameroon) on annual testing requirements
Resolving Challenges around Scaling Up Transmission Assessment for Onchocerciasis and Use of Xenomonitoring after MDA	Lymphatic Filariasis and Onchocerciasis	• Which mosquito population is most amenable to fecal testing for LF? • How can fecal testing be standardized and validated? • What is the best way to adapt test-strip detection strategies for fecal testing? • What effect does trap placement have on the number and status of vectors caught?	• Conduct additional studies on the effect of trap placement, compounds in dirty socks, performance of the EWT across species and improved ITT tent design • Establish the number of vector collection points per evaluation area to establish onchocerciasis endemicity. • Determine the best timing to collect

	• How can Ifakara Tent Traps (ITT) be better designed? • Which compounds in dirty socks (via Esparanza Window Trapping, or EWT) are most effective at catching flies? • How do EWT perform in catching species outside of the *S. damnosum* complex? • What is the appropriate trapping position for EWT? • How many vector collection points per evaluation area are required to establish onchocerciasis endemicity? • What is the best timing to collect xenomonitoring data in relation to MDA for onchocerciasis? • How can programs apply xenomonitoring in onchocerciasis hypo-endemic areas? • How can programs scale up xenomonitoring for onchocerciasis when deciding to stop MDA? • What is the relationship between filarial prevalence in mosquitoes and human lymphatic filariasis infection? • How many mosquitoes must be caught to conduct xenomonitoring for LF in the context of MDA stopping? • What guidelines should be in place to confirm the absence of LF transmission via xenomonitoring? • How should programs respond when LF-positive mosquitoes are identified during post-MDA surveillance? • How can the community be engaged in xenomonitoring?	xenomonitoring data in relation to MDA for onchocerciasis. • Evaluate methods for xenomonitoring in areas hypo-endemic for onchocerciasis • Collect data on human and mosquito filarial presence in the same locations • Develop mathematical models to interpret the relationship between human LF and mosquito infection • Collect mosquitoes at different times post-MDA for LF • Develop low-cost systems to detect reintroduction or increase of infection in mosquitoes • Determine the number of vector collection points per evaluation area required to establish LF endemicity • Study ways to engage community members in xenomonitoring efforts

		• What standards should be applied for tools and mosquito collection methods, community selection and laboratory techniques/sample processing?	
Schistosomiasis Elimination: Where are we? (and) Where do we go from here?	Schistosomiasis	• The cause of persistent hot spots • Are parasites in hot spots stronger parasites? • The role of non-compliant and migrant community members in sustained transmission • Does migration increase parasite diversity? • Worm count in infected individuals • Whether or not worms with no egg fecundity contribute to transmission • Whether or not a lack of morbidity can be attributed to no egg fecundity • Whether worms with no egg fecundity could start producing eggs again • What is the implication of *S. mansoni* infection in animal reservoirs? • Is verification of elimination a priority in the context of endemic countries' needs? • What indicators and activities are needed to get to elimination?	• Follow up on infection intensity data for the same individuals longitudinally • Evaluate potential PZQ requirement for people entering a community • More POC-CCA evaluations: class analysis, cassette batch variation, intra-reader reliability, inter-reader reliability, variability in individuals day-to-day, POC-CCA evaluations post-PZQ • Conduct mapping considering the level of granularity required for the implementation unit • SCH hybrid research • Conduct community-wide PC • Greater engagement with WASH sector • Stratify national programs within countries, tailoring individual locations • Develop guidelines for programmatic interpretation of POC-CCA results (including trace readings) • Determine preventive chemotherapy treatment strategies at local levels (especially in low-transmission areas where KK results do not indicate treatment) • Define cut-offs for morbidity • Develop goalposts for countries which have not yet started moving towards elimination

			• Involve countries in the policy decisions surrounding the shift from control to elimination • Develop and validate models to predict stopping MDA • Evaluate the test and treat strategy for maintaining morbidity control • Develop sampling methods for verification of interruption of transmission surveys
Strategies to Combat Drug Resistance in STH	Soil-Transmitted Helminthiasis	• What is the frequency of resistant alleles globally? • When is reduced drug efficacy truly caused by antihelmintic resistance (AR) and not by another factor? • What are the minimum criteria that a new drug or combination regimen needs to satisfy to supplant current protocols and be supported financially?	• Develop genotypic protocols for the early detection of the emergence of AR • Begin systematic and consistent monitoring of AR • Develop and apply a standard operating protocol to confirm anthelmintic drug efficacy and to systematically exclude confounding factors related to reduced drug efficacy • Improve upon molecular and *in vitro* diagnostic assays to track the impact of STH treatment • Use next-generation sequencing to develop genotypic assays that can detect the early emergence of AR • Develop new drug classes for the eventual failure of available anthelmintic drugs
Addressing STH in Areas Transitioning to Post-MDA Surveillance Status for LF	Soil-Transmitted Helminthiasis	• Operational research and implementation science research is necessary to learn how to sustain the gains of the LF program on STH	• Further define the goal of the global STH program and corresponding indicators to measure success • Collect data on STH prevalence/intensity

		transmission. • Evidence is needed to determine under which conditions it might be possible to interrupt transmission of STH. • Further research is needed to validate the modeled transmission breakpoint of <2% prevalence of STH. • Tools are needed to help countries develop national deworming plans and transition deworming activities in the LF post-MDA phase.	in the post-LF era • Increase the use of existing opportunities to assess STH prevalence and intensity, particularly the use of the STH-TAS protocol outlined by WHO • Prioritize support to countries without national deworming programs in order to help them plan for a strengthened STH platform in the LF post-MDA phase.
WASH on worms: integrating and strengthening multi-disciplinary actions on schistosomiasis and soil-transmitted helminths	Schistosomiasis and Soil-Transmitted Helminthiasis	• More information on the WASH impact on STH and schistosomiasis • Appropriate use of human-water contact studies • What is the level of environmental contamination with fecal matter and helminth eggs? • Why do schistosomiasis hotpots exist?	• Conduct epidemiological and mathematical modelling on elimination and focal transmission dynamics • Apply updated molecular epidemiology and diagnostic techniques to determine focal transmission dynamics • Shift the paradigm and rethink the control approach for schistosomiasis • Encourage collaboration between WASH and NTD programs
Trachoma Elimination	Trachoma	• District-level datasets are needed to help standardize methods for laboratory testing, determining cut-offs in serology testing, assessing the level of infection for cessation of interventions, and defining re-emergence of infection. • What is the long-term impact of a one-time MDA? • What is the effect of high treatment coverage? • How can programs improve coverage and	• Continue to investigate alternative indicators of progress towards elimination • Develop gold standard for serology, including standardized definitions of negative and positive • Conduct additional surveillance to assess the long-term impact of MDA in Malawi • Determine the reasons for sub-optimal impact of A, F, and E interventions • Conduct a national review of the

		means for determining coverage? • Why do A, F, and E interventions sometimes have sub-optimal impact? • How can researchers determine the main routes of transmission and best targets for F and E interventions	Ethiopian program • Collect empirical evidence to validate model for double-dose strategy Conduct • research to determine the main routes of transmission and best targets for F and E interventions
Building a future with accessible treatment for all affected by Chagas	Chagas	• Is it better to treat or not treat chronic patients? • What are the correct dosages of benznidazole and nifurtimox for adults? • What are the impacts of benznidazole and nifurtimox on adults? • How can diagnostics be improved? • What is the comprehensive burden of Chagas disease? • What are the potential cost savings of screening and treating?	• Conduct clinical trials for benznidazole and nifurtimox in adults • Seek approval for benznidazole and nifurtimox in the United States • Validate and perform active case detection and treatment • Conduct economic studies on cost and burden • Advocate for early case detection in children and infants, as well as for screening of pregnant women
New Tools to Accelerate Elimination of Leprosy	Leprosy	• Lack of a standard PCR test for leprosy • How can wide adoption of a leprosy vaccine be achieved? • What is the effectiveness of a combination of chemoprophylaxis and immunoprophylaxis • Is it possible to develop a more powerful preventive chemotherapy regimen that would also cure pre-clinical disease? • How can the programs coordinate across the India-Nepal border?	• Develop a standard PCR test and immunological test that would include an antibody assay with a cytokine assay • Continue research on combining chemoprophylaxis and immunoprophylaxis • Test the PEP++ package in a multi-country trial • Emphasize early detection through contact screening and leprosy prevention • Continue scaling up the single dose of rifampicin (SDR) program in Nepal

Field Experience from India, Bangladesh and Nepal on Visceral Leishmaniasis. Operational Research on integrated approaches to break transmission	Visceral Leishmaniasis	• Where should success in VL reduction be attributed? • What is the impact of new VL interventions? • What is the source of sandfly (*Phlebotomominae*) infections? • What determines infection versus disease? • Is current surveillance enough to establish disease control? • What alternative treatment options could be used in the event of LAmB resistance?	• Gather greater field data • Focus on transmission dynamic models • Coordinate programs within continents where migration is common • Strengthen health systems to better identify infections and attract infected persons away from alternative sources of care • Develop a VL vaccine • Investigate persistent infections in areas where VL was declared eliminated
Moving Towards the End Game for Intensified Disease Management Diseases	IDM Diseases	• What are the effects of non-participation and disease risk variation? • What is the baseline endemicity for IDM diseases, and how are they distributed? • What is the geographical overlap of different NTDs? • How can programs integrate their whole systems around SMS, and SMS with DHIS 2? • What is the best way for programs to record results of multiple diagnostics from a single survey? • How can diagnostics be more field-friendly, especially as incidence declines?	• Improve routine data collection • Report additional data over case numbers (e.g., staging for HAT) • Combine passive case reports and active case detection • Collect more data from institutional active surveillance studies • Develop an interoperable suite of tools for countries to select from • With support from WHO, develop standard integrated training guidelines, modules and tools for data and supervisory evaluation • Compile and share photographs of NTD symptoms with communities and schools to help with early identification and case finding • Combine screening of individual NTDs with that of other diseases. • Address critical gaps in availability of suitable screening strategies and tools

			• Develop integrated NTD case management training • Integrate mapping of remaining case-management NTDs • Monitor during implementation of new diagnostics and/or surveillance strategies
Maximizing the number of districts with good treatment coverage	Cross-Cutting	• How should programs implement supervision? • How do we encourage compliance, particularly in areas with prior PZQ adverse events? • Compliance in cities remains low; should it be a priority? • How can programs address delay? • How should programs decide on denominators for coverage calculations? • How can programs utilize existing data to improve coverage estimates and programs overall? • What is the optimal supervisor training and training cascade? • How should supervision be supported if cut from programs' budgets? • How should programs handle locations that come back indeterminate via the Supervisor's Coverage Tool? • Is Epi or program coverage applicable in a conflict area? • What strategies are already being implemented in conflict areas? • How can programs incorporate geographic coverage given the possibility of microfoci?	• Define the scope of the supervisor's work – use written mini job descriptions • Optimize use of the Supervisor's Coverage Tool, Data Quality Assessment and coverage surveys for during and between MDA supervision • Integrate PC supervision with IDM activities • Ensure that supply chain managers are experts in logistics, and that denominators are known • Use UN population estimates as denominators or ranges that benchmark on UN estimates and more recent or local estimates • Conduct operational research on methods for population measurement such as mobile data footprint, capture-recapture and satellite methods • Validate coverage via surveys • Make data available locally and publicly • Make drugs available in conflict areas • Determine the population of conflict areas via censuses

Feasibility of integrated surveillance for parasitic and neglected tropical diseases	Cross-Cutting	• There are no existing guidelines for LF Post-Treatment Surveillance with ongoing oncho MDA. • Can LF and oncho targets be reconciled to conduct simultaneous post-treatment surveillance? • Can antigen testing be supplemented or replaced with a biplex test? • With bed nets for malaria and albendazole for STH, when are communities ever truly post-treatment? • How can skin NTDs be mapped, diagnosed and controlled? What are the opportunities for training and community management in these processes? • What is the role of communities in driving down NTDs of the skin? • How does the multiplex perform under real-world conditions? • How do we sample for low-prevalence diseases or if antigens included in the panel have low sensitivity and/or specificity? • Is integrated vector management possible? • What are the costs and benefits of the multiplex bead assay?	• Develop guidelines for LF Post-Treatment Surveillance with ongoing oncho MDA • Reconcile LF and oncho targets to conduct simultaneous post-treatment surveillance • Evaluate effectiveness of supplementing or replacing antigen testing with a biplex test • Determine the effects of bednets and albendazole on disease transmission in post-treatment areas • Conduct operational research on mapping, diagnosis, training, community management and control of NTDs of the skin • Evaluate absence of skin NTDs as a point of entry into communities • Evaluate the Luminex-based platform in four PAHO countries • Conduct operational research on sampling for low-prevalence diseases and on antigens with low sensitivity and/or specificity • Build technical capacity in entomology • Conduct an analysis of potential cost-savings with considerations of personnel and reagents
Defining operational research needs to improve access to quality MMDP services for NTDs globally	Cross-Cutting	• How does quality of services effect surgical uptake and what strategies can be used to improve surgical quality? • What effect does incorporating simulation training (HeadStart and FASTT) have on long-term outcomes?	• Identify strategies to provide quality MMDP services through integration with other programs and better incorporation into the primary health system. • Validate survey methodologies to identify cases, considering opportunities for

		• What are the best strategies to manage recurrent trichiasis and hydrocele cases? • How can NTD programs better utilize current systems (e.g. HMIS and primary health care systems) to generate burden data and assess availability of MMDP services for patients? • Which tools are appropriate to measure stigma in the context of NTDs and to evaluate the impact of stigma reduction interventions?	integration with other diseases/programs and through the use of novel technologies (e.g. SMS). • Define tools to assess stigma and evaluate optimal interventions to address NTDs in the context of stigma and mental health. • Utilize existing data collection opportunities (e.g. HMIS and disease-specific assessments) to acquire case estimates. Develop cost-effective strategies to estimates cases when opportunities for integration are not possible.
Maps and Models for Program Decision-Making	Cross-Cutting	• There are many regions, in which there is little or no data, to infer the burden of disease. • Many regions lack data up-to-date measures of infection and disease. • There are issues surrounding confidentially and security of data. • Some tools will likely need training to understand the outputs and use effectively, however these tools also have the most flexibility to allow the user to tailor interventions.	• Generate new mapping tools for both the PC and IDM diseases • Determine how to liaise effectively between modelers, researchers and program implementers so that tools in development can be used by local stakeholders to answer priority questions.
Examining the Demands Placed on Community Drug Distributors	Cross-Cutting	• What alternative methods of CDD motivation and incentivization work best? • What are the programmatic impacts of increased multitasking and added responsibilities for CDDs?	• Identify the opportunity cost of volunteering • Study the differences in circumstances faced by female and male CDDs • Define the role of the community in offering support to CDDs and promote

	• How should volunteerism be redefined? • What are the issues related to CDDs in South America and Asia? • How can countries standardize CDDs' remunerations and incentives? • How can discussions and actions involving CDDs apply outside of NTDs?	best practices • Conduct high-level dialogue with case studies showing linkages, standardization and management of the volunteer workforce