

Accelerating the Elimination of LF using IDA: Lessons Learned from Early Adopters

Session Date & Time:	Monday, November 18 at 1:00 PM
Session Location:	MGM Salon A
Session Description:	With publication of the WHO guidelines for the use of IDA for LF elimination in 2017, there have been seven countries considered as early adopters who implemented IDA in late 2018 and early 2019: Samoa, American Samoa, Fiji, Kenya, India, Malaysia and Papua New Guinea. These LF programs are trailblazers who developed the tools, processes and implementation considerations appropriate to their contexts to ensure the goal of 80% coverage. Each country also had specific challenges that are important to understand as new countries consider IDA in 2019/2020. To accelerate LF elimination to reach global goals, we need to learn from these early adopters and use their experiences to guide the formulation of the operational research challenges as the community moves forward with IDA.
Session Chairs:	Jonathan King and Alison Krentel
Session Rapporteur:	Teresa Tufte

KEY DISCUSSION POINTS

“Kenya: continuum from planning to MDA IDA implementation,” Dr. Sultani Matendechemo/
Prof Sammy Njenga

Kenya successfully implemented its first round of mass drug administration (MDA) rollout with ivermectin, diethylcarbamazine, and albendazole (IDA) in November 2018 with 82% coverage achieved across three sub-counties. This came after several rounds of inconsistent and ineffective MDA from 2001-2011. Several major factors for success were identified with effective social mobilization seen as the principle driver. Other important elements included the introduction of a dosing pole for increasing the community’s confidence in the treatment, building strong and effective partnerships with national and local players, early planning, frequent communication with stakeholders, and a high-level launch officiated by a local government official who took the drug publicly to promote trustworthiness in the community.

“Novel delivery strategy for high coverage IDA MDA in 4 districts in India,” Dr. Neeraj Dhingra
India successfully piloted IDA in four districts. Success strategies identified for reaching high coverage and compliance include effective planning with emphasis on ownership given to state and local governments, extensive media campaigns and engagement to raise awareness and support for IDA rollout, implementation of directly observed treatment (DoT), and applying lessons learned on improved microplanning from polio campaigns.

“The evolution of lessons learned from Samoa through Fiji, Malaysia to PNG,” Dr. Aya Yajima
Implementation strengths and challenges were discussed in the rollout of MDA with IDA in several countries in the Western Pacific region from 2018-2019. Effective (>65% of total population) coverage was reported or estimated after coverage evaluation surveys for the 5 countries implementing IDA. Some of the key lessons noted include the importance of dosing strategy and careful micro-planning, re-training of health staff, reinforcement of DoT, intensive social mobilization and consultations with relevant stakeholders to ensure ownership by local government and communities, and public launching by high-level officials. Remaining challenges noted were operational high turnover in health systems, hard-to-reach populations in remote communities, and implementation delays due to concurrent public health emergencies and delay in arrival of medicines. Real financial challenges included, competition for resources with other national priorities, high operational cost of MDA in low-infrastructure settings and lack of and slow release of project funding at national and sub-national levels.

“IDA for LF elimination: A good start, but miles to go before we sleep,” Dr. Gary Weil
Dr. Weil proposed several key areas for further research on IDA to reach elimination of lymphatic filariasis (LF). It is known that IDA is superior to DA and IA but the underlying mechanism for this effectiveness against LF is presently unknown. The validity of current transmission assessment survey (TAS) guidelines as an accurate measure for IDA MDA stopping decisions was raised as an issue warranting further investigation, especially as the number of countries using IDA increases. Other potential valid indicator alternatives suggested for further exploration included: antibodies, circulating filarial antigen surveys of adults and testing for positives for microfilaremia, and molecular xenomonitoring. It is also still unknown exactly how many rounds of IDA MDA are necessary for reaching stopping targets and this will vary depending on the target in question (e.g. TAS vs. interruption of transmission, etc.). An important area for further research is determining whether administration of IDA is safe to potentially accelerate LF elimination among countries co-endemic for onchocerciasis where IDA is currently not recommended.

KNOWLEDGE GAPS IDENTIFIED

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 microfilaria (Mf) without clearing circulating filarial antigen (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.