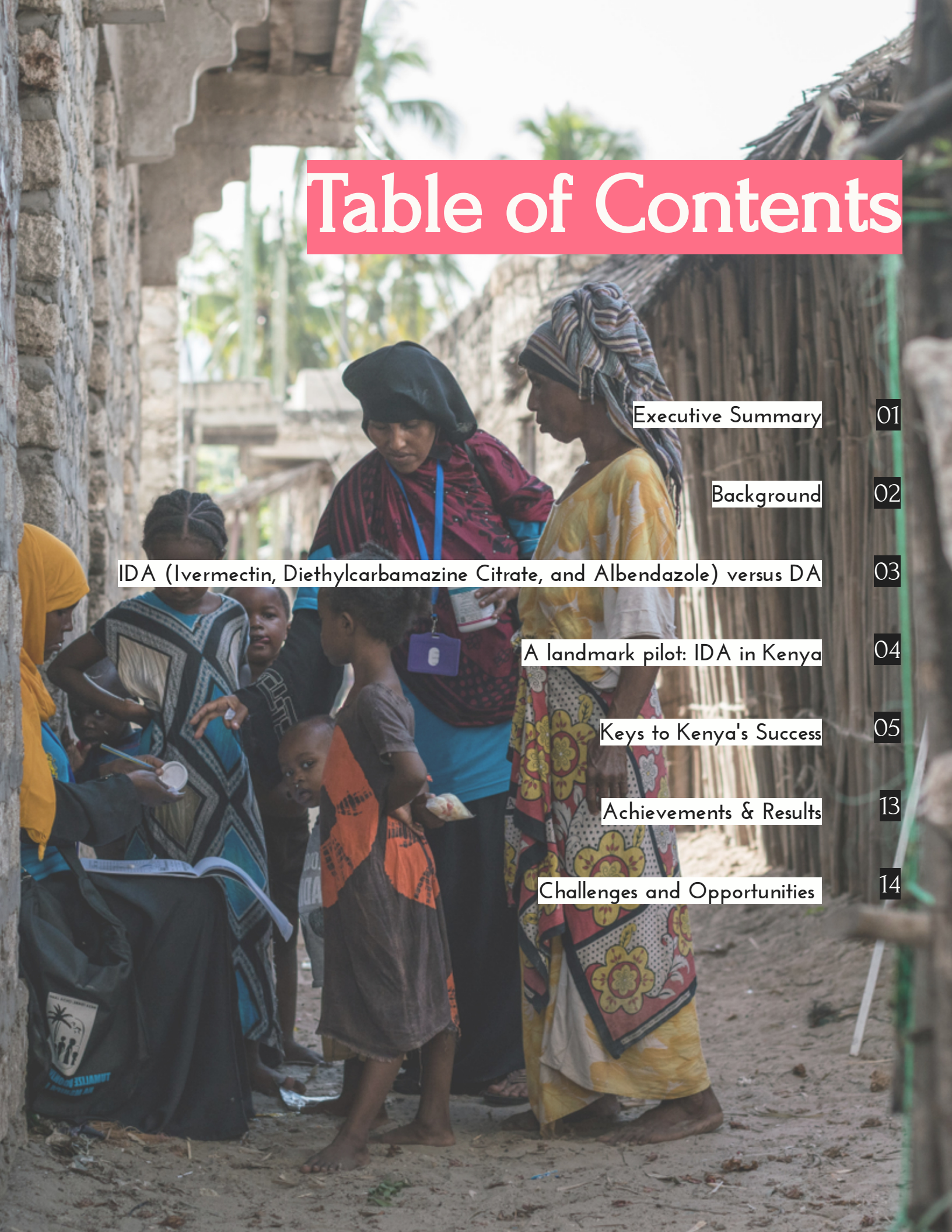
Charting the path for a new evidence-based approach to combating Lymphatic Filariasis

Piloting triple-drug therapy in Kenya

Evidence Action



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Executive Summary

Approximately 3.9 million people are at risk for lymphatic filariasis (LF) in Kenya. Kenya's Neglected Tropical Disease (NTD) Unit has implemented a National Programme to Eliminate LF (NPELF) since 2002. However, prior to 2015, mass drug administration (MDA) was irregular and limited in reach—implemented every two to three years instead of within 18 months as globally recommended—and covered fewer than 17 of the 23 endemic sub-counties. Kenya's program has markedly improved its quality and coverage achievements in recent years, but as of 2018, still required at least three additional rounds of consistent and effective MDA in most of the endemic communities to reach elimination, falling short of the World Health Organization (WHO)'s 2020 elimination target.

To explore possibilities of accelerating LF elimination, three sub-counties on the Kenyan coast (Jomvu in Mombasa County, and Lamu East and West) were selected in 2018 to pilot IDA—a new, intensified, and evidence-based treatment combination of ivermectin, diethylcarbamazine citrate, and albendazole, with heightened coverage requirements (therapeutic coverage must reach 80% or higher in IDA settings, compared to the standard 65% threshold in traditional LF programs). Evidence Action has provided fiscal management and technical assistance to Kenya's NPELF since 2016, and was proud to support Kenya as it became the first African country to pilot the new IDA regimen at public-health scale. This case study is meant to serve as an implementation blueprint for other nations considering IDA to accelerate the elimination of LF, pointing out some of the inputs and preparations that made a difference in the overall outputs and results. While further analysis is ongoing to determine cost-effectiveness and potential for future scale-up, it is clear that the Kenyan pilot reached its target population, with 100% geographic coverage and average treatment coverage of 87%.

At a glance: The problem

59 endemic countries have not eliminated LF

3.9 million people in Kenya are at risk of contracting LF

2020 is WHO goal for eliminating LF as a public health problem

Background

LF is an NTD that targets the lymphatic system and can often lead to elephantiasis (thickening of skin and tissue) or swelling of the limbs (lymphedema). It is a painful and profoundly disfiguring disease that can affect any individual, regardless of age, in communities where filariasis is transmitted. The disease is caused by microscopic parasitic thread-like worms known as microfilariae that are transmitted to humans through mosquito bites. The parasites develop into infective larvae in the human host and live for approximately 6–8 years, producing millions of microfilariae that circulate in the blood. While the infection may be acquired at any point in time, visible manifestations can be delayed until later in life, causing temporary or permanent disability in infected adults.

In 2000, the WHO launched the Global Programme to Eliminate Lymphatic Filariasis (GPELF), working towards elimination of LF as a public health problem by 2020. The WHO recommended large-scale treatment of entire at-risk populations in areas where the disease is of public health concern with a combined dose of two drugs: albendazole (ALB; 400 mg) with ivermectin (IVM; 150–200 mg/kg), or with diethylcarbamazine citrate (DEC; 6 mg/kg). This dual-therapy approach requires five to seven years of consecutive rounds of MDA at 65% therapeutic coverage or higher, and as of January 2019, the WHO had validated that 14 of 73 endemic countries had successfully eliminated LF as a public health problem using this treatment regimen. The majority of these are outside Sub-Saharan Africa, which constitutes 40% of the global disease burden.

With the year 2020 approaching and many countries still fighting LF, the global community of LF partners realized that the goal of elimination by 2020 could not be achieved in some regions and sought tactics to accelerate progress. Based on rigorous efficacy and safety trials (Weil et al., 2019), in 2017 the WHO recommended a triple-drug treatment of ivermectin, diethylcarbamazine citrate and albendazole (abbreviated as "IDA") as a more potent regimen that could quicken LF elimination (WHO, 2017). Evidence from large-scale randomized trials suggested that IDA has the potential to clear microfilaria at all life stages from the blood and can eliminate the disease from a population after two consecutive years' treatment with at least 80% coverage (Irvine et al., 2016). Compared to traditional treatment with only DEC and ALB (DA) or only IVM and ALB, which requires at least five consecutive annual rounds of treatment and 65% coverage of the target population, IDA presents a major opportunity.

DA versus IDA

Dual therapy (DA)	Triple therapy (IDA)
Two drugs administered	Three drugs administered
65% treatment coverage required to be considered "effective"	80% treatment coverage required to be considered "effective"
5 - 7 years of mass drug administration required	**As few as 2 years of mass drug administration may be sufficient**

In August 2018, Samoa became the first country to implement IDA through its national health system. However, it had never been implemented in a public health program in Africa until November 2018, when the Government of Kenya's Ministry of Health, through the NTD Unit, built upon an increasingly successful LF MDA program to pilot Africa's first mass IDA distribution in a subset of endemic areas. Meeting the coverage targets required careful adjustments to the LF program's design, additional financial investments, and strong coordination among multiple partners.

A landmark pilot: IDA in Kenya

Approximately 3.9 million people are at risk for LF in Kenya, residing in six counties (23 sub-counties) of the coastal region - Kilifi, Kwale, Lamu, Mombasa, Taita Taveta, and Tana River. The IDA pilot was conducted in three sub-counties, within two counties, where prevalence is high but MDA treatment coverage had previously been inadequate. One sub-county represented an urban setting (Jomvu, in Mombasa county), while the other two were rural (Lamu West and East, both in Lamu county). Lamu comprises of a mainland area and an archipelago of many islands situated on Kenya's northern coastline near Somalia, and therefore required some unique approaches to accessing all at-risk communities.

Keys to success: Kenya's implementation of IDA

For successful IDA implementation, based on existing evidence, a program target of 80% therapeutic coverage was set. To maximize Kenya's chances of achieving these higher targets, a range of new program strategies were adopted, including:

- Robust partnerships
- Advocacy, communication and social mobilization
- Adverse event management and pharmacovigilance tools
- Heightened supervision of drug distribution
- Customizing implementation and delivery to meet intensified program targets
- Improving implementer selection and training to achieve ambitious program goals

Robust partnerships

Several international partners collaborated to support the planning, design phase, and preparation for Kenya's IDA pilot, while the national NTD Unit was ultimately responsible for implementation. Evidence Action provided fiscal management and technical assistance in the following areas: a) design and procurement of training materials and advocacy, communication, and social mobilization (ACSM) materials; b) logistics for drug distribution; c) budget management for county and sub-county training and sensitization; d) customization and production of reporting forms; and e) coverage evaluation surveys. The NTD Support Center at the Task Force for Global Health and the END Fund provided technical and financial support (partially enabled by funding from the Bill and Melinda Gates Foundation), while the Kenya Medical Research Institute (KEMRI) conducted parasitological monitoring and evaluation. The African Institute for Health Development (AIHD) conducted formative research that influenced the review of ACSM materials and identified specific population segments with lower program engagement that could benefit from intensified mobilization.

Advocacy, communication, & social mobilization

The NPELF already used a suite of information, education, and communication tools including a flyer, poster, trainer's guide, and implementer's handbook. The program team also provided talking points to County Directors of Health to use in radio shows or news announcements. AIHD's formative research aimed to build on these tools by convening focus groups and community surveys that would allow the implementation team to better understand communities' knowledge and attitudes about LF and MDA, including perceived vulnerability to the disease and potential concerns about taking a larger number of tablets during the IDA pilot (because DEC and IVM dosage varies by height, some individuals would receive up to nine pills).Through these interactions, AIHD found that within Lamu and Jomvu, men and youth were more likely than other groups to turn down treatment, and recommended that in addition to intensifying the program's standard awareness materials such as posters and fliers, town announcements, community meetings, and radio talk shows, the program develop customized messages for these groups.

Advocacy, communication, & social mobilization (Continued)

For instance, some believed that LF is caused by witchcraft or can be inherited, that hydrocele is a sexually-transmitted disease, that hydrocelectomy surgery causes infertility, or that LF only affects the old and the poor. Messages were tailored to directly refute these common misperceptions. A hydrocelectomy is a procedure to repair a hydrocele, which is a buildup of fluid around a testicle that can be caused by LF infection.

The Evidence Action team set up WhatsApp groups for county level teams and sub-county teams, which were used to both "push" and "pull" information. The sensitization videos were shared through this platform as well as reminders of key dates or responsibilities. At the community level, similar groups were formed on an ad hoc basis, while individuals also forwarded the videos and messages to their existing groups or social contacts.

In IDA-implementing sub-counties, area chiefs and Community Health Extension Workers (CHEWs) worked in pairs to carry out in-person community sensitization, so that the CHEW could respond to any medical or technical question that arose but was also supported with a sense of authority from their local leader. As shown in Figure 1, they undertook a variety of methods to announce and explain the changes in treatment strategy and reasoning behind the shift, encouraging people to take the tablets during MDA.

Figure 1: Sensitization methods conducted by CHEWs prior to MDA

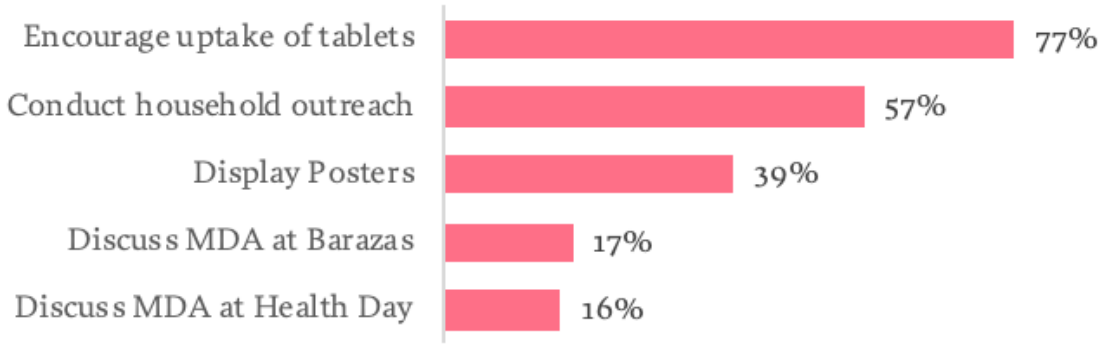


Figure 2: Household members' sources of information about the LF MDA

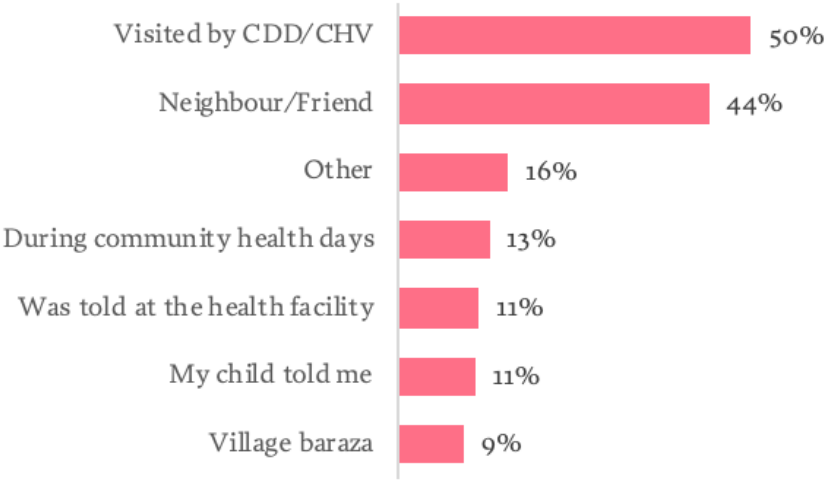


Figure 2 illustrates that most community members heard about LF treatment through their CHEWs and Community Drug Distributors (CDDs), but also that they successfully enabled individuals to pass along key messages to others.

Drawing on the successes that other public health programs have seen from developing logos and slogans, partners coined a program catchphrase: "Meza Tembe, Okoa Jamii!" which roughly translates to "Swallow the tablets to protect your community!" A new logo (Figure 3) depicts a family standing near a palm tree and coastline, showing that the program was meant for this specific community, residing in the Kenyan coastal region, comprising of all ages and genders.

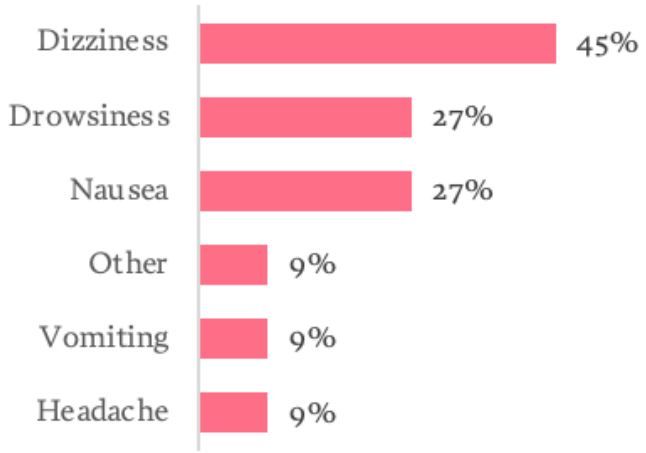
Respected figures such as politicians and Muslim and Christian faith leaders also reminded their followers to participate. The governor of Lamu County attended the IDA launch event along with the County Commissioner and Member of County Assembly, swallowing the tablets to prompt others to do the same, and to increase communities' confidence in the MDA campaign.

Figure 3: Program Logo

Adverse event management & pharmacovigilance tools

Based on research findings, partners knew that an increase in mild or severe adverse events was possible alongside the increased number of tablets being consumed. To ensure rapid and robust reporting and response to such events, the NTD Program collaborated with Kenya's Pharmacy and Poisons Board (PPB) and adopted tools (such as reporting forms) that were appended to both the Training of Trainers (ToT) manuals and CDD handbooks, and formed part of the training content. To ensure that any community members' questions or concerns about the drugs could be adequately addressed, the PPB provided hotline numbers that individuals could call with any questions or in case of any adverse events observed. Medication (cetirizine, paracetamol, and prednisolone) was also procured and distributed to health facilities so that providers would be ready to manage any reactions. Ultimately, no severe adverse events were reported and mild side effects were observed in only 2% of 675 households visited during MDA monitoring. Dizziness was most common (45%) among the 11 households where side effects were seen (Figure 4).

Figure 4: Side effects observed at MDA households (n=11)



Heightened supervision of drug distribution

In previous years, and in sub-counties using the DA treatment regimen, the LF program directed each CDD to target 500 individuals for treatment during the MDA. By recruiting more CDDs and reducing this target from 500 to 300 in IDA areas, each CDD was able to spend more time with their targeted households to answer any questions, ensure accurate dosing and recording, and to directly observe the treatments being swallowed. There was also closer supervision of CDDs, with one CHEW overseeing 10 CDDs, compared to 20 in prior years or in the sub-counties applying the DA approach. Finally, in IDA areas, treatment activities lasted for six days, compared to five days in the DA areas. All of these adjustments allowed the implementers to pay closer attention to detail and assured community members of the safety and importance of taking the medicines.

Customizing implementation and delivery to meet intensified program targets

Fixed posts and door-to-door treatment approaches were both used in the IDA implementation strategy. Both of these approaches had generally been used in prior years of treatment but were iterated upon during the 2018 round. For instance, MDA was taken directly to factories in Mombasa's industrial areas for the first time. This was an innovative way to capture a portion of systematic non-compliers by meeting them where they usually spend their days. However, one challenge to highlight is that because the drugs could make some individuals feel drowsy, some workers preferred to carry the medication home for later consumption, despite the program's recommendation to conduct "directly observed treatment" (DOT).

DOT enhances compliance with treatment – i.e., confidence that targeted individuals have swallowed the tablets – which cannot be confidently extrapolated from coverage measures that only reflect the distribution of medicines to targeted individuals. Before the 2018 MDA round, Kenya's program did not explicitly highlight the need for DOT, but leading up to the IDA pilot, partners agreed that it would be critical to emphasize this guideline during all implementer trainings and in the accompanying manuals – this may have contributed to resulting coverage levels. During this round of treatment, more boats were hired than in previous years to reach all targeted island areas, including those that were previously missed, given the extra time or resourcing required to access these hard-to-reach areas. As in prior years, some CDDs distributed medicines on or near the ferries that coastal communities often use to commute to and from work. While the particulars may differ in other countries, these are all examples of how the team in Kenya adapted "typical" program delivery structures to their local context and way of life.

Careful CDD selection processes also contributed to the success of the pilot. The NTD Unit and county teams provided guidance for CDD recruitment and gave inputs to communities' selection criteria; fundamentally, it is critical that CDDs are trusted and familiar to the neighbors they will be serving during the MDA. Some CDDs were chosen on the basis of being retired health professionals, or having worked as private chemists, ensuring their communities' confidence in their skills and potentially boosting treatment uptake. In some higher-class or gated communities, prior appointments had to be made, and it was useful to engage well-known and "experienced" CDDs to increase the community members' trust in the program. Training for CHEWs and other sub-county IDA implementation teams was centralized and conducted simultaneously for all. This was to ensure that accurate information on the new triple-drug therapy was conveyed, and to minimize information loss further down the training cascade.

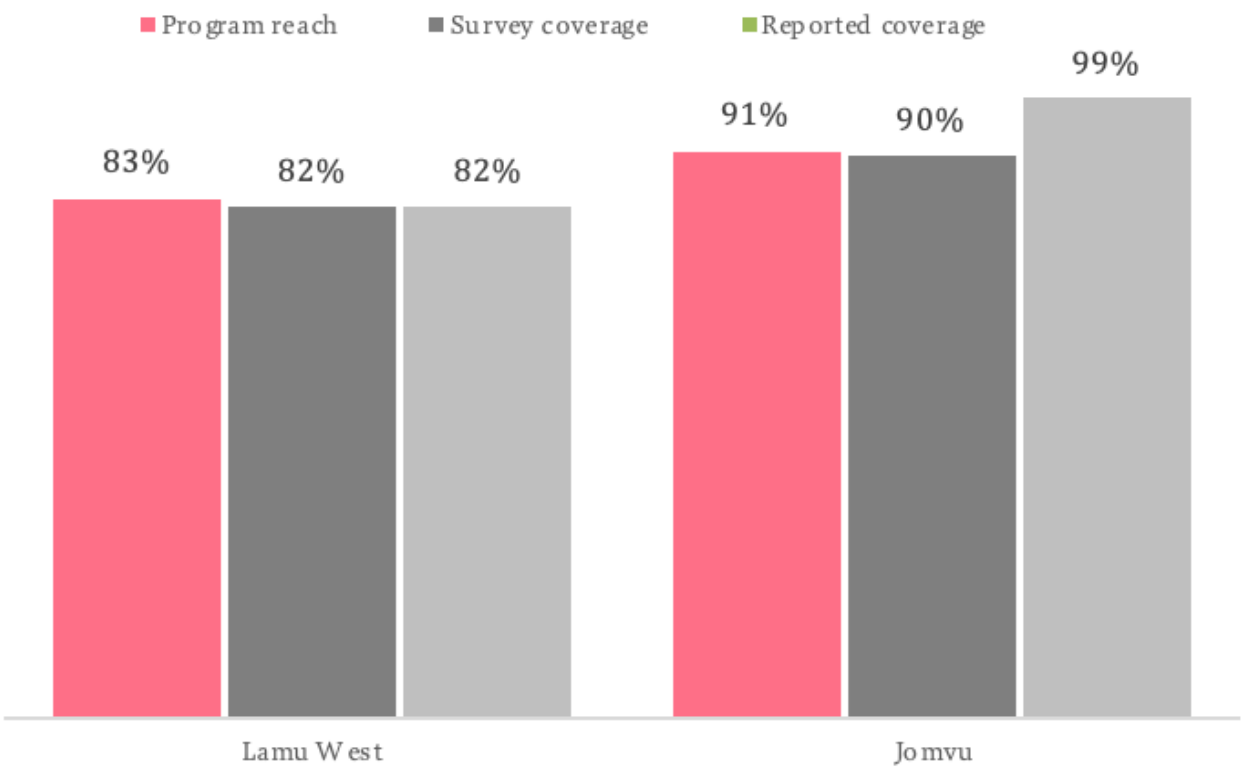
Improving implementer selection & training to achieve ambitious goals

Identifying champions, including victims of LF, at multiple points in the program cascade and awareness-raising process encouraged others to participate in MDA. At the launch event in Lamu, several of these individuals openly spoke about their lives with LF including hydrocele, a symptom of filariasis infection, and their previous belief that a hydrocelectomy would render them infertile. They shared about the surgery's positive impact on their quality of life and self-esteem, and encouraged their peers to take the LF medicines. To reinforce the training processes and messages delivered during the weeks and months before MDA, frequent mass SMS messages were sent to the CHEWs and chiefs reminding them of the LF and IDA information they needed to share with their constituents, and to emphasize the need for thorough social mobilization to meet the treatment targets.

Achievements and results

Program treatment reports showed 100% geographic coverage and indicated that the recommended 80% therapeutic coverage mark for IDA was met in all the targeted areas (Jomvu 98.6%, Lamu West 82.3%, and Lamu East 80.4%), with an average coverage of 87.1% in IDA target areas. were conducted in Jomvu and Lamu West, where results also showed high surveyed coverage – the proportion of surveyed individuals who ingested the IDA drugs - of 82% for Lamu West and 90% for Jomvu. Taken together, these data points give a sense of confidence that the actual treatment coverage in these sub-counties reached beyond the 80% target, implying successful implementation of the IDA MDA (see figure 5). Meanwhile, a similarly structured coverage evaluation survey that was conducted in a DA treatment area revealed 83% reported coverage and 73% surveyed coverage, suggesting a lower achievement than the IDA areas by comparison, while still achieving the 65% coverage target for the two-drug regimen.

Figure 5: Coverage evaluation survey results: program reach, surveyed coverage, and reported coverage



Challenges observed

The details of drug supply chain management at the sub-national implementation level has been an area of difficulty in the past and continues to be a challenge. Despite the recommendations for a reverse cascade as documented in the program's operating procedures, specific steps are not implemented effectively at all levels; for instance, some CHEWs do not send all remaining drugs post-MDA to the sub-county pharmacist for centralized storage. This makes it difficult to establish a reliable estimate of the number of drugs that remain in the sub-counties post-MDA. Although the NPELF has been able to recall treatment data within about a month of the MDA, tAs with many MDA programs, myths, misconceptions, and religious beliefs about medication caused a small minority of community members to refuse the drugs despite the intensified ACSM approaches informed by local formative research. While CDDs were directed to personally observe each individual swallowing the drugs, this was also challenging in some instances, including where drugs were distributed in workplaces, and especially in factories where workers were concerned about drowsiness. Just as the "cascade" model channels program information and materials from a centralized (i.e., national or county) level to lower (i.e., sub-county and community) levels of a program, the "reverse cascade" provides a structure for relaying program data or outputs from the communities back to a central node.

Lessons & Future Opportunities

Results from Kenya's pilot confirm the feasibility of surpassing the 80% coverage target with the IDA treatment regimen at public health scale. Key factors to a successful implementation included a smaller ratio of community health workers to targeted individuals; customizing and intensifying community mobilization activities; and increasing investments in logistical areas such as efficient local (ground or water) transportation and a greater number of MDA days. Using NPELF's treatment reports, , KEMRI's xenomonitoring results, and Evidence Action's process monitoring reports and coverage evaluation surveys, the Government of Kenya and partners will be able to assess the inputs, outputs, and benefits of the IDA pilot across several categories and contexts. This detailed analysis will allow the NTD Unit to decide how the triple-drug approach will be best incorporated into its future treatment strategies for Kenya's endemic counties. Kenya's NTD Unit and its partners also look forward to opportunities to share experiences with other countries working to shift from the traditional "DA" LF treatment model toward inclusion of the IDA regimen. Xenomonitoring detects the presence of the LF parasite in mosquitoes and allows programs to assess disease transmission dynamics.

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References:
Weil J. G. et al, The safety of double- and triple-drug community mass drug administration for lymphatic filariasis: A multicenter, open-label, cluster-randomized study, PLOS Medicine, June 24, 2019
WHO, Guideline: Alternative Mass Drug Administration Regimens for Lymphatic Filariasis, 2017
Irvine, A. Michael, et al. Effectiveness of a triple-drug regimen for global elimination of lymphatic filariasis: a modelling study, Lancet Infectious Diseases, December 21, 2016

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