




Navigating the way to onchocerciasis elimination: the feasibility and affordability of Onchocerciasis Elimination Mapping

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Background: Onchocerciasis is targeted for elimination of transmission by 2030 in at least 21 countries. To achieve this, recent and accurate data on the extent and intensity of onchocerciasis transmission are required. This will include mapping areas previously unassessed, or remapping of areas that were last visited as part surveys aiming to prevent blindness, not assess transmission in totality. There is near universal acceptance of the need to carry out these mapping reassessments, to achieve equitable and lasting elimination of onchocerciasis transmission. However, there is no consensus on how to conduct onchocerciasis elimination mapping (OEM), and little published data to inform policymakers and programme managers, including on cost.

Methods: Here, we summarise the methods and cost implications of conducting pilot OEM surveys in Ghana and Nigeria in 2018. We have included a breakdown of costs incurred overall, per person and per implementation unit in each country, as well as detailed analysis of the cost categories and the main cost drivers.

Results: The procurement and logistics of diagnostics accounted for more than one-third of the total cost, a significant cost driver.

Conclusions: This information will be valuable to policymakers and donors as they seek to prioritise onchocerciasis elimination and plan to complete OEM.

Keywords: cost, elimination, Ghana, mapping, Nigeria, onchocerciasis.

Introduction

Onchocerciasis is a neglected tropical disease (NTD), common in multiple discrete transmission foci across sub-Saharan Africa. It is caused by the parasitic filarial worm *Onchocerciasis volvulus*, which is transmitted by the bite of infected female black-flies. More than 218 million people live in areas known to be endemic for onchocerciasis, and >20 million people are currently estimated to be actively infected, not including residents

of areas requiring mapping.^{1,2} Onchocerciasis causes a range of skin symptoms including severe itching, and if untreated for a long period of time, can cause irreversible visual impairment and blindness.

Control of onchocerciasis symptoms and pathology can be achieved through delivering repeated doses of Mectizan, donated by Merck and Co., Inc. through the Mectizan Donation Program (MDP). For >30 y, national, regional and local governments, the WHO, MDP and other non-governmental organisation partners

have been scaling up efforts to control onchocerciasis, achieving remarkable success in many countries and foci. New cases of onchocerciasis-related blindness are now increasingly rare. This success has seen a shift in policy and programme focus from controlling onchocerciasis symptoms to eliminating transmission. In 2020, onchocerciasis was targeted for elimination of transmission in the new WHO NTD 2030 roadmap.¹ With this shift in focus, the need to extend previous onchocerciasis mapping surveys and accurately delineate all areas in need of treatment becomes more urgent.

During the control era, large-scale rapid epidemiological mapping of onchocerciasis (REMO) took place in a concerted effort to map high transmission areas in >20 countries, spearheaded by the African Programme for Onchocerciasis Control (APOC).³ REMO provided invaluable data allowing Ministries of Health to target Mectizan distribution in areas where the risk of onchocerciasis transmission and blindness was greatest. However, areas with medium to low transmission that were not the focus of REMO activities, for good reason, must now be identified and treated, to ensure no pockets of disease remain to jeopardise elimination and serve as reservoirs of infection. This requires optimisation of existing tools and strategies and the development of new methods and approaches. There is near universal acceptance of the need to carry out these mapping reassessments, because ensuring that all areas in need of ivermectin treatment receive it is a key component of achieving equitable and lasting elimination of onchocerciasis transmission. However, there is no widely agreed consensus on how to conduct onchocerciasis elimination mapping (OEM), and little data to inform policymakers and programme managers, including on cost. Concerns have been raised regarding the cost of conducting OEM in the estimated 1223 implementation units (IUs) that require it.⁴

In collaboration with ministries of health in Nigeria, Ghana and Mozambique, the WHO/Expanded Special Project for Elimination of Neglected Tropical Diseases (ESPEN), the Bill and Melinda Gates Foundation, Sightsavers and other partners have begun a series of pilot studies to test and refine the tools and strategies that will be needed for OEM. The overall aim is to operationalise and scale up the draft OEM protocols outlined by the WHO Onchocerciasis Technical Advisory Subgroup (OTS), and to provide data and learning to support their refinement and wider use. The first phase of OEM pilot studies was successfully completed in 2018 in Ghana and Nigeria and is the focus of this paper. Work in Mozambique is expected to conclude in early 2022.

Thus, we have collected and analysed the expenditure of OEM pilots in Ghana and Nigeria, to inform the NTD community on the cost and affordability. Detailed epidemiological results of mapping will be reported in subsequent publications. The aim of this study is to describe and compare the operational and economic lessons learnt through conducting OEM according to recommendation of the first WHO OTS meeting.

Methods

Sampling methods

Onchocerciasis is endemic in 147 districts of Ghana, with 7 621 642 people living in at-risk areas and requiring mass drug administration (MDA) with ivermectin (Mectizan).² According to ESPEN,

in 2017 there were 30 districts in Ghana not currently receiving MDA that could potentially be endemic and in need of OEM to confirm prevalence. Onchocerciasis is endemic in 436 local government areas (LGAs) in Nigeria, with 50 567 805 people living in at-risk areas requiring MDA. LGAs (the district equivalent) in Nasarawa, Plateau, Kaduna, Kebbi Zamfara and Delta states have officially stopped MDA for onchocerciasis and are entering into post-treatment surveillance.

The following methodology for elimination mapping using serologic testing was guided by recommendations made at the WHO OTS 1 meeting, where the district or subdistrict is both the assessment area for mapping and the potential IU for any MDA treatments.

Desk review

The ESPEN portal provides detailed district-level onchocerciasis data for Africa region countries. Alongside that, a thorough review of national databases, national reports, published literature, WHO, ESPEN, APOC and Onchocerciasis Control Programme reports was conducted for each IU. If there was no onchocerciasis information available for a chosen IU, information on bordering IUs or areas was collated for consideration. Mectizan-naïve districts (i.e. no previous treatment with ivermectin) were prioritized for mapping over districts under Mectizan treatment for lymphatic filariasis. Then environmental suitability models and satellite maps were used to aid district selection and subsequent identification of suspected first-line villages.⁵

Following the review and determination of areas to be surveyed, a 10-km buffer around rivers and tributaries suspected to have black fly breeding sites was visualised. An entomologist conducted a short, confirmatory visit of the area to identify potential vector breeding sites. A simple survey of village residents living within the 10-km buffer zone regarding the presence of biting black flies, seasonality of flies and areas along rivers known for particularly intense blackfly biting, was used to pinpoint suspected breeding sites and provide essential information to confirm the proximity of suspected 'first-line' communities to actual breeding sites confirmed by the entomologist. Communities located within 5 km of the putative breeding sites identified on the maps were designated as suspected first-line villages eligible for inclusion in elimination mapping exercises. These communities meet all the criteria for first-line villages, apart from confirmation of circulating *O. volvulus*. If local onchocerciasis transmission is confirmed during OEM, these villages will be confirmed as first-line villages.

Serological surveys

In Nigeria and Ghana, sero-surveys were conducted using an IgG4 Ov16 Rapid Diagnostic Test (RDT) at each survey site (SD Bioline, Abbott, South Korea), and SD Bioline Ov16 ELISA kits (SD Bioline Abbott), carried out in a laboratory using dried blood spot (DBS) samples collected on TropBio Filter paper (Cellabs, Australia). Each RDT and DBS was labelled with a unique QR code identifier assigned to each individual during the consent process, to ensure data confidentiality.

Two-tiered sampling approach

Rationale

Onchocerciasis is a focal disease, with the intensity and proximity of blackfly biting correlated to risk and severity of disease. This biology means OEM must focus on first-line villages, where the risk is assumed to be highest. For this reason, the first tier of sampling proposed for OEM is that in first-line villages, where, if onchocerciasis transmission is taking place locally, it should be easiest to detect. However, it is also important to note that the majority of onchocerciasis epidemiological and entomological data have been gathered from medium to high transmission areas. The biology and epidemiology of onchocerciasis transmission is ill defined and understood in lower transmission areas. Many countries and areas will not have recent or detailed data from hypoendemic areas to enable first-line villages to be selected with confidence. For this reason, the desk review and confirmatory entomologist inspections are required, as well as tier 2 sampling. Tier 2 sampling is a spot check on the remainder of the IU, to ensure no potentially suitable locations have been missed during the desk review, confirmatory entomology and tier 1 sampling. To have confidence that transmission is not taking place within the IU, a rigorous approach is required. Otherwise, future achievement of onchocerciasis elimination is at risk.

Tier 1 first-line villages

Three to five first-line villages were purposely selected within each IU, following breeding site identification. A convenience sample of 100 adults, aged ≥ 20 y, approximately 50 males and 50 females who had lived in the village for >10 y, were selected in each first-line village. Fingerprick blood samples were collected, applied directly to the RDT, according to the manufacturers' guidelines, then applied to filter papers to form DBS for subsequent ELISA analysis. If the selected first-line village did not have the required 100 resident adults, additional adjacent and nearby communities were included until 100 adults were recruited.

Tier 2 random sampling

From a list of all communities within the assessment IU, 30 were randomly selected. These could include potential first-line villages not sampled in tier 1, and others not previously considered. Any selected village could only be included in one tier, so if a randomly selected village had already been sampled in tier 1 it was excluded and another random selection was made. In each village, a convenience sample of 50 adults, approximately 25 females and 25 males, who had lived in the village for >10 y, was selected. Fingerprick blood samples were collected, applied directly to the RDT, according to the manufacturer's guidelines, then applied to filter papers to form DBS for subsequent ELISA analysis. If the selected village did not have the required 50 resident adults, additional adjacent and nearby communities were included until 50 adults were recruited.

Data collection

Serological, geographical and participant data were collected using the Android-based app *ESPEN Collect*. Data were structured

into three forms: one for each village, one for each participant and one for RDT results recording.

Training and operational learning

Training was conducted using a training manual and power-point modules specifically developed for the pilots. The modular structure allows easy adaption for future protocol iterations recommended by the WHO OTS committee. The training materials were first used in Nigeria and the feedback collected was then used to update them before training in Ghana. Training lasted for 3 days, two classroom-based days and one practical session. Feedback on training content, scope and delivery was collected using a standardised rating matrix and an open-ended comment section. Postmapping feedback on the OEM process as a whole was gathered from supervisors and ministry staff using semistructured questionnaires/feedback forms.

Costing methods

As part of the pilot phase, selected districts in Ghana and Nigeria were mapped. All actual pilot implementation expenditure was exhaustively collected and analysed.

Costing perspective

A service provider (project) perspective was adopted for this costing study. The in-country incremental cost for conducting onchocerciasis prevalence surveys using the OEM protocol was estimated.

We included all direct expenditure that occurred during the mapping activities and those linked to the OEM project. All indirect expenditures related to the normal running of a functional NTD elimination programme were excluded. Therefore, opportunity costs, including in-kind donations and time of Ministry of Health (MoH) or partner staff that were incurred but not charged to the OEM project, were not included, similarly to other NTD costing studies.^{6,7}

Finally, capital expenditure, here defined as items that will last for >1 y, were annualised by dividing its total cost by 5, the chosen average lifetime of capital items.⁸

Activities

OEM expenses were allocated to six activity categories (the detailed intervention pathway is available in Supplementary Information S1): (1) desk review activities, with each targeted IU requiring a review of historical *O. volvulus* point prevalence data, identification of suspected river basins (rivers and tributaries) and a definition of buffers, confirmation of the environmental suitability of areas within the buffer and identification of potential breeding sites and suspect villages; (2) training of technicians, including readers and recorders, community guides, drivers, supervisors and coordinators; (3) mapping activities, including personnel and transport costs of field staff, but also community sensitisation, divided into two subactivities (a) mapping of tier 1 villages and (b) mapping of tier 2 villages; (4) procurement activities, consisting of all expenditure related to the purchase and shipment of equipment and supplies used across all activities (e.g. supplies of RDTs, mobile phones); (5) supervision,

Table 1. Number of people screened by tier and country

Samples collected	Ghana		Nigeria		Grand totals (IU average)
	Dormaa West	Asunafo North	Wammako	Aleiro	
Tier 1	304	300	292	298	1194 (298.5)
Tier 2	1500	1491	1476	1413	5880 (1470)
IU total	1804	1791	1768	1711	7074 (1768)
Country total	3595		3479		

which mainly included personnel and transportation costs of the supervisors when travelling to supervise the designated teams; and (6) laboratory activity-related costs of the collection of dry blood samples for ELISA confirmatory testing, including shipment, supplies, analysis and quality assurance. Further details are provided in Supplementary Information S2.

Currency

For cross-country analysis, all costs were converted into US\$ 2018 using the average yearly exchange rate for the mapping period.

Data collection

Project expenditures were retrieved using the standard Sight-savers accounting system, where actual expenditures were reported against budgeted expenditure. Narrative information provided by in-country teams was also used. Data on the number of districts, IUs, villages and people examined were obtained from regular project monitoring using Metabase.

Results

Pilot mapping was successfully carried out in one LGA in Nigeria in July 2018, two districts in Ghana in August 2018 and one LGA in Nigeria in November and December 2018. In total, 7074 people were surveyed, 3595 in Ghana and 3479 in Nigeria (Table 1).

Training and operational learning

A total of 34 people were trained on the OEM mapping protocol, 16 in Nigeria and 18 in Ghana. Based on the feedback received, the field teams found the workload for collecting both RDT and DBS samples, entering village and individual results onto mobile phones, drying and packaging DBS, and communicating RDT results to individuals, manageable. To collect 100 samples in a village it was necessary for two teams of three people each to work together in Nigeria, whereas in Ghana 100 samples in first-line village were collected by one team of three people in a single day. In random villages, where the sample size was easily completed in 1 d by one team of three people, the time taken to travel to the next village often precluded starting work on another random village on the same day as the first. In both countries the

survey teams were keen to stress that good mobilisation of villages was key to successful sampling.

The use of *ESPEN Collect* to monitor data as they were collected and assist in supervision and data analysis was appreciated in both countries. WhatsApp was used as the primary means of communication between the ESPEN Data Manager and survey teams. Teams felt the rapid and specific feedback on their entered data helped them improve their technique, limit minor errors and consolidate the techniques learnt during training. The most common types of errors were the use of the same QR code for more than one participant, the entry of wrong cluster ID and confusion about the recorder ID, the cluster ID, the participant age and the time the participant spent in the village. To resolve these issues, user feedback was critical and was captured through daily interactions with the ESPEN Data Manager, field teams and supervisors.

Cost of surveys

Table 2 displays a breakdown of the total financial cost of conducting OEM pilots in four IUs in Ghana and Nigeria: US\$163 563. In terms of activities, fieldwork represented the majority of total financial costs (35%, US\$85 609), followed by procurement of equipment and supplies for activities (including tier 1 and tier 2 sampling) with 31% of total expenditure, then training with 22% of total expenditure.

In terms of the cost categories, personnel expenditure reached 52% of project expenses, costs associated with equipment and supplies were the second highest (34%) and, finally, transportation-related expenditure accounted for 14% of the total cost.

OEM implementation costs were further disaggregated to compare the cost of tier 1 and tier 2 sampling, as well as the cost of different diagnostic methods. As indicated in Figure 1, the overall cost of conducting this research, on average, was US\$40 891 per IU or US\$23 per person, using both SD RDT and ELISA for diagnosis (country details are available in Supplementary Information S3 and S4).

Looking at different sampling approaches and diagnostic methods, conducting tier 1 sampling as a stand-alone activity and using RDTs only is estimated to cost US\$92 per person in Ghana and US\$45 per person in Nigeria, resulting in an average cost per person of US\$69 (Figure 1, Supplementary Information S3 and S4).

Table 2. Total financial cost of OEM pilots by activities and inputs (in current US\$)

Activities\inputs	Personnel	Equipment and supplies	Transportation	Total
Fieldwork, subtotal	44 651 (27%)		12 256 (7%)	56 908 (35%)
Tier 1 villages	8904 (16%)		5193 (9%)	14 097 (25%)
Tier 2 villages	35 747 (63%)		7063 (12%)	42 810 (75%)
Procurement		49 925 (31%)		49 925 (31%)
Training	21 900 (13%)	5251 (3%)	9288 (6%)	36 439 (22%)
Laboratory	11 583 (7%)			11 583 (7%)
Desk review	5636 (3%)		305 (0%)	5941 (4%)
Supervision	1838 (1%)		930 (1%)	2768 (2%)
Total	85 609 (52%)	55 176 (34%)	22 779 (14%)	163 563 (100%)

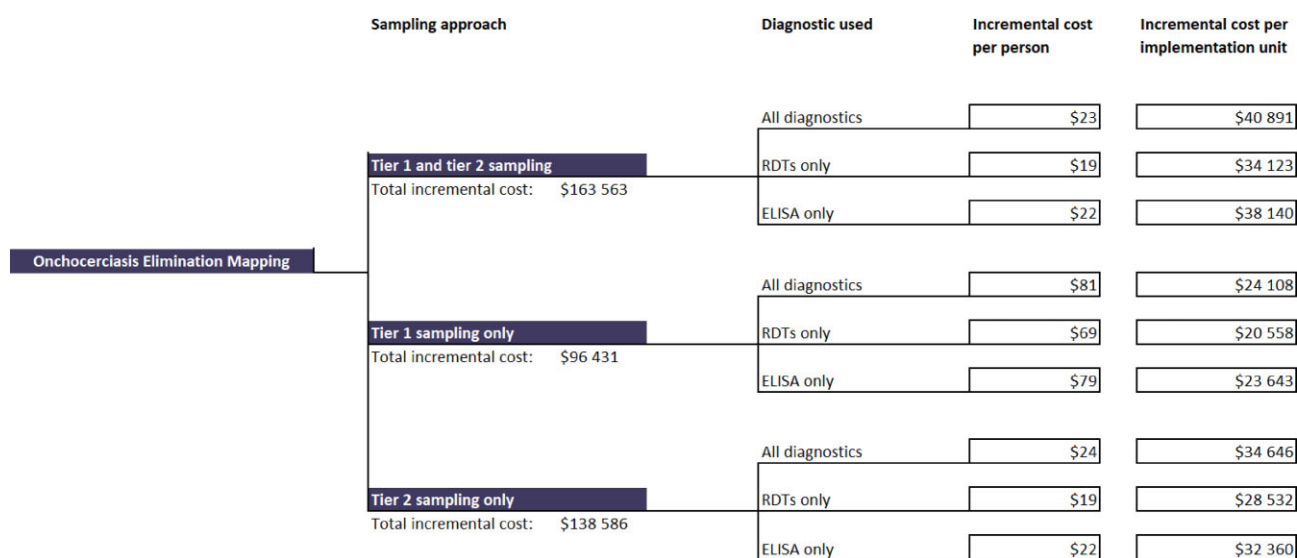


Figure 1. Total OEM unit costs by intervention and diagnostic.

Discussion

During the pilot OEM studies in 2018, detailed financial data were collected, disaggregated to expenditure category and type to allow accurate and comparative appreciation of the actual cost of OEM implementation and sample analysis. This analysis focuses on the costs of OEM activities, identifies the key cost drivers and helps to assess the affordability of addressing the unmet mapping needs. This evidence will help inform decision making regarding the prioritisation and resource needs for future OEM activities. Without completing OEM in areas of uncertain transmission, it will not be possible to achieve the elimination of onchocerciasis transmission by 2030. There are undoubtedly some unmapped areas that will need to start treatment. These areas must be identified as soon as possible to ensure that the health, and in particular the skin and eye health, of people living in such areas is not compromised. Moreover, eliminating onchocerciasis would represent significant cost savings for Ghana, Nigeria and other endemic countries, creating important fiscal space for financing other health interventions.⁹

The OTS recommendations have been iteratively updated since this study was carried out. The OTS 3 and OTS 4 recommendations make clear that the precise approach for tier 2 needs additional research.¹⁰ Therefore, it will be most informative for countries and implementing partners to be able to appreciate the costs of tier 1 mapping alone, while the community awaits further OTS recommendations on tier 2 random sampling. The costing information on tier 2 will be helpful to inform future recommendations in that area. The current OTS 3 recommendations on OEM also state that RDT on DBS samples eluted in the laboratory should be the primary diagnostic approach, while alternatives are investigated, validated and approved.¹⁰ We do not have data that would allow us to directly estimate a cost for the laboratory RDT approach, but it would be most comparable with the cost of performing RDT in the field. Cost savings during village sample collection would probably be realised through the streamlined workflow in this approach: only DBS samples would be collected, and there would be no need for the additional time to communicate RDT results and refer to health centres when required. This would be offset by minimal laboratory costs; however, running

laboratory RDT does not need much specialised equipment, other than a refrigerator in which to store reagents and carry out elution incubations, plus basic pipettes and laboratory plasticware. These costs would likely be less than the ELISA processing costs in the laboratory.

To put our findings in the most useful context, the cost of training, supervision, sample collection and SD RDT analysis for a tier 1 survey of 300 people was, on average, US\$20 558 per IU, or US\$69 per person screened. This is the cost estimate most likely to be closest to current recommendations. If SD ELISA kits are used as the primary diagnostic method, then the average cost per IU for tier 1 sampling would be US\$23 643, or US\$79 per person screened. There are significant cost savings realised through economies of scale by carrying out tier 1 and tier 2 sampling together, rather than carrying out only tier 1 sampling and completing tier 2 sampling at a later date. The cost per person screened when conducting tier 1 and tier 2 sampling together is estimated to be US\$34 123 per IU (US\$19 per person) for SD RDT as primary diagnostic and US\$38 140 (US\$22 per person) if using SD ELISA. Carrying out the two tiers of sampling as two separate surveys would lead to a total cost of at least US\$49 090 per IU using RDT only and US\$56 003 per IU using ELISA only.

As well as the OTS 3 recommendation against the use of RDTs directly on whole blood, there is also a lack of certainty around the optimal ELISA method. Here, we used commercially available kits. Both the SD ELISA and SD RDT kits are supplied by the same manufacturer, Abbott. They need to be shipped from their manufacturing base in South Korea. This adds considerable shipping costs, particularly for the ELISA kits, which need to be kept at 4°C throughout transit. There is no global donation or diagnostic discount scheme for onchocerciasis, unlike for lymphatic filariasis, so this is a cost that falls on each country wishing to carry out OEM. Additionally, in many countries onchocerciasis diagnostics are not on the official MoH exemption list, meaning additional importation and customs costs are included within the shipping cost category. Arranging import, collection and transport of the diagnostics within each country also has a personnel time cost. This cost is not well captured in our study, due to an underestimation of the time-consuming nature of this activity during the planning phase of the work, but we conservatively presume it corresponds to an additional US\$832 of staff time (8 d) for each country.

It is difficult to compare OEM costs to other disease-mapping interventions. Comparing cost estimates between disease mapping studies can be deceiving, as survey methodologies, mapping protocols and even costing methodologies can differ. For instance, OEM requires procurement of diagnostic materials, and this is often not required for other NTD mapping. However, it is interesting to note that OEM mapping costs are three times as expensive as trachoma mapping carried out by the Global Trachoma Mapping Project (GTMP).¹¹ The financial cost of screening a person for trachoma cost, on average, US\$6.4 (converted to US\$ 2018 using World Bank annual inflation consumer prices) or US\$18 632 (US\$ 2018) per evaluation unit (around 2500 people) against US\$19 (US\$ 2018) for OEM tier 2 sampling by RDT or US\$28 532 per IU (around 1470 participants). This is largely explained by the fact that trachoma mapping does not require the same level of equipment and supplies as OEM mapping as it is a clinical examination rather than a diagnostic test; GTMP required less personnel and per diems, which are, in both projects, signif-

icant cost drivers; and finally, GTMP was a standard large-scale project, whereas the surveys analysed here are pilots including different testing methods.

Alternatively, and to compare with a similarly material intensive mapping intervention, the Brady et al. study on the costs of transmission assessment surveys (TAS) for lymphatic filariasis, found the average cost per IU to be US\$23 547 (converted to US\$ 2018 using World Bank annual inflation consumer prices) per TAS or evaluation unit.¹² This is comparable with the similar sample size and approach of tier 2 sampling by RDT for OEM, which cost US\$28 532 (US\$ 2018) per IU. This does not take into account the fact that filariasis test strip kits used for TAS are donated and there is no similar donation programme for onchocerciasis diagnostics. There are other differences, including the fact that in the OEM costing, supervision and 'out-of-country' shipping expenditure have been included, while the study of TAS of lymphatic filariasis costing did not.

Given that procurement and shipping of diagnostic material is a significant cost driver (34% of total incremental costs), the choice of diagnostic method has an important cost implication. As shown in Figure 1, the average cost per IU of conducting tier 1 and tier 2 sampling at the same time varies from US\$34 123 to US\$38 140 whether we use RDTs only or ELISA kits, which, at a larger scale, could have significant cost and affordability implications.

The variations in cost per person tested between Ghana and Nigeria are mainly explained by the cost-of-living differences between the two countries, particularly the official MoH per diem rate, and the higher price for venue rental in Ghana. In addition, in Ghana an entomologist was contracted for the desk review, whereas in Nigeria an entomologist from the MoH did the work required and hence only received per diems.

In the context of the WHO 2030 NTD roadmap and the global drive to eliminate onchocerciasis, this research provides useful information on the cost and practicalities of conducting OEM mapping according to the latest WHO OTS guidance. Completing OEM is a vital step towards achieving the elimination of onchocerciasis transmission and providing an accurate and up-to-date epidemiological assessment of transmission in all potentially endemic or at-risk areas, whether currently under treatment or not. Through careful desk review, countries can minimise the number of IUs that need to have physical OEM surveys, greatly reducing costs. Some mapped IUs could still be below the threshold and will not need to begin treatment. Therefore, conducting OEM will allow us to rapidly 'shrink the map' and focus on areas that need treatment. In that regard, completing OEM is an important issue for equity, and ensuring all those who need treatment for onchocerciasis can receive it, protecting them from potential skin disease, itching and eye health problems later in life.

This research also highlights the need for affordable, accurate point of care diagnostics for onchocerciasis, to make an assessment of treatment needs through OEM, and eventual stopping decisions, achievable. The procurement of Ov16 diagnostics, and associated costs, accounts for more than one-third of the total mapping incremental costs across the two pilot countries. This is a significant cost driver and may result in OEM being unaffordable outside of a research setting unless the procurement costs can be lowered. For programmes to be able to conduct OEM and take that crucial step closer to achieving nationwide elimination,

research on new diagnostics, and support for affordable access to them, is paramount to the global elimination agenda.

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Data availability: None.

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