Integrated Surveillance Planning Toolkit for Neglected Tropical Diseases in Post-Validation or Verification Settings

Landscaping report
May 19, 2023
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### Abbreviations

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<th>Description</th>
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<tr>
<td>AGT</td>
<td>Anopheline gravid traps</td>
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<tr>
<td>BGS</td>
<td>Biogents Sentinel</td>
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<td>CDC</td>
<td>Centers for Disease Control and Prevention</td>
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<tr>
<td>CO2</td>
<td>Carbon dioxide</td>
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<td>DBS</td>
<td>Dried blood spots</td>
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<td>DEC</td>
<td>Diethylcarbamazine</td>
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<td>DHIS2</td>
<td>District Health Information System</td>
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<tr>
<td>DHS</td>
<td>Demographic and health survey</td>
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<tr>
<td>DNA</td>
<td>Deoxyribonucleic acid</td>
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<tr>
<td>ELISA</td>
<td>Enzyme-linked immunosorbent assay</td>
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<tr>
<td>ESPEN</td>
<td>WHO AFRO’s Expanded Special Project for Elimination of Neglected Tropical Diseases</td>
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<td>GPELF</td>
<td>Global Program to Eliminate Lymphatic Filariasis</td>
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<td>HIV</td>
<td>Human immunodeficiency virus</td>
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<tr>
<td>HLC</td>
<td>Human landing catch</td>
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<td>HMIS</td>
<td>Health management information systems</td>
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<td>ICT</td>
<td>Immunochromatographic test</td>
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<td>IDSR</td>
<td>Integrated disease surveillance and response</td>
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<td>IgG4</td>
<td>Immunoglobulin G4</td>
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<td>LF</td>
<td>Lymphatic filariasis</td>
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<td>LTS</td>
<td>Lohmann Therapie-Systeme AG</td>
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<tr>
<td>MDA</td>
<td>Mass drug administration</td>
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<tr>
<td>mIVRS</td>
<td>Mobile phone-based interactive voice response system</td>
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<td>MMDP</td>
<td>Morbidity management and disability prevention</td>
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<td>MX</td>
<td>Molecular xenomonitoring</td>
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<tr>
<td>NLFEFP</td>
<td>National Lymphatic Filariasis Elimination Program</td>
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<tr>
<td>NTD</td>
<td>Neglected tropical diseases</td>
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<td>PAHO</td>
<td>Pan American Health Organization</td>
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<tr>
<td>PC-NTD</td>
<td>Preventive chemotherapy neglected tropical disease</td>
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<tr>
<td>PCR</td>
<td>Polymerase chain reaction</td>
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<tr>
<td>PTS</td>
<td>Post treatment surveillance</td>
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<td>PVS</td>
<td>Post verification/validation surveillance</td>
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<tr>
<td>Q-PCR</td>
<td>Quantitative polymerase chain reaction</td>
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<tr>
<td>RDT</td>
<td>Rapid diagnostic test</td>
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<tr>
<td>STH</td>
<td>Soil-transmitted helminths</td>
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<tr>
<td>TAS</td>
<td>Transmission assessment survey</td>
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<tr>
<td>TB</td>
<td>Tuberculosis</td>
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<td>TF</td>
<td>Trachomatous-inflammation follicular</td>
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<td>TPP</td>
<td>Target product profile</td>
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<td>WHO</td>
<td>World Health Organization</td>
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Executive summary

The World Health Organization (WHO) includes 21 neglected tropical diseases (NTDs) in its 2030 road map to prevent, control, eliminate or eradicate disease. As part of this road map, more than 40 countries will be in their post-verification or validation phase for at least one disease in the next three years, including four for onchocerciasis, 17 for lymphatic filariasis (LF), and 33 for trachoma. Given that disease-specific funding is likely to decrease after a country attains elimination, this presents a critical window to identify and invest in post-validation or verification surveillance (PVS) systems.

One approach to improving the sustainability of PVS is to integrate surveillance with other existing surveillance platforms or to develop new integrated platforms that share resources. Under WHO leadership and with funding from the Bill & Melinda Gates Foundation, PATH is supporting the design of an integrated PVS planning toolkit to assist national NTD programs in assessing options for sustainable and integrated approaches to NTD surveillance after elimination has been verified or validated. To guide the toolkit development, PATH conducted landscaping activities to review existing NTD surveillance platforms and strategies, with an initial focus on LF, onchocerciasis, and trachoma.

Through a semi-structured review of published and grey literature, evidence was gathered to understand current and planned NTD PVS strategies and best practices for NTD surveillance, particularly for the three priority NTDs, including case studies detailing the practical application of these approaches. This evidence base was validated and expanded through the stakeholder consultation process, which included global NTD experts, NTD program staff, WHO and donor representatives, and stakeholders with surveillance or modeling expertise. The semi-structured interviews helped identify high-quality, effective NTD surveillance systems and countries that have implemented them successfully, particularly in PVS settings. The project team also gathered input on how an integrated system could work, what components are needed, and what considerations should be taken into account when developing the PVS planning toolkit for NTDs.

The literature indicated the potential benefit of molecular xenomonitoring (MX) and next-generation serological testing for both LF and onchocerciasis in conjunction with more traditional population surveys (i.e., transmission assessment surveys) for PVS. These strategies may provide logistical and financial efficiency that will be key to sustaining PVS as funding for validated or verified diseases is likely to diminish over time. Additionally, tools such as PoolScreen for MX and the biplex LF-Onchocerciasis antigen rapid diagnostic test for serological testing offer potential opportunities for integration between these two diseases, which may create additional gains in efficiency for programs conducting integrated PVS for NTDs. Investments in new biomarkers may also contribute to integrated PVS by expanding the utility of integrated serological platforms (i.e., Luminex®). Key areas of uncertainty remain where additional research and global guidance on PVS will be needed. For example, monitoring for post-validation reintroduction of disease via migrant populations or zoonotic sources is a critical component of PVS, however it is not yet well understood. Serosurveillance presents important opportunities for increased efficiency, specificity, and sensitivity in identifying subpatent infections, but guidelines for the use of serosurveillance must be sensitive to age and geography-dependent factors.

This landscaping exercise identified several key themes to consider in the development of the PVS planning toolkit for NTDs. Multiple stakeholders agreed on the importance of keeping the toolkit flexible and agile, remaining adaptable to local country contexts and responsive to the varying needs of different NTD control programs. There were also consistent recommendations to design the toolkit to facilitate sustainable integration of PVS strategies into routine reporting systems and existing data analysis platforms wherever possible. Lastly, the need to consider well thought-out responses to cases identified through a potential surveillance system was stressed by several stakeholders.
Looking ahead, the PVS planning toolkit will be most useful if it effectively combines guidance from WHO and other global stakeholders with the contexts, needs, and innovations of NTD program managers and staff in the geographies where it is initially implemented. As such, the voices of those who best understand the local realities and challenges inherent in conducting PVS for NTDs will be centered and prioritized during the upcoming toolkit development process.
Introduction

The World Health Organization (WHO) includes 21 neglected tropical diseases (NTDs) in its 2030 road map to prevent, control, eliminate or eradicate disease. An estimated 1.74 billion persons globally are still at risk for these diseases, which disproportionately affect populations in poverty and cause significant disability among those affected. The WHO road map sets disease-specific goals in three categories: eradication (i.e., permanent global reduction to zero); elimination of transmission (i.e., reduction to zero in a defined geographical area); and elimination as a public health problem (i.e., achievement of measurable targets). Two NTDs (dracunculiasis and yaws) are currently targeted for eradication, three (onchocerciasis, leprosy, and African trypanosomiasis [gambiae]) for elimination of transmission and eight for elimination as a public health problem. Countries use these goals to set their own targets and to prioritize resources for program and surveillance activities, ensuring that they can meet the requirements for validation, verification, or certification of elimination.

Achievement of the disease-specific criteria for eradication, elimination of transmission, or elimination as a public health problem is an important public health success, and WHO officially acknowledges this achievement after an external review is conducted. Each goal is associated with a specific term to describe the level of achievement: certification is recognition of countries that have eliminated a disease targeted for eradication; verification refers to the elimination of transmission; while validation refers to the elimination of a disease as a public health problem. Achievement of WHO certification, verification, and validation, however, does not mean that there is no future risk of disease: although countries may meet the criteria for verification of elimination of transmission, they will remain at risk of re-introduction from imported cases as long as transmission continues elsewhere, while countries validated for elimination of disease as a public health problem are at risk of resurgence.

As part of this road map, more than 40 countries will be in their post-verification or validation phase for at least one disease in the next three years, including four for onchocerciasis, 17 for LF, and 33 for trachoma. Surveillance after elimination of NTDs is critical to protect the gains that have been achieved. Signs of re-establishment and resurgence that are identified early can lead to timely and effective responses that address the increased incidence. However, once the verification or validation processes have been completed, resources are often depleted and funding for post-verification or validation surveillance (PVS) may not be available or may be insufficient to cover the long period of time over which surveillance may be required.

One approach to improving the sustainability of PVS is to integrate surveillance with other existing surveillance platforms or to develop new integrated platforms that share resources. Under the leadership of WHO and with funding from the Bill & Melinda Gates Foundation, PATH is supporting the design of an integrated PVS planning toolkit to assist national NTD programs in assessing options for sustainable and integrated approaches to NTD surveillance after elimination has been verified or validated. It should be noted that this toolkit is not intended to define best practices or guidelines for PVS of NTDs, which is WHO’s responsibility and role, but rather to support national NTD programs in developing a sustainable approach to PVS using the resources available.

This work focused initially on three target NTDs: onchocerciasis, lymphatic filariasis (LF), and trachoma. These three NTDs represent diseases that have seen substantial progress toward elimination, have different transmission pathways, and are in most immediate need of PVS approaches. While the integrated surveillance planning toolkit being developed was initially conceived with an emphasis on these three focal NTDs the potential exists to incorporate additional aspects for

1 Countries that are certified free of disease also remain at risk of imported (or zoonotic cases) and post-certification surveillance is required until global eradication is achieved.
other NTDs.

Onchocerciasis, or “river blindness,” is a parasitic disease that threatens the health of 240 million people living across 31 endemic countries, 99% of whom live in sub-Saharan Africa.²,³ The disease is caused by the parasitic worm *Onchocerca volvulus* and is transmitted to humans through repeated bites of infected *Simulium* black flies.⁴ Those who are infected may develop symptoms such as a skin rash, nodules under the skin, or eye disease, with the most serious manifestations from long-term and repeated infections being visual impairment and permanent blindness.³ Verification of elimination is granted once all detected foci under long-term ivermectin treatment have been verified as free of transmission and after sufficient evidence has been provided that all areas of potential transmission have been identified through appropriate testing of black flies and serological evaluation of children under 10 years of age, as necessary.⁵ To date, four countries have been verified as onchocerciasis-free by the WHO: Colombia, Ecuador, Mexico, and Guatemala (Figure 1). Once verification has been achieved, a PVS system should be established to detect any recrudescence in formerly endemic areas and introduction in formerly non-endemic areas. The WHO-recommended approach to PVS for onchocerciasis is based on the capture and testing of black flies using O-150 polymerase chain reaction (PCR) to determine the proportion of the vector population infected with *O. volvulus*. This works by using *O. volvulus*-specific DNA probes targeting the O-150 repeat family sequence.⁵ Based on WHO guidance, surveillance should continue until the risk of reintroduction of the disease no longer exists in any country in that region. However, recommendations on what cadence and duration is most appropriate and feasible for entomological surveillance in each setting, as well as what additional approaches, such as serology, could be implemented in addition to entomological surveillance, remain unclear.

![Map of countries that have been validated or verified for elimination of onchocerciasis, lymphatic filariasis, and/or trachoma.](image)

LF is a parasitic disease transmitted to humans through mosquitoes infected with nematodes (roundworms) of the *Filarioidea* family.⁶ While those with LF are often infected during childhood, chronic manifestations such as lymphoedema and hydrocoele tend to appear later in life, requiring lifelong care.⁷,⁸ As of 2020, 863 million people across nearly 50 countries are at risk for LF, with over 36 million people living with chronic manifestations of the disease.⁷ Countries must meet two milestones in order to achieve validation: (1) stop the spread of infection through mass drug administration (MDA), and (2) alleviate suffering by managing morbidity and preventing disability (MMDP).⁹ To date, 17 countries have been validated by the WHO for elimination of LF as a public health problem, including Cambodia, Egypt, Malawi, Togo, and Yemen.¹⁰ An additional seven
countries—Bangladesh, Brazil, Brunei, Dominican Republic, Laos, Mali, and Uganda—are close to validation (Figure 1). Once validation is achieved, WHO recommends that the country continue conducting PVS and integrate MMDP into health services, though additional clarity is needed on specific surveillance activities recommended for PVS.

Trachoma is the leading cause of blindness worldwide and a public health problem in 44 countries, with an estimated 136 million people at risk.11 Caused by the bacterium *Chlamydia trachomatis*, trachoma spreads to humans through personal contact, shared towels or clothing, or through infected flies.12 Trachoma predominantly affects those in the poorest and most rural parts of the world, with young children and their caregivers being the most at risk of infection.12 WHO validation of elimination of trachoma requires that trachomatous-inflammation follicular (TF) in children aged 1–9 years remains at <5.0% for at least two years after interventions to control trachoma have ceased.13 As of October, 14 countries have been validated as having eliminated trachoma as a public health problem (Figure 1).11 There are currently no formal guidelines on how to conduct PVS for trachoma.14

To guide the development of an integrated NTD PVS planning toolkit focused on these three diseases, PATH sought to compile evidence on existing NTD surveillance platforms and strategies through a desk review and informal stakeholder discussions. The team also conducted an initial review of existing surveillance toolkits to identify components or structural considerations that might be relevant for the PVS planning toolkit. The literature review and a semi-structured stakeholder consultation process served to generate evidence on the current state, barriers, and opportunities for integrated PVS of onchocerciasis, LF, and trachoma, including utilization of surveillance systems outside of NTDs. A thorough review of PVS guidance and approaches for non-priority NTDs fell outside the scope of the literature review and stakeholder consultations for this project. The methodologies and key findings of both the literature review and the stakeholder interview process are included in this report. The findings from the landscaping activities will inform the development of the integrated NTD surveillance planning toolkit.
Methodology

Literature review

The objective for the literature review was to review the existing evidence base to understand current and planned NTD PVS system strategies and best practices for NTD surveillance, particularly for the three priority NTDs in PVS settings, including case studies detailing the practical application of these approaches. Peer-reviewed publications and grey literature were both reviewed in this process. The review also incorporated an examination of existing routine and active surveillance systems that could serve as platforms for PVS such as the Integrated Disease Surveillance and Response system (IDSR), community- and event-based surveillance systems, periodic population-based surveys such as the Demographic and Health Survey (DHS) program, entomological surveillance platforms that track relative vector composition and distribution patterns, xenosurveillance platforms that analyze captured vectors for the presence of pathogens, and facility- or location-based surveys and available platforms in the District Health Information System (DHIS2), as well as digital tools currently being used for both NTD and non-NTD surveillance.

The literature review consisted of a non-systematic, "semi-structured" review of published literature available via the PubMed® online database and a supplementary grey literature search for relevant literature that had not undergone peer-review or was otherwise uncaptured by the original search terms. The published literature search involved devising appropriate combinations of search terms in PubMed’s advanced search builder, reviewing the titles and abstracts of the initial results for relevance, and then performing a full-text review of the initial inclusions. The search terms for the review included key terms for surveillance and disease monitoring as well as terms for the three NTDs that formed the focus of this review, along with exclusion terms to ensure that all papers returned had abstracts available and were published in the 10 years prior to the review (see Appendix 1 for search terms in their entirety).

The grey literature review consisted primarily of reviewing resources on PVS recommended to the project team by key stakeholders during the consultation process. In addition to these two initial steps, a reference or "snowball" sample of relevant literature was reviewed by identifying highly useful publications listed in the reference sections of the papers reviewed in the published literature search that were not captured by the initial PubMed search terms.

The outputs from the published and grey literature searches were collected into spreadsheets where metadata such as author information, disease focus, elimination setting, and study type were extracted alongside key takeaways from the full text review for each identified document or resource.

Semi-structured stakeholder interviews

The aim of the semi-structured interviews with key stakeholders was to understand current and planned NTD surveillance strategies. Given the lack of historical emphasis on PVS, the interviews discussed all surveillance systems used for various disease transmission settings. Through the consultation process, the project team aimed to: 1) identify NTD surveillance systems (including data platforms) that have been used in the past, as well as countries that have implemented those systems successfully, particularly in PVS settings; 2) gather input on how an integrated PVS system might work and what components are needed; 3) gain insight into any NTD PVS surveillance approaches or guidelines currently in development; and 4) identify any other toolkits that might be relevant, from both a structural and technical perspective.

Key informants were identified from global institutions (i.e., academic institutions, implementing partners, donors) and a few national NTD programs that are approaching elimination or are in the PVS stage for at least one of the three disease areas. The initial stakeholder list was developed with input from the Bill & Melinda Gates Foundation and WHO. Special attention was paid to ensure variation in expertise across stakeholders consulted, with representation from NTD technical experts,
non-NTD surveillance experts, and modeling fields. An initial set of priority stakeholders were contacted via email to request their participation in the stakeholder consultation process to inform the development of the NTD surveillance planning toolkit. For stakeholders willing to participate, a 45-minute virtual meeting was scheduled with at least two interviewers from the PATH team.

During the interview, PATH introduced the project, the purpose of the interview, and requested verbal consent to record the interview. The interviewers then followed a standard script with interview questions. As semi-structured interviews, the interviewers had the flexibility to deviate from the script as they saw fit. Additional stakeholders were identified using a snowball approach throughout the consultation process, where participants were asked to name any other stakeholders that they would recommend contacting for the project. Additional stakeholders were contacted for participation until content saturation was reached for the various interview topics.

The interview guide was designed to confirm current and planned NTD surveillance strategies and gather insight on what a successful surveillance system looks like for the three NTDs. Stakeholders were further probed to gather information, if known, about both integrated and non-integrated surveillance approaches in elimination or non-elimination settings, as well as the challenges in implementing PVS approaches. The interviews also explored any new or emerging tools, approaches, or guidelines that are currently in development and could impact the future toolkit deployment process. Finally, the interviewees were asked to share their suggestions for an integrated NTD surveillance system in PVS settings, as well as key components and considerations to include in the development of the planning toolkit. The key takeaways from each interview were summarized into a spreadsheet to identify key themes that would inform toolkit development.

**Toolkit review**

As noted above, during stakeholder interviews, interviewees were asked to share any existing planning toolkits for NTDs or other health areas that might be informative in the development of the PVS planning toolkit for NTDs. These toolkits were then compiled for review. A spreadsheet was created to systematically capture information about each toolkit (Annex 1). Information recorded included disease focus, geographic focus, recommended tools, toolkit format, audience, and approach. All toolkits were reviewed to help establish a baseline understanding of pre-existing toolkits and to also identify limitations of current toolkits.
1. Literature review

The final search terms for the literature review returned 240 published papers, all of which were published in the English language. The inclusion criteria used to evaluate the relevance of these papers in the title and abstract review were quite broad, and somewhat subjective. A publication was deemed to be relevant if it provided insight into NTD surveillance approaches, guidelines, or toolkits in development, or highlighted relevant digital or novel tools that may contribute to integrated NTD surveillance. Of the 240 papers returned by our search terms, 128 met our initial inclusion requirements for further full text review (Figure 2). For the grey literature search, 26 documents were identified in the project’s initial scope of work from the Bill & Melinda Gates Foundation, 8 were identified by WHO or other stakeholders, and 52 papers were identified in the snowball search using references from previously identified resources. After cross-referencing the published literature, 18 of these were removed as duplicate records prior to full text review.

Figure 2. PRISMA-style exclusion flowchart for the literature review.

Between published peer-reviewed literature and grey literature, a total of 196 documents were reviewed at the full-text stage. LF-tagged papers were the most common in the initial search results and make up the bulk of the included papers (47% for LF, 17% for onchocerciasis, and 24% for trachoma). The papers documented research evenly across various transmission settings (pre-
elimination, post-treatment, and post-elimination). The majority of papers focused on field research or cross-sectional studies, although some of the included papers documented systematic reviews, tool/product testing, or modeling results. The studies generally looked at three different categories of surveillance—serological surveillance, entomological surveillance, or population-based surveys.

Some of the main themes coming from the literature review included: 1) monitoring for post-validation reintroduction via migrant populations or zoonotic sources is critical but not well documented; 2) xenomonitoring can provide significant value to surveillance programs, but methods and results vary widely across settings and vectors; 3) serosurveillance guidelines should be sensitive to age and geography-dependent factors.

2. Stakeholder interviews

In total, 31 interviews (a mix of key informant and small group discussions) were conducted with 42 individuals from WHO, research institutions, funding agencies, and national NTD programs.

Individuals interviewed brought a variety of expertise, including surveillance, modeling, toolkit development, and control and elimination of neglected tropical diseases. Stakeholders identified promising surveillance activities that could be applied in PVS settings, some of which have been piloted by national NTD programs in countries on the leading edge of elimination of LF, onchocerciasis, and trachoma. Most of the emerging surveillance tools identified through stakeholder consultations focus on improved diagnostics and serosurveillance approaches as well as improved vector surveillance and molecular xenomonitoring (MX). Additional WHO guidance for PVS of LF and trachoma are in development and anticipated to be shared within the next few years. While no NTD programs have fully implemented an integrated surveillance system for PVS of NTDs, some operational research activities have been conducted in PVS settings to explore opportunities for integrated surveillance (i.e., integrated serosurveillance with HIV and malaria platforms).

Findings from the literature review, stakeholder interviews, and toolkit review have been synthesized and organized by key thematic areas that will inform the development of the planning toolkit for integrated NTD surveillance in PVS settings.

3. Disease specific findings

3.1. Onchocerciasis

3.1.1. General surveillance approaches and guidance

Serology and MX are the predominant tools used for surveillance of onchocerciasis. According to WHO, elimination of onchocerciasis should be documented through (i) appropriate testing of black flies and (ii) corroborated through serological evaluation of children under 10 years of age as necessary. After elimination, current WHO guidance for PVS recommends employing entomological monitoring of black flies to detect possible renewal of parasite transmission both in previously endemic and in non-endemic areas as well as in areas where imported cases might be expected to occur. Using O-150 PCR, the entomological assessments can demonstrate the absence of infective-stage larvae of O. volvulus in Simulium flies that serve as vectors for the causative pathogen. In this case, detection of O. volvulus DNA serves as a proxy for the presence of parasites in the human population. The entomological criteria used in these guidelines include an upper limit of the 95th percentile confidence interval for prevalence of infective larvae (stage L3) of 0.1% in parous flies, or a 95th percentile confidence interval of prevalence of infective larvae less than 0.05% in all flies, with an assumed parity rate of 50%. For implementing serological surveillance, the guidelines recommend utilizing Ov-16 serology to detect the presence of antibodies to the O. volvulus specific antigen Ov16 in a sample size of at least 2000 children under 10 years of age, with selection occurring through a multi-stage stratified sampling method at the lowest local administrative unit in the foci of interest. It should be noted that some studies have suggested the statistical methods underlying the cutoff
prevalence of 0.1% exposure in children should be re-examined. With investments from the Bill & Melinda Gates Foundation, the OV-16 RDT has been optimized by Drug & Diagnostics for Tropical Diseases in San Diego, California. The test requires additional field validation, which is planned for 2023, but stakeholders familiar with the project note that the test appears likely to meet the target product profile (TPP) for onchocerciasis stopping decision.

It should be noted that to-date, only countries in Latin America have eliminated onchocerciasis. Additional guidelines are needed to define approaches for verification of elimination in Africa. In the Latin American context, the Onchocerciasis Elimination Program for the Americas identified sentinel hyper-endemic communities in each focus along with previously agreed-upon epidemiological and entomological indicators for elimination of transmission in those sentinel communities. This was deemed to be appropriate in Latin America where the foci were generally isolated from one another, but in Africa well-defined foci boundaries were not identified before the onset of onchocerciasis control activities, and those foci that exist are often not isolated from one another, making reintroduction of the parasite through human migration or vector population drift likely. Therefore, the definitions of how foci should be sampled, and the time and numerical criteria that should apply to insect collection sites, should be determined for countries in Africa prior to conducting systematic PVS for onchocerciasis.

3.1.2. Diagnostics

Recent developments in onchocerciasis detection include the diethylcarbamazine (DEC) skin patch, as well as a pre-prepared version called the Lohmann Therapie-Systeme AG (LTS)-2 patch, and a pair of rapid diagnostic tests (RDT)—one for Immunoglobulin G4 (IgG4) detection of onchocerciasis and one that serves as a biplex antigen-detection RDT for both onchocerciasis Ov16 and W. bancrofti Wb123 antigens. The DEC patch has not been recommended by WHO for verification due to part in wide-ranging sensitivity levels depending on the comparator test used, with particularly low sensitivities being shown in low prevalence areas.

For the new RDTs, the single IgG4 product insert reported the sensitivity of the Ov16 standalone test to be 81.1% compared to 81.3% for the Ov16 line on the biplex test. Initial specificities were listed as 99.0% and 100% respectively, although early prototype studies measured specificity to be 1-2% lower than initially assumed. A 2016 study in Senegal comparing the Ov16 rapid test to skin-skip microscopy found that the rapid test was highly acceptable (99.7% vs 32.7%) and cheaper on a per-test basis ($3.14 vs. $7.48) than skin-snips. It is worth noting that the biplex test is not in wide use and will likely require additional field validation to determine if it can meet the TTPs for LF and Onchocerciasis stopping decisions.

A potential development in onchocerciasis surveillance is the combination of three standard minimal epitopes into a single peptide called OvNMP-48 that can be measured using ELISA. The performance of ELISA targeting this peptide has been shown to be sensitive (76.0%) and specific (97.4%) but with a high level of cross-reactivity in individuals infected with soil-transmitted helminths (STH) (11.1%). A critical aspect of this multi-epitope peptide is that it may allow for a better characterization of filarial exposure compared to immunochromatographic test (ICT) and Og4C3 ELISA antigen tests that are only designed to detect current infection.

3.1.3. Molecular xenomonitoring

For MX, the PCR-based O-150 test can detect O. volvulus DNA in pools of more than 100 flies, in conjunction with an algorithmic tool (PoolScreen), which can reliably calculate the proportion of black flies containing parasite DNA in the pooled sample. PoolScreen technology has made a significant difference in the feasibility of MX for onchocerciasis in black flies, allowing for the bypassing of standard dissection techniques that are expensive and time consuming. The difference in time and money is significant, as the reagent cost for processing a pool of 100 flies is only about US$ 0.07 per insect, and a single individual can process roughly 4000 pools or 400 000 individual insects annually. Additionally, PoolScreen analysis precludes the issue of having to account for overestimation of transmission intensity due to the presence of Simulium species that only transmit zoonotic non-human Onchocerca parasites with morphologically indistinguishable larvae from those that infect humans.
limitation to the use of MX generally, and for onchocerciasis in particular, is the difficulty in interpreting MX results in the context of the disease indicators that guide programmatic decision-making.23

There are potential improvements on the way for insect collection techniques that may benefit MX efforts. Substitutions to traditional human landing catch (HLC) techniques such as sticky targets baited with scent markers such as POCA or carbon dioxide (CO2) mixtures could prove practical and economical to onchocerciasis MX in the future.24 and another product, the MosqTent®, has been demonstrated to be more efficient than HLC (p = 0.031) at capturing blackflies, with daily capture means of 799.4 blackflies versus 217.6 blackflies for HLC.25

3.1.4. Modeling

The role of mathematical modeling in characterizing onchocerciasis dynamics has continued to evolve in recent years. For example, one study evaluating two different onchocerciasis models has shown that the most informative age groups for onchocerciasis seromonitoring vary depending on age-dependent exposure patterns. These exposure patterns are different for different models, with children <10 years being the most informative under EPIONCHO-IBM exposure patterns, and 5–14-year-olds being the most informative for ONCHOSIM patterns.26 Considerations about what model inputs to incorporate into PVS for different settings are a potential area in which new guidance could be informative. Current investments in geospatial mapping with Lancaster University are focused on helping shrink the map for MX for onchocerciasis.

Another avenue where mathematical modeling could prove beneficial to onchocerciasis surveillance is in the field of remote sensing. Evaluation of satellite-based remote sensing for environmental variables such as rainfall, temperature, and vegetative indices has shown demonstrated success in identifying the most conducive locations for Simulium larvae breeding grounds and could potentially help surveillance programs target human or vector-based surveillance activities.27,28

3.1.5. PVS activities

In PVS settings, countries are also exploring different approaches to implement Ov-16 serology and entomological monitoring of black flies. Colombia, Ecuador, Mexico, and Guatemala, which have eliminated onchocerciasis, have leveraged the available guidance from WHO and established protocols for onchocerciasis surveillance based on the detection of positive cases. For example, as part of Mexico’s PVS plan, they have included the examination of formerly endemic communities for onchocercomas.29 By contrast, Ecuador has deployed Ov16-based serosurveys in school children to support post-elimination surveillance of onchocerciasis.30 Stakeholders noted that cost and time pose the greatest challenges to incorporating PVS for onchocerciasis into routine surveillance. Such an endeavor would likely demand significant investments of time and financial resources.

While some guidance does exist for onchocerciasis PVS, informants interviewed for this work agreed that existing guidance needs to be more precise to provide utility in multiple contexts. New guidance from WHO is coming soon, but in the meantime, there are significant new and upcoming developments in the onchocerciasis surveillance space to consider when planning for integrated surveillance opportunities.

Numerous countries that are still affected by onchocerciasis have made considerable progress subnationally in eliminating the disease, often relying on integration with other disease programs.4 For example, transmission of onchocerciasis was eliminated in 2018 in Plateau and Nasarawa states in Nigeria.31 In their continued effort to reach elimination, Nigeria, with support from Sightsavers International, piloted integrated serological screenings for HIV and onchocerciasis, leveraging HIV/TB laboratories that have the capacity to conduct Q-PCR and ELISA. Stakeholders familiar with this project noted that the country level laboratory capacity, willingness/ability to change consent forms, and country-level buy-in facilitated the implementation of this approach. Other countries have explored the use of MX to provide sentinel indicators of LF and onchocerciasis.
3.2. Lymphatic filariasis

3.2.1. General surveillance approaches and guidance

According to WHO guidelines, countries must meet two milestones in order to achieve validation for elimination of LF: (1) stop the spread of infection through MDA with annual diethylcarbamazine and albendazole in LF only geographies, annual triple drug therapy with ivermectin in WHO eligible geographies, ivermectin and albendazole in LF and Oncho co-endemic countries, or biannual MDA with albendazole in LF in Loiasis co-endemic settings; and (2) alleviate suffering through MMDD.9

Current LF elimination guidance, published in 2011, states that after the minimum of 5 years of annual MDA, transmission assessment surveys (TAS) should be conducted among 6–7-year-olds to determine whether transmission has been reduced below sustainable levels and MDA can be stopped.32 In areas where *W. bancrofti* is endemic, the previous WHO guidance was to administer ICT to all surveyed individuals to measure levels of antigenemia. However, the ICT has recently been replaced in field usage by the comparatively higher-performing Abbott filariasis test strip.19 In areas where *Brugia* spp. is endemic, the *Brugia* Rapid™ test should be administered to all surveyed individuals to measure levels of antibody prevalence. Studies indicate that current stop-MDA guidelines appear sufficient for achieving transmission interruption in both settings with *W. bancrofti* and those with *Brugia* spp. that maintain high MDA coverage and widespread bed net usage.33,34

Once MDA has been stopped, WHO recommends conducting TAS two to three and five to six years after stopping MDA in order to gather evidence of elimination to inform WHO validation.35 It has been recommended that the assessment of transmission interruption following cessation of MDA for LF be conducted in an integrated fashion to combine both serologic and vector-based techniques.36

Currently, WHO does not make recommendations for additional post treatment surveillance (PTS) or post stopping MDA beyond the TAS protocol.38 However, researchers have noted two major complexities in conducting LF PTS in onchocerciasis co-endemic areas: 1) complications in forming evaluation units when LF epidemiological similarity is prioritized over the co-endemicity status of onchocerciasis resulting in mixed endemicity evaluation units; 2) timing of PTS activities given that ivermectin monotherapy, which reduces both onchocerciasis and *W. bancrofti* microfilaraemia in circulation, may be undergoing implementation at the same time. Therefore, researchers propose that additional integrated surveys should be conducted after the halt of both Albendazole and Ivermectin or DEC MDA in formerly co-endemic areas to substantiate claims of LF transmission interruption in the absence of further interventions.33

Emerging guidance on surveillance for LF highlights the importance of four key principles to incorporate: (1) adaptation to the needs and capacities of the country, (2) coverage of all at-risk areas, including those areas that may have been initially mapped as non-endemic, (3) implementation before cessation of MDA if possible, and (4) a well thought out response to cases that may be identified through surveillance.37 Another area where specific guidance does not exist but which may need to be taken into account is the contribution of zoonotic reservoirs of *B. malayi* to LF recrudescence. Cases of re-emergent *Brugia* species infection in Sri Lanka have been found to exhibit nocturnal sub-periodicity, which suggest possible zoonotic origins.38

3.2.2. Molecular xenomonitoring

MX has emerged as another key pillar of PTS and PVS systems for LF. MX at scale is a relatively new practice for measuring parasite distribution in local vector populations.39 The vector analysis tool, PoolScreen (discussed above) appears to be practical and reasonable for LF surveillance where *Culex* mosquitoes are the primary vector.39 MX generally has been demonstrated to be economically and epidemiologically viable, both as a complement to existing TAS surveillance activities and in PVS for LF. Several key informants reiterated the anticipated utility of combining TAS-like population survey approaches and MX in PVS settings to monitor for recrudescence of LF.

Insect capture and quantification may soon benefit from non-HLC techniques, such as the Biogents Sentinel (BGS) trap for *Aedes* spp, although programmatic expansion of MX efforts into *Anopheline, Culex*, and *Aedes*-dominated contexts will require additional operational research.40 MX has often outperformed traditional night-blood screening surveys at detecting the presence of *W. bancrofti*,41 demonstrating 100% sensitivity with mosquito sample sizes of 1000 or more, even in low microfilaraemia prevalence areas. Additionally, MX rates and microfilaraemia prevalence have been
shown to have a significant relationship, the strength of which is higher in areas having completed MDA, making it ideal for peri-elimination settings.\textsuperscript{23} That said, the WHO Diagnostics Technical Advisory Group is still working to identify a validated MX threshold that is correlated with risk of transmission in humans and develop a TPP for this use case.

Gaps in current understanding of MX for LF include elucidating the relationship between \textit{W. bancrofti} DNA prevalence in mosquitoes and subsequent infection and transmission rates in humans.\textsuperscript{42} Additionally, the impact of MX seems to depend largely on setting-specific seasonal behavior differences, vector composition, and feeding preferences.\textsuperscript{42} While MX has seen growing acceptance in recent years, there are still significant obstacles in the path of widespread O- 150 PCR assay use, most of which are technical or logistical in nature such as international shipping requirements, cold chain storage, and technical expertise. A common technical issue is amplicon contamination which can often lead to false-positive result on the test.\textsuperscript{40}

There are several new tools in development that could contribute to PVS for LF in the future. For standard entomological data collection, one potential advancement is the field-deployment of high-functioning traps for Anopheline mosquitoes that perform similarly to Centers for Disease Control and Prevention (CDC) gravid traps that are typically used for collection of Culex mosquitoes. One study of Anopheline gravid traps (AGT) showed high efficiency for anopheline collection in comparison with other trap types but also highlighted clear limitations such as the bulkiness of the AGT and the fact that it requires the use of a 12 volt car battery which is not very portable.\textsuperscript{43} Meanwhile for MX, a new tool that has shown potential for collecting and analyzing samples is backpack PCR, a rapid, point-of-collection-based diagnostic platform that runs on a sodium hydroxide–based methodology for the extraction of total DNA from pools of parasite-spiked vector mosquitoes and can fit inside of a small backpack.\textsuperscript{44} This would potentially open up field MX settings to rapid PCR deployment and analysis without the need for a centralized laboratory.

Another potential avenue for resource and labor-minimizing “first alert” MX systems is the testing of mosquito excreta or feces.\textsuperscript{45} This is still a very experimental method of detecting disease markers in mosquito populations, but the high-throughput and highly sensitive nature of excreta testing warrants future evaluation. Additionally, L3-specific real-time PCR assays, which currently exist for both \textit{W. bancrofti} and \textit{B. malayi}, if appropriately utilized for intermittent re-mapping, may become useful as a means of monitoring the changing transmission landscape.\textsuperscript{40}

3.2.3. Diagnostics

Serology is a critical component of PTS of LF, and there is growing support for its utility in post validation settings. There are several available techniques for identifying LF elimination endpoints in the field. Comparing OG4C3 ELISA, ICT, Alere, and PCR techniques, one study showed OG4C3 ELISA to be the most sensitive test but ICT, the second most sensitive, was the most field applicable. PCR was found to be the most specific, but with significant cost and logistical requirements. Critically important is to understand what populations and age groups are most relevant for sampling in PVS settings, which can be very location and country dependent.\textsuperscript{46}

Potential new data collection methods for human disease endpoints are also in development. Urinary ELISA of anti-filarial IgG4 combined with GPS tracking has been demonstrated to successfully monitor LF transmission and indicate potential transmission foci as well as areas where transmission is unlikely. This may provide value as a relatively low-cost surveillance tool to monitor for rerudescence that is comparatively non-invasive and highly sensitive and specific when compared with traditional CFA tests.\textsuperscript{47} Additionally, data collection via community health workers may be enhanced by the use of tools such as a mobile phone-based interactive voice response system (mVRS) used by community health volunteers in Ghana for LF surveillance and MMDP.\textsuperscript{48} Community health collectors, who are often a key component in traditional surveillance programs, were also found to substantially lower the cost of mosquito collection for MX, while collecting similar numbers of mosquitoes as study teams in some districts.\textsuperscript{48}

Future guidance may need to take into account recent findings from studies that identify improvements in surveillance performance and efficiency. For example, a recent modelling study for LF found that small, low-intensity microfoci may not be detected by current post-treatment
surveillance approaches, and that detection efficiency for these microfoci was maximized by simple random sampling, ICT, and the sampling of adults. Adult-TAS and MX surveillance methods have also been shown to be more sensitive than school-based TAS for detecting residual LF following MDA.

3.2.4. Modeling

The impact of geospatial modeling on LF surveillance in peri-elimination settings is also an area of ongoing research. A recent study in American Samoa, which is still endemic for LF, showed that a targeted sampling strategy guided by predictions from a spatial model was more efficient for identifying residual LF infection at a household level than purely random sampling, although factors such as infection prevalence and the cost of collecting and analyzing geo-referenced data will determine whether a modeling-informed approach will provide a net benefit.

3.2.5. PVS activities

After validation is achieved, WHO recommends that countries conduct PVS and integrate MMDP into routine health services, although detailed guidance on what PVS activities should be conducted is still under development and not yet been shared with national NTD programs. In December 2022, an initial draft of proposed guidance was shared at WHO Lymphatic Filariasis Post Validation Surveillance meeting in Bangkok, Thailand. The proposed guidance would give countries the option to choose a combination of at least two of the following for platforms to be implemented for PVS: 1) health facility screenings, 2) existing standardized surveys, 3) MX, 4) targeted surveys to high-risk areas or high-risk groups.

While official WHO guidance is still being finalized, as noted by key informants, countries are doing what they think is best for PVS, resulting in a wide range of PVS implementation based on varied human and financial resources available. Some countries are conducting sentinel site monitoring while others, such as the Solomon Islands, are carrying out intensive indoor sampling. Some activities being implemented in South East Asia include additional country-funded TAS surveys, xenomonitoring, cluster-based surveys, health facility screening, and nationwide seroprevalence surveys repurposing dried blood spots that were collected for tetanus surveillance. Leveraging domestic funding, Thailand and Malaysia NTD programs are using serology to monitor LF transmission in humans and cats. Evidence from China’s efforts with the Global Program to Eliminate Lymphatic Filariasis (GPELF) showed the effectiveness of utilizing a mix of surveillance techniques to monitor for recrudescence of LF, including cross-sectional stratified cluster sampling, longitudinal data for fixed populations, and surveillance of floating or migratory populations.

Togo was noted by multiple stakeholders as an exemplar for integrated PVS of LF, and their successful PVS implementation has been similarly documented in the published literature. Leveraging the existing malaria surveillance system, the National LF Elimination Program (NLFEP) established a PTS system including epidemiological investigations of all microfilaria-positive individuals leveraging a routine surveillance network of 47 laboratories and 20 peripheral health facilities that collected blood smears and dried blood spots for Og4C3 antigen. Surveillance data gathered from these activities are stored on a national platform. By establishing the PVS system for LF alongside its existing malaria framework, Togo was able to establish nation-wide surveillance rather than focusing solely on historically endemic areas or transient disease hot spots. This was viewed as being particularly important due to the effect of potential cross-border migration on hot spots for LF.

To further explore the impact of migration on recrudescence of LF post-treatment, Togo is conducting operational research on migratory populations traveling between countries. Stakeholders did note that LF was only endemic in some districts, not all, which made it easier to manage elimination and post elimination efforts.

One potential challenge in PVS settings noted by stakeholders was the sensitivity of diagnostic tools available and the declining expertise of microscopists over time. Another identified gap in PVS for LF is the need for better integration of routine platforms and data to track milestones. Currently, there is no centralized storage or management of data for LF. To address this challenge, the WHO African Regional Office’s Expanded Special Project for Elimination of Neglected Tropical Diseases (ESPIEN)
has been working to integrate NTD indicators into country-specific health management information systems (H MIS) and DHIS 2 platforms.

3.3. Trachoma

3.3.1. General surveillance approaches and guidance

Current WHO recommendations for trachoma surveillance include carrying out impact assessments at least two years following MDA to confirm that the district-level prevalence of TF3 is less than 5%. However, the accuracy of TF field grading in low-prevalence settings has been a cause for concern historically, as seen in the case of Ghana’s implementation of WHO recommendations for trachoma surveillance. There have been calls for re-evaluation of these criteria and for re-initiating MDA using non-TF markers of C. trachoma transmission such as those leveraged by trachoma serology. The utility of serological markers for trachoma surveillance has been supported by a 2016 study from West et al, which confirmed that prevalence of less than 6% pgp3 antibody in children ages 1–3 years was associated with the absence of re-emergence of trachoma transmission. However, guidance on serological surveillance for trachoma have yet to be released. While momentum for serology use in PVS settings continues to build, the lack of established guidance and the presence of significant questions around its implementation make it difficult to prognosticate effectively about when and how serology will fit into PVS for trachoma.

3.3.2. Diagnostics

While no official guidelines have been published for the use of serological data in trachoma surveillance, any future guidance for trachoma PVS is likely to outline approaches to serosurveillance. In the absence of official guidelines, recent studies have undertaken to provide operational thresholds for interpretation of serological data in low-transmission and post-elimination settings. A key area for which upcoming guidance will be critical is the operationalizing of data around seroreversion and seroconversion.

Seroconversion of disease status from seronegative to seropositive has been considered as a possible stand-in measure of transmission intensity in areas formerly endemic for trachoma, with results from Pinsent et al, suggesting that seroconversion rates below 0.015 per year correspond to TF <5%, at which level the mean sero-prevalence for 1–9-year-olds is <7%. Using that mean estimate, a sample size of at least 51 sero-negative samples would be required for confirmation of a maintained status of trachoma having been eliminated as a public health problem. Confirming sero-prevalence levels to be below a more stringent threshold of 1% would require much larger sample sizes. On the other hand, seroreversion, where disease status in an individual changes from seropositive back to seronegative, may lead to mischaracterization of Ct transmission by serology, by contributing to low seroprevalence rates that are erroneously assumed to represent lack of exposure. One study showed up to 6.4% reversion to seronegativity for pgp3 antibodies.

While serosurveillance for trachoma has many distinct advantages related to integration with other diseases and the usage of stored specimens, existing models are considered to be over-informed by small Pacific Island contexts. Another drawback of the most robust serosurveillance techniques for Pgp3 and CT694 antigens, using multiplex bead assay analysis of dried blood spots on the Luminex platform, is that the techniques are very expensive to perform. By contrast, the Pgp3 black latex LFA does not require advanced instrumentation and may be a useful tool for providing national trachoma programs with the flexibility to monitor seroprevalence on a variety of platforms.

One non-serological advancement that may have a role to play in post-validation surveillance for trachoma is smartphone photography, which is relatively inexpensive and requires lower training barriers when compared to traditional TF field grading. Hired trachoma surveillance workers were able to master photography skills in 30 minutes compared to the 3-hour training normally required for trachoma grading, and additional studies have shown high levels of agreement between field and photo grading. However, recent evidence suggests that drivers other than Ct may cause the TF phenotype, which may reduce the utility of TF ocular photography in characterizing underlying Ct infection. Additionally, the utility of photography may be limited in PVS settings due to the fact that
no clear association exists between TF prevalence and ocular Ct infections at low levels of TF prevalence.\textsuperscript{66}

Given the lack of established guidelines for surveillance of trachoma recrudescence, researchers have attempted to evaluate the effectiveness of several potential sampling strategies. In a 2021 study in Ghana, the standard approach of random sampling taken by the Ghana Health service for assessing TF prevalence was compared to a second strategy whereby communities hypothesized to be at potential risk of recrudescence were identified by serological or infection data from previous investigations and pre-validation surveys. While both strategies identified at least one community with probable post-validation transmission of Ct, it was determined that the use of infection and antibody data in the sampling process added value to a purely random sample approach.\textsuperscript{66}

3.3.3. PVS activities

For those countries that have achieved validation for elimination of trachoma, PVS activities have focused on conducting surveys in previously endemic settings. For example, Morocco, which was validated as having eliminated trachoma in 2016, conducted post-validation surveys in 2019 wherein eye examinations and antibody tests were conducted in two previously endemic districts.\textsuperscript{14} Given the lack of PVS guidelines for trachoma, further investigation is needed to better understand how to best implement PVS surveys, how to mitigate costs of these surveys, or if additional PVS tools, such as a standardized serological approach, are needed. Prior studies have noted that current diagnostic approaches, such as the eye exam, are becoming more expensive, and that the sensitivity and specificity of these tests are declining as the prevalence of trachoma and the severity of clinical manifestations decrease.\textsuperscript{67} Stakeholders noted that some work has been done to nest surveillance for other NTDs (i.e., scabies) into trachoma surveys. Further research is needed to determine the viability of incorporating these integrated NTD surveys into routine surveillance within the health system.

Due to the wide-ranging and potentially transformative nature of emerging techniques for trachoma PVS, and the hope of stakeholders in this space for the arrival of anticipated WHO guidance on serological surveillance, it may be prudent to delay the inclusion of trachoma in this iteration of the integrated PVS toolkit until such time as research in this field has coalesced around the new guidelines.

4. Systems for surveillance data reporting and management

4.1. NTD systems

Leveraging digital tools and data visualization is a critical component of responding to outbreaks and accelerating burden reduction and elimination; however, the uptake of these tools has been limited and there is a lack of standardization across the NTD portfolio. A recent scoping review of the role of digital health technologies in case detection and management of NTDs found that digital health technologies enhance case detection and disease diagnosis and treatment in places where these are used, but that the study of these tools is limited.\textsuperscript{68} An example of the tools identified include the use of mobile messaging in Ghana and Malawi to report basic information on case detection of lymphatic filariasis.\textsuperscript{48} The advancement of mobile data collection techniques has allowed for the expansion of smartphone-based platforms based on Open Data Kit (ODK) technology such as the LINKS system, which has been used to map NTD prevalence in 37 countries and specifically incorporated into integrated TAS assessments.\textsuperscript{19}

There are other data management platforms that countries can use for particular purposes. For example, the WHO ESPEN portal is also increasingly being used by countries in Africa and supports improved data management, data sharing, and epidemiological and entomological data collection through electronic collection methods such as the ODK-based ESPEN Collect tool. The ESPEN Portal enables health ministries and stakeholders to share and exchange subnational program data on a WHO-supported system in support of the NTD control and elimination goals.\textsuperscript{69}

Finally, the Tropical Data is another data platform used by national NTD programs, which supports surveillance activities for trachoma.\textsuperscript{70} Using the platform, countries implement standardized trachoma
transmission assessment surveys and collect data using a phone-based app. That data is then integrated into the tropical data platform to facilitate easy synthesis of surveillance information and to inform decision-making. Several stakeholders noted the utility of this tool, given that it supports national trachoma programs in nearly all transmission settings to conduct a variety of surveillance activities—baseline surveys, impact surveys, surveillance surveys, and trachomatous trichiasis-only surveys. The primary limitations of this platform for integrated surveillance are that it is only focused on trachoma surveillance and that funding may be difficult to sustain for use of the platform in PVS settings.

4.2. Non-NTD systems

One of the most widely used HMIS is DHIS2, a global open-source platform used by more than 76 countries to collect and analyze health data. Stakeholders noted that countries are successful at maintaining high-quality data in DHIS2 when sufficient investments in training, logistics, and infrastructure have been made. The main limitation of DHIS2 for the purposes of this work is that NTD data are not routinely incorporated into DHIS2 data platforms.

Preventive chemotherapy NTD (PC-NTD) data are often not incorporated into health facility registers and online HMIS such as DHIS2. Instead, these diseases are often lumped together into a category for “other” conditions. A major reason for this issue stems from a lack of appropriate data collection tools such as clearly defined PC-NTD case definitions, disease-specific physical case registers, and surveillance report training and feedback mechanisms. All of these factors, along with the presence of well-equipped laboratories, have been associated with higher odds of conducting analysis of surveillance data at the facility level. Additional guidance from WHO is needed to support countries in determining what data they should report on, and which indicators should be prioritized for inclusion without overburdening data collectors.

One particularly promising instance of integrated surveillance outside of NTDs has been the implementation of the regional Integrated Disease Surveillance and Response (IDSR) system throughout Africa since its inception in 1998. The IDSR framework was designed to serve as an early warning system and prioritizes surveillance of diseases capable of causing epidemics, although it is also used to monitor diseases targeted for elimination and eradication (dengue, chikungunya, dracunculiasis, leishmaniasis, snake bite envenoming, leprosy, onchocerciasis, STH, LF and trachoma). The system was implemented by the WHO-AFRO region to strengthen surveillance, diagnostics, and response efforts in line with the International Health Regulations (IHR), which provide a global legal framework to prevent, detect, and respond to the international spread of diseases. In this context, the IHR creates an enabling environment to support integrated surveillance efforts.

Of the countries that have implemented the framework, about 85% initiated trainings at sub-national levels, and more than two-thirds of countries had also initiated community-based surveillance using the IDSR approach. Due to this success, a University of Praetoria assessment of NTD surveillance in Kenya specifically touted the IDSR framework as the most pragmatic approach to improving PC-NTD surveillance.

There are some limitations with integrating PVS for NTDs into the IDSR. For example, the IDSR sets standards for reporting for clinical case data, which for NTDs, would not function as an early-warning system due to the delayed nature of clinical progression in most PC-NTDs. That said, regular facility reporting of clinical visits and MMEDP service provision could serve to fill gaps in standard NTD reporting for areas where sero prevalence surveys are not available, as shown by recent work indicating that morbidity clusters may be important as proxy markers of ongoing disease transmission. An additional challenge highlighted by stakeholders is that there are some diseases that require significant amounts of surveillance data (i.e., HIV and malaria, which previously had parallel systems). The IDSR data collection tool is already regarded as long, cumbersome to use, and challenging to train new staff on. As a result, efforts to incorporate additional questions or diseases may put an added strain on implementation staff.
4.3. Integrated approaches to data systems

For integrated PVS to be successful, case detection tools need to link to an integrated data reporting platform. In the absence of clear guidance, countries are determining on an individual level what data to include in DHIS2 and how much information to gather on a specific disease. Ethiopia, for example, has integrated a few NTD indicators into their HMIS, mostly related to LF or onchocerciasis. Nigeria is looking to roll out DHIS 2 data collection that incorporates some NTD data shortly. Multiple stakeholders mentioned there is interest in developing more comprehensive tools for PC-NTDs data collection. DHIS2 and the ESPEN portal are promising tools to build on and integrate additional indicators into. In fact, the PMI-funded ACT-WEST project is currently exploring work to support integrated DHIS2 platforms.

In recent years, WHO and the global NTD community have been working to increase data sharing to monitor cross border transmission. For example, Unitedengue is a website run by the governments of 11 countries in South East Asia to share cross border information on dengue transmission, providing excellent regional surveillance at a confidential level. The Pan American Health Organization (PAHO) is currently in the preliminary stage of developing a similar collaborative website that allows each participating country to share data on several diseases.

5. Opportunities for integrated surveillance approaches

There are a variety of approaches to integrated surveillance, although most of these approaches are emerging from operational research activities. Within the NTD surveillance space, key integrated surveillance approaches focus primarily on vector surveillance and serosurveillance.

5.1. Vector surveillance

In 2017, WHO set the global vector control response strategy for 2017-2030, promoting an integrated vector surveillance program. To support this, investments have been made in recent years to improve vector traps and diagnostic tools. The WHO vector control advisory group is tasked with reviewing various traps and other tools in the development pipeline to see whether any new tools provide public health value. Concurrently, according to key informants, WHO is developing an integrated surveillance manual for NTD vectors at the request of national NTD programs.

Some research has been done to look at how to approach integrated vector surveillance programs. Considerations for designing grid-based MX systems include underlying human infection prevalence, spatial scale, and transmission dynamics. Xenomonitoring can be applied for both LF and onchocerciasis to estimate disease prevalence in real time but needs for integrated assessments include standardized thresholds. In South East Asia, stakeholders noted that some NTD programs are working to integrate xenomonitoring for LF and other diseases such as malaria and dengue.

Challenges with integrated vector surveillance noted by key informants include the overall lack of trained vector control staff and limited laboratory capacities. These informants added that some countries are looking at options to leverage malaria vector control staff, particularly in areas where malaria burden has been significantly reduced. Another challenge is that climate change has impacted the movement patterns of various vectors. This has made it challenging to rely upon historical prevalence as a guide for where to conduct vector surveillance.

5.2. Serosurveillance

Integrated serosurveillance has garnered significant interest in recent years, particularly with the development of the multiplex bead assay. Studies have demonstrated that integrated epidemiological surveys can be performed on co-endemic parasitic diseases for surveillance, including integrated serosurveys on Trachoma, LF, and 9 other disease biomarkers using the multiplex bead assay in Haiti. Additional pilot activities have been conducted in Ghana, Bangladesh, Cambodia, Nigeria, and several countries in the Americas. In Nigeria, the multiplex bead assay was integrated into a national HIV serological survey in 2018, which examined 37 antigens including trachoma. This effort allowed the trachoma team to gain access to data from regions of the country that their team had not
previously been able to reach. Limitations to this approach still exist, of particular concern for trachoma teams is that the granularity of sample collection may not be sufficient for trachoma programs to identify pockets of recrudescence in a post validation survey.

To support uptake in the Americas, PAHO developed the Toolkit for Integrated Serosurveillance of Communicable Diseases in the Americas, which was highlighted by several stakeholders as a key resource both for its content and structure.83 This toolkit was published in September 2022 and subsequently piloted in Mexico, Paraguay, Brazil, Guyana, and Guatemala.84 Several countries are collecting dried blood spots (DBS) in conjunction with national surveys and using the multiplex bead assay to look for 13 antigens, from vaccine preventable diseases to stronglyoides. For example, the national NTD program in Guyana utilized the LF TAS surveys to collect DBS to test for other diseases using the multiplex bead assay.

PAHO is now in the process of developing training materials and disseminating the guide globally, with plans to deploy the multiplex bead assay as part of national serological surveys in all PAHO countries. Stakeholders noted that Brazil and Mexico plan to start using samples from blood banks. These efforts require strong laboratory capacities and the ability to conduct PCR testing. One key informant noted that there may be an opportunity to leverage PCR labs that were built up to respond to the COVID-19 pandemic. This should be investigated further to determine if it’s a viable resource to leverage. It is also worth noting that while it might be available now, if not utilized in the next few years it may no longer be available.

One challenge noted by stakeholders is that while integrated serology has a lot of clear benefits, it is dependent on the quality of information available on target antigens. More research is needed to expand the evidence base around target antigens and possible cross reactions within the multiplex bead assay. To continue to support diagnostic development, WHO is building out TPPs for diagnostics manufactures, which are available through a searchable database on the WHO website.85,86

5.3. Modeling

Mathematical modeling can help evaluate potential strategies for integrated disease surveillance. Some considerations for which modeling can provide insight include when, where, who, and how to sample; whether to implement active or passive case detection, what diagnostic tests to use, and which sampling schemes will be most appropriate in a given context.87 In Peru, recent efforts led by PAHO and UCSF have used modeling to support trachoma mapping in the Amazon region. WHO is also supporting the expansion of DHIS2 by building disease-specific modules to capture and analyze data.

5.4. Enabling environment for integrated surveillance

As new opportunities for integrated surveillance of NTDs become available, it is important to foster a positive enabling environment in order to move beyond operational research or pilot activities toward sustainable implementation at scale. Key enabling conditions include the following:

1. **Political buy-in:** Recognition of the importance of PVS, demonstrated by its inclusion in national strategic planning documents, policies, and standard operating procedures for NTDs. Political will from national and subnational governments can facilitate sustainable development and implementation of PVS approaches. As shown in efforts to integrate WASH activities with NTD control and prevention efforts, advocacy at the government level can help to increase country ownership of integrated surveillance approaches and underscore the need for national strategic plans.88

2. **Alignment and active coordination:** Establishment of a multi-stakeholder governance and coordination mechanism such as a PVS sub-committee can help ensure successful collaboration between two programs (i.e., NTD program and non-NTD programs). This coordination effort can facilitate the development of national guidelines and a dedicated annual data review process to inform decision-making. Successful collaboration between the
two programs or sectors being integrated depends on commitment to a shared vision, as well as clear, measurable benefits for each sector.  

3. **Workforce:** Effective training and supervision of staff or volunteers implementing integrated PVS activities at all levels of the health system will be critical to the program’s success. Such training should help address any knowledge gaps for those not familiar with the two sectors being integrated, as well as the purpose and specific mechanism of integration-related changes to existing workflows.

6. **Toolkit review findings**

In addition to the key themes identified from published literature and stakeholder interviews, 15 existing toolkits were reviewed for potential structural elements and approaches that may be applicable to the PVS surveillance planning toolkit for NTDs. The focus on the toolkit review was on NTD’s with specific interest in: LF, onchocerciasis, trachoma, and leprosy. Once combined, the review consisted of 12 toolkits from: WHO, PAHO, CDC, RTI International, USAID, The World Bank and SPEAK India (see Appendix 2 for a full list of toolkits reviewed). Of note, the “WHO WASH and Health Working Together” toolkit contained 21 individual tools. Toolkits included information about addressing NTD’s in specific geographic locations while others highlighted examples of toolkit implementation in specific countries. Some examples of the planning resources that have been particularly helpful in conceiving this work are the WHO Malaria Surveillance Assessment Toolkit and the PAHO Integrated Serosurveillance Toolkit. While these resources are not wholly compatible with this project’s desired output, they have each provided valuable examples of how to approach the display of structural or technical elements that will be crucial to the success of an integrated PVS toolkit for NTDs.

Toolkit formats included checklists, step-by-step overviews, informational tables, questionnaires, survey guides, country specific manuals, templates, spreadsheets, presentations, and additional resources. Most toolkits were tailored for program managers of specific NTD surveillance or elimination programs, while two toolkits were targeted at Ministries of Health and donors. One common approach among the toolkits was to identify the target population and stakeholders and then evaluate current applications of prevention, control, and elimination to highlight strengths and challenges of those approaches to better understand the impact of NTD work. Another theme woven throughout the toolkits was establishing the focus of specific projects, utilizing monitoring and evaluation data of surveillance systems. Many toolkits focused on supporting the organization and planning of programs and program-related events such as workshops. Uniquely, a few toolkits provided SOP’s and guidelines for laboratory workflow, qualitative and quantitative data storage and management and compiled resource lists for data analysis and result dissemination. Lastly, the toolkits included information about the complexities of funding and emphasized the usefulness of collaboration and partnerships with pre-existing programs, value of budgeting and anticipating budget cuts in elimination phases and how to record project outcomes in a way that can be leveraged for additional funding. Although the toolkits complied varied on disease focus and format, a main challenge identified in the review was the level of detail provided in the toolkit and its overall relevance to the audience. General tools may not provide the intended audience with sufficient details on how to organize, plan, and implement, yet specific tools may be too narrow to apply to other topics or diseases. The complete findings from the toolkit review, including the potential utility for the NTD PVS planning toolkit, can be found in Annex 1.

7. **Considerations for an integrated surveillance planning toolkit**

During stakeholder consultations, key informants identified several ideological, structural, and technical considerations to inform the design of the NTD surveillance planning toolkit. These inputs have been summarized within two general focus areas—guiding principles and overarching structure, as well as more specific toolkit content.
7.1. Guiding principles and overarching structure

Several themes were identified to guide the toolkit development. Some themes, like the importance of national NTD program ownership and ministry of health buy-in, as well as the critical timing of using the toolkit during the WHO dossier development process, were echoed by the majority of informants. However, in some instances, stakeholders held differing opinions on guiding principles for the toolkit. For example, some key informants proposed keeping the toolkit broad, outlining a general framework to follow for designing and implementing PVS, whereas other key informants stated that specificity and concrete guidelines and outputs that national NTD programs can follow are necessary to ensure the toolkit is used. In the development of the toolkit, it will be important to balance the need for flexibility and the desire for clear, data-driven guidance. Table 1 outlines the foundational elements that key informants felt should underpin the toolkit.

Table 1. General themes to guide the development of the toolkit and inform its structure.

<table>
<thead>
<tr>
<th>Theme</th>
<th>Considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>NTD country program ownership &amp; wider MOH buy-in</td>
<td>High interest from the national NTD program is critical, both for the development of the toolkit and for implementing it in pilot countries and beyond. Ensuring we have strong input from key national stakeholders early on will help promote uptake of the toolkit down the line. Investment from the ministry of health at large will help facilitate coordination and collaboration with other disease programs, paving the way to explore opportunities for integration with other surveillance systems.</td>
</tr>
<tr>
<td>Flexibility</td>
<td>Flexibility will be a key aspect of the planning toolkit, given that the development of new diagnostic tests or other surveillance approaches and guidelines may impact the target age groups, focus regions, and testing strategies for PVS. One approach suggested by stakeholders was to keep the toolkit broad, outlining cross-cutting components of a surveillance system regardless of the target disease.</td>
</tr>
<tr>
<td>User-friendliness</td>
<td>User friendliness is also an important consideration to ensure the toolkit will actually be utilized by national NTD programs. Stakeholders that had worked with a similar toolkit, the WHO malaria surveillance assessment toolkit, noted that the components of the toolkit that do not get used often are complex graphs or plots with embedded excel macros because generating tables and graphs automatically is very difficult to do properly.</td>
</tr>
<tr>
<td>Informed by best available technical evidence</td>
<td>People want quantitative, data-driven guidance on what to measure when. One stakeholder cautioned to stay away from flimsy recommendations about what you “could” do. Another noted concerns that toolkits without very concrete outputs or guidelines do not end up being useful and just collect dust on the shelf. While WHO recommendations for PVS are not yet available for this project’s focus NTDs, it will be important to leverage the existing body of evidence from ongoing program implementation and operational research to guide programs on what data surveillance systems need to gather in order to be sensitive enough to detect reemergence of target diseases.</td>
</tr>
<tr>
<td>Defined scope</td>
<td>The toolkit should have a clear, defined scope outlining its target audience (i.e., NTD program managers), goals, and intended output. It is equally as important to outline what this planning toolkit is NOT designed or equipped to do. For example, this toolkit is not intended to provide new WHO Guidelines for PVS. Rather, it is a tool/framework to help countries figure out what to do with their existing resources in order to monitor for recrudescence of their target NTD.</td>
</tr>
<tr>
<td>WHO leadership</td>
<td>Ensuring WHO ownership of the toolkit will be critical throughout its development. Several stakeholders reiterated that countries would follow WHO guidelines/leadership, and without WHO approval, the toolkit may not be used by national NTD programs. Furthermore, WHO ownership could help formalize the use of the tool during dossier development.</td>
</tr>
</tbody>
</table>
The planning toolkit has the greatest potential utility when a country is approaching elimination of a target NTD and is preparing their dossier for WHO validation or verification. One stakeholder emphasized that PVS needs to be in place BEFORE the verification/validation is confirmed, given that resources and interest for the target disease often go away after elimination.

The toolkit should be structured to be able to gather all the relevant information in one place to assess options for PVS. It would be beneficial to provide a template that allows users to standardize incoming data into one suggested format. This will allow users to make data-driven decisions about their PVS plan in a streamlined fashion.

### 7.2. Toolkit content considerations

During the stakeholder consultations, participants provided various suggestions for an integrated system and identified key components. Suggestions pertaining to the toolkit content have been divided into four potential sections of the planning toolkit—gather, integrate and synthesize, plan, and implement.

#### 7.2.1. Gather phase

The initial gather phase would support NTD programs in identifying what they need in order to conduct effective PVS surveillance for their target NTD and what resources they may have in their country to leverage for PVS. Table 2 below outlines suggested components to include in the gather phase, including a needs assessment, situational analysis, and capacity self-checklist.

<table>
<thead>
<tr>
<th>Component</th>
<th>Considerations</th>
</tr>
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</table>
| Self-checklist | Before implementing a PVS system, NTD programs need to ensure that the basic enabling conditions and capacities of the existing health system are sufficient. To support this, the toolkit should include a checklist on feasibility/readiness that includes asks NTD programs to determine if they have sufficient political buy-in, access to diagnostic tools, adequate human resources and lab resources, and effective data management systems. These enabling conditions will be critical to developing an effective PVS system. Key questions for NTD programs may include:  
  - Do you have sufficient political support from the NTD program and ministry of health leadership to develop and implement an integrated PVS system?  
  - How easy is it to import and purchase antibody tests, PCR tests, reagents, etc.? (Stock flows, etc.)?  
  - What is the human resource and technological capacity of existing labs and entomologists?  
  - How many well-equipped labs are available for sample processing within the country?  
  - What is the clinical diagnostic capacity of health workers for your target NTD in country?  
  - What is the quality of data available at the community level?  
    - There are concerns about the human resource element of integrated data entry. Ensuring everyone knows all the indicators and how to store them in DHIS2 will require training.  
  - What is the capacity of country programs for data interpretation? |
| Identification of PVS development team | Given that NTD ownership is critical to successful implementation of the toolkit and subsequent PVS plan, identifying what local or national officials within the MoH/NTD program will drive the work forward, and who needs to be targeted for increased engagement, is an important first step of the gather phase. |
**Key questions to include in this section of the toolkit may be:**

- Is there a steering committee to support PVS planning?
- Who are the key players in the health system?
- Which authority in MoH is responsible for surveillance, etc.?

**Baseline Information for Target NTD**

During the gather phase, the NTD program will need to identify what kind of data they need to collect. To support this, the toolkit should include clear definitions of what elimination means for each target NTD (elimination as public health problem vs elimination defined as breaking transmission, etc.) and outline any known PVS guidance, noting that it may be subject to change as new tools or guidance is developed. Stakeholders noted that when NTD programs are determining what to monitor, they should prioritize types of surveillance that can identify asymptomatic cases and other early signals (i.e., xenomonitoring and serosurveillance), and where possible, they should include morbidity surveillance, particularly for NTDs that cause chronic health issues.

The toolkit should also include a comprehensive list of potential indicators that may be relevant for each focal disease. This was identified by stakeholders as one of the most helpful components of the malaria surveillance assessment toolkit. The indicator list should also include a prioritization of the indicators and make note of where/when an indicator is particularly important. Existing literature can be leveraged to inform this list. For example, one study highlighted that quantitative antibody levels may prove useful in measuring differences in exposure for populations where PC-NTD seroprevalence is less informative, such as very high or very low-level transmission settings.

An overview of baseline risk factors and potential high-risk populations should be included in the toolkit (i.e., refugee camps or mobile populations, such as miners that are often not present during MDA). Risk mapping may be a helpful tool to identify areas to target for surveillance. It may be relevant for NTD programs to consider what neighboring countries are doing and assess what impact these activities might have on possible recrudescence in their country (i.e., current MDA implementation or migration patterns). Where relevant, mapping of morbidity should also be considered. It should be noted that a country’s risk map may change and should be periodically updated. The toolkit should also highlight cultural and environmental factors, including seasonality of disease transmission, for NTD programs to consider factoring into their PVS plans.

NTD programs will then need to answer the following questions:

- **What**: what disease is the program looking to monitor for? What indicators should be used to assess that?
- **Where**: what are the high-risk areas? (i.e., historically endemic areas, areas impacted by migration, etc.)
- **Who**: who is the target population for surveillance? (i.e., human or vector, specific age groups, certain occupations etc.)
- **When**: When should surveillance activities be conducted? (detailing both what season and at what frequency)
- **How**: what tests/surveillance tools should be used? What sample size is needed and what sampling regimens will be required?

**Situational analysis of potential systems, surveys, or approaches**

Several stakeholders noted the importance of a standardized landscaping tool for countries to identify ongoing surveillance activities that might be relevant for their target NTD. The toolkit should include a tool that lists current surveillance systems that might be present in a given country and a series of key questions to explore for each surveillance system that will help inform whether it will be useful for PVS of the target NTD. This tool could then be used to map sample collection efforts across the country.

The list of sample sources currently available in a country should be gathered, with possible suggestions in the tool including: xenomonitoring, maternal and child health surveillance activities, health facility screening, school surveys, step surveys (5-6 years), blood bank surveillance, MDA surveillance, serological surveys, community health information system,
IDSR surveillance systems, and event-based surveillance, among others. Additionally, the tool could provide sample collection timelines and populations to target for each of these potential sampling avenues.

The most effective integration opportunities will likely leverage platforms that conduct ongoing routine surveillance (i.e., Malaria and DHS surveys, Maternal and Child Health routine visits), are relatively inexpensive to run, cover a wide geographic area (ideally nationwide) or overlap with areas that harbor traditional reservoirs of NTD burden. NTD programs should first look to see what exists, assess how strong a particular surveillance platform is, and explore what it would take to integrate the target NTD into this system. If there isn’t an opportunity to integrate, it’s important to understand and document why it wasn’t feasible.

In addition to mapping sample collection points, it would be useful to document the following as part of the situational analysis:

- Regional/national public health labs, satellite labs or district labs to map testing facilities and their lab capacities (what does the lab look like, what is the structure, what tests are they able to do, what data systems do they use). Post covid, there may be additional PCR machines in-country that can be leveraged for NTD surveillance.
- Biomarkers and diagnostic tools available for the target NTD
- Vector collection points or sentinel sites

Key questions that national NTD programs will need to answer:

- What: what data is being collected from current surveillance activities (i.e., indicators)?
- Where: where is sample collection taking place for current surveillance activities?
- Who: who is being sampled during current surveillance activities? (human or vector; what age groups?)
- When: when is sample collection happening for current surveillance activities?
- How: what surveillance approaches or diagnostic tools are being used for the ongoing surveillance system?
- Where is data from current surveillance activities being stored?

### Timing/ frequency of surveillance

Timelines will be an important component of an effective PVS plan. The integrated toolkit should be able to provide guidance on the type and timing of surveillance activities for the target NTDs. For example, it has been recommended that programs repeat cross-sectional serological surveys for PC-NTDs up to 10 years apart in order to provide more accurate estimates of epidemiological endpoints. When known, the toolkit should include the recommended number of years between surveys, although more research is currently needed to determine the ideal cadence and duration of PVS.

Nearly all of the diseases have randomly chosen sampling frames (distinct from true random sampling). Therefore, there may be opportunities to align sampling frames between surveillance activities that have similar targets (number of people, age groups, settings).

### 7.2.2. Integrate & synthesize phase

The integrate and synthesize phase would guide NTD programs to organize and prioritize the information collected during the gather phase. The NTD programs could then use these data to identify gaps and opportunities for integration. Table 3 below outlines suggested components to incorporate into the integrate and synthesize phase, including a synthesis guide, gap analysis, and process to identify opportunities to bridge the gap between what data the program has and what they need.
Table 3. Key components for an integrate and synthesize phase of planning for NTD surveillance in PVS settings.

<table>
<thead>
<tr>
<th>Component</th>
<th>Considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Synthesis guide</td>
<td>The toolkit should include a guide on how to organize and prioritize all the information from the gather phase in order to make programmatic decisions. One example consideration mentioned by a stakeholder would be to prioritize surveillance approaches that do not create an undue burden on the general population for PVS, given that countries are already seeing some fatigue with interventions/MDA more generally.</td>
</tr>
<tr>
<td>Gap analysis</td>
<td>Using inputs from the situational analysis, a gap analysis should be conducted to assess overlap between the disease risk maps and the sample collection maps generated during the gather phase. This analysis can also help identify areas where existing data are not sufficient for conducting PVS.</td>
</tr>
<tr>
<td>Identification of opportunities to bridge the gap</td>
<td>A likely source for collection of new data to cover identified gaps will be standardized survey collection. This could involve an NTD program leveraging existing surveys for other diseases such as malaria, or creating additional survey vehicles as funds allow. Another option could be to leverage geospatial modeling to help fill in the gaps.</td>
</tr>
</tbody>
</table>

7.2.3. Plan

The plan phase of the NTD surveillance planning toolkit would support NTD programs in outlining their approach to PVS surveillance, given all the inputs from the gather and synthesize phases. Once the proposed PVS surveillance system is outlined, the NTD programs would then outline next steps for cross-sectoral engagement and other planning steps needed before implementation of the new PVS system. Table 4 outlines key components and considerations for the plan phase of the toolkit.

Table 4. Key components for a plan phase for the development of NTD surveillance in PVS settings.

<table>
<thead>
<tr>
<th>Component</th>
<th>Considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Outline integrated surveillance plan</td>
<td>Once viable surveillance activities have been identified in the integrate and synthesize phase, NTD programs need to prepare a PVS plan. Considerations for the PVS plan may include:</td>
</tr>
</tbody>
</table>
|                                         | • A study from Means et al, made 10 specific recommendations on structural, process, and technical integration for NTD programs, with one recommendation in particular emphasizing the importance of standardizing subnational reporting systems to avoid confusion among health workers and supervisors.  
92 • A joint paper from U.S. CDC and American Samoa public health officials and Australian university researchers proposed a multi-stage surveillance strategy for LF post-MDA surveillance that begins with population representative sampling before targeting operationally efficient survey sites with low numbers needed to test, or that contain strategic subpopulations.  
93 • Ideally the PVS plan and data collection approach should be accessible for staff at the primary health care level.  
• A review of event-based surveillance systems noted that incorporating feedback loops to inform stakeholders about findings and actions was an essential process for sustaining motivation and improving cooperation of local health staff, particularly in routine surveillance settings.  
94 • A framework designed to improve surveillance and response to PC-NTDs at the sub-national level in Kenya relied on previously defined conceptual frameworks and a stakeholder-oriented approach to component identification and interconnection. The framework was validated in a multi-phased approach that included: (i) consultative meetings with stakeholders at the sub-national and |
The PVS plan should include the planned approach for responding to possible resurgence. Key questions for NTD programs would include:

- Have drugs for treating recrudescent disease been sourced appropriately?
- How do people get treated if discovered “post-elimination”? (Clinical treatment may not be part of the routine health system anymore)
- How will morbidity and prevention be incorporated into the PVS plan?
- What kind of reporting will be most effective for focal MDA?

| Implementation feasibility assessment | As part of the toolkit, it is important to identify opportunities for integrated surveillance, but it is equally important to identify when NTD programs don’t have enough data, resources, or capacity to implement integrated surveillance. After all the information from the gather phase has been synthesized and analyzed for gaps and opportunities for PVS, an assessment will be needed to determine whether the identified surveillance resources/integrated surveillance plan will be sustainable for PVS surveillance in the absence of clear WHO guidance. |
| Outline pathway to implementation | NTD programs must outline a plan for piloting and ultimately fully implementing the proposed PVS system. As part of the pathway to implementation, cross-sector engagement will be critical (including factors such as education, sanitation, etc.). Ideally, NTD programs would engage other programs and key stakeholders within MOH early in the process and build the survey approach together so that the appropriate information is being collected to maximize survey benefits for all users.

If the most sustainable solution to integrated PVS involves partnering with other vertical disease programs within the MoH, NTD programs will need to be able to highlight the utility of integrated surveillance for the potential partner programs (likely the program paying) in order to convince them that incorporating additional work to survey for NTDs will benefit them in the long run. The NTD program should look for ways to work within the dominant disease’s survey structure to get the data they need, either by triangulating data from different surveys/platforms or by using the same surveys over time.

It is also important to incorporate a feedback mechanism into the PVS plan that creates opportunities for various stakeholders to provide feedback on the quality and effectiveness of the PVS approach. This iterative approach will also keep the surveillance system flexible to incorporating new tools and guidance as they become available. |

7.2.4. Implement

Minimal suggestions were provided during the stakeholder consultations relating to implementation of PVS once plans have been developed. One stakeholder noted the importance of community engagement and clear messaging around stopping MDA and maintaining surveillance activities for PVS. Several others highlighted the importance of data management and storage, ideally through an integrated, nation-wide digital platform. In addition, once the surveillance system is in place, NTD programs should conduct health care provider trainings to refresh them on how to identify cases and record them in the reporting systems.

The planning toolkit also presents an opportunity to share data across neighboring countries to strengthen regional surveillance of NTDs. Such platforms to monitor cross-border transmission could include the PLISA platform used to share country data within the Americas; the WHO ESPEN Collect portal, which enables health ministries and stakeholders to exchange subnational program data in support of the NTD control and elimination goals; or the UNITEDengue confidential website of disease surveillance run by the governments of 11 countries in South East Asia.
7.3. Dissemination of the toolkit

Once the toolkit is developed, it will be important to have an effective, WHO-approved, platform to host the toolkit and share results when reasonable. According to key informants, the malaria surveillance assessment toolkit was intended to be hosted on a web-based platform that has a better user interface option, such as RShiny, but this was ultimately not accomplished. Stakeholders familiar with the process reiterated the benefits of a web-based platform and suggested it would be worth considering for this toolkit. Lastly, training resources should be developed, both for in-person and online trainings, to support the use and uptake of the toolkit by NTD program staff and other stakeholders from ministries of health.

8. Challenges for integrated PVS

Some suggestions gathered from key informants fall outside the scope of this toolkit and are activities that this project team is not equipped to act upon. However, these suggestions present important aspects of a sustainable integrated surveillance system that should be taken into consideration by WHO, funding agencies, and NTD programs.

First, funding and other incentives need to be restructured to encourage and support integrated programs. If financial investment has so far been dedicated to activities that are mostly single disease oriented, future investments should prioritize a set of interventions aimed at integrating NTD management within the primary health care system, at least in those areas where the disease burden has already decreased and vertical programs targeting specific diseases may no longer be cost effective. A shift towards an integrated approach, fully endorsed by donors, would also facilitate integration of diseases at the national level, especially where financially supported vertical health programs may pose a challenge for operationalizing this shift. To maintain effective surveillance systems, investments are needed to establish a capacity building system for data analysis and to support re-training for reporting on NTDs more generally.

Second, national NTD programs and their partners seek clear, quantitative, and data-informed approaches and guidelines for what to measure for PVS and when. For example, for LF, stakeholders are seeking a better understanding of target antigens in varying contexts to improve diagnostics. Serologic reactivity to Wb-Bhp-1 varied widely with samples from different regions (sensitivity range 32–92%), with 77% sensitivity for 116 samples collected from microfilaremic individuals outside of sub-Saharan Africa. This variable sensitivity highlights the importance of validating new diagnostic tests for parasitic diseases with samples from different geographical regions. In addition, NTD programs need clear case definitions included in updated guidelines to inform mandatory reporting practices.

Finally, there’s a need for improved cross-border data sharing and support for data platforms that facilitate data sharing. This toolkit can encourage countries to be mindful of reintroduction from the surrounding region in the post validation space, but establishing and maintaining cross-border data sharing practices is outside the scope of this work. This cross-border surveillance could potentially pull from the ESPEN portal, automatically showing countries the disease transmission status of their neighbors. This might be difficult to make the investment case for unless the surveillance data available becomes truly multi-disease and geographically granular enough to show trends in border districts or health facility areas.
Conclusion

Throughout this review, peer-reviewed scientific papers and grey literature sources were examined and interviews with key stakeholders were conducted to collect a substantial body of knowledge relating to PVS for three focal NTDs. This evidence pertains to both established and emerging approaches to surveillance before and after verification or validation of elimination, as well as diagnostic tools that are currently in development.

From the literature, there is strong evidence in favor of incorporating MX and next-generation serological testing for both LF and onchocerciasis in conjunction with more traditional TAS-style population surveys. These strategies may provide logistical and financial efficiency that will be key to sustaining PVS as funding for validated or verified diseases is likely to diminish over time.

Additionally, tools such as PoolScreen for MX and the bplex LF-Onchocerciasis antigen RDT for serological testing provide potential opportunities for integration between the two diseases that may create additional gains in efficiency for programs conducting integrated PVS for NTDs.

Meanwhile, this review identified key areas of uncertainty where guidance on PVS will need to be supplemented by emerging research and local contextual information to be maximally effective. For example, it is clear that monitoring for post-validation reintroduction of disease via migrant populations or zoonotic sources is a critical component of PVS but is also not yet well understood. And while xenomonitoring can provide significant value to surveillance programs, it is also the case that methods and results vary widely across geographic settings and disease vectors. Additionally, serosurveillance presents important opportunities for increased efficiency and sensitivity in identifying subpatent infections, but guidelines for the use of serosurveillance must be sensitive to age and geography-dependent factors. Importantly, serological targets also vary between those aimed at identifying recent infection and those aimed at identifying past exposure, and these differences will have significant implications when identifying which diagnostic is most appropriate for use in a given elimination context.

In synthesizing the compiled evidence, this work identified a number of key themes to consider in the construction of an integrated NTD surveillance toolkit. For example, multiple stakeholders agreed on the importance of bearing flexibility in mind for the design phase, with an emphasis on adaptability to local country contexts and responsiveness to the varying needs of different NTD control program structures and needs. There were also consistent recommendations to tailor the toolkit in such a way as to facilitate the sustainable integration of PVS strategies with routine reporting systems and existing data analysis platforms such as DHIS2 wherever possible. Lastly, the need to consider well thought-out responses to cases identified through a potential surveillance system was stressed by several stakeholders.

One point on which sources shared different perspectives is the level of complexity that the toolkit should ideally use for the options it will present to country NTD programs. Some stakeholders indicated a need for the toolkit to make recommendations simple and accessible, with an emphasis on presenting options to potential end-users at the primary health-care level, whereas others suggested targeting high-level recommendations to NTD program managers. In either case, both the literature review and interview responses highlighted a need for concrete recommendations rather than an overly general collection of options that would prevent straightforward use of the toolkit in program implementation.

There were several limitations inherent in the process of this review, including the limited scope of the three focal NTDs considered. Since the intended focus of this project was on LF, onchocerciasis, and trachoma, the landscaping activities did not meaningfully cover surveillance activities for non-focal
NTDs. While this limits the applicability of our findings for other NTDs, the project aims to develop the toolkit using a structure that easily converts to include new diseases, and there may be aspects of this work that provide insights into the eventual integration of PVS for non-focal NTDs. Additionally, this work is limited by the static nature of retrospective evidence evaluation. Recommendations and assumptions from this work were made based on previously compiled knowledge, whereas any toolkit that aims to guide PVS implementation in the future will need to be adaptable in order to take into account the generation of new evidence and approaches from the public health research community in the coming years. Lastly, while the goal of this review was to compile all existing PVS guidance for our focal NTDs, the evidence base for trachoma has not yet permitted for the creation of distinct WHO guidelines on PVS. This limits the utility of a toolkit designed to highlight sustainable approaches to integration of PVS based on WHO recommendations, and therefore trachoma will not be included in the initial toolkit construction and rollout.

The next steps for this work include a deeper review of existing planning toolkits identified through our landscaping activities (Appendix 2) to glean relevant structural or technical elements that may increase the utility of the eventual end product. The general structure will also be modified in accordance with feedback on a draft version of the toolkit from WHO stakeholders and partners in national NTD programs prior to a piloting phase where the toolkit will be implemented in three initial geographies.

Looking ahead to the toolkit development process, consideration of local context and the needs of eventual end-users of the toolkit will be central to its creation. Any product composed from this process will only achieve its aims if guidance from WHO and other global stakeholders is carefully combined with the contexts, needs, and innovations of NTD program managers and staff in the geographies where it is initially implemented. This can be accomplished by heeding and prioritizing the voices of those who best understand the local realities and challenges inherent in conducting PVS for NTDs throughout the toolkit development process.
Appendices

Appendix 1: Detailed search terms for literature review


Annex 1: Relevant toolkits reviewed

There are several tools and approaches that have been used (or are in development) to assess or plan surveillance systems for infectious diseases. The list of tools and toolkits reviewed and relevant findings from the review are captured in Annex 1, including the disease focus, geographic focus, recommended tools or approaches, format, audience, approach, potential relevance to the integrated NTD PVS planning toolkit, and limitations.
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