COR-NTD 2020
Virtual Meeting, November 12 – 14
Integrating for Impact

**TAS to the Future: New Approaches for the Last Mile of LF**

**Session Date:** 11/14/20

**Session Time:** 9:00 AM - 12:00 PM EST

**Session Description:** The Global Program to Eliminate LF has seen tremendous gains in recent years, thanks to a strong M&E strategy and promising new treatment approach (triple drug therapy). The final frontier for LF programs is determining how to conduct surveillance in a way that is both sufficient and sustainable. This breakout session will present new solutions for conducting LF surveillance that build off the present approach of repeating the TAS survey for a 2nd and 3rd time. A key theme of this session is that better utilization of existing data can lead to an improved ability to find hotspots, greater resource savings, and a strengthened case for demonstrating verification of elimination.

While the presentations in the first half of the session will focus on new tools and approaches to come out of current research efforts, the latter half of the session will be focused on the program implications and challenges associated with adopting these tools in a surveillance setting. The group will be divided into four smaller sections, each with a facilitator and access to a virtual whiteboard for brainstorming, and will be given a topic for discussion. The goal of these smaller breakout groups is to generate a list of the information available, information gaps and OR next steps in order to address their topic. The list of topics for discussion includes:

**Session Chairs:** Katie Gass and Ernest Mensah

**Session Rapporteur:** Kira Barbre

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**KEY DISCUSSION POINTS**

*What key findings and data did the group identify via presentations? What issues were raised in discussions?*

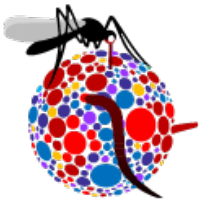
The main discussion for this session focused on four areas: operational research (OR) to improve post-validation surveillance (PVS), OR to improve evaluation unit (EU) formation during transmission assessment surveys (TAS), OR to prioritize PVS within countries, and OR to guide hotspot response during PVS.

OR to improve PVS

- Before designing a method for PVS, it is important to define the end goal. It is unclear whether the only goal of PVS is to maintain the current objective of elimination as a public health problem or if it can also be used to move towards the likely future goal of elimination of transmission.
- Countries already have a wealth of data across mapping, pre-TAS, and TAS. It is likely that these data are currently underutilized.
- It is essential to have georeferenced data. All countries should be collecting this if they are not already.
    - It may be worthwhile to go back and collect GPS data for surveyed schools/communities where they are unavailable.
- There is a need for new diagnostic tools that meet the new World Health Organization (WHO) target product profile (TPP) performance characteristics for stopping mass drug administration (MDA) and for PVS.
    - There is also a need to prepare for PVS to be conducted with the new tools.
- There is a need to develop capacity to conduct PVS among program implementers in endemic countries.

OR to improve EU formation during TAS

- Currently defined EUs are often too large; smaller EUs are better.
- Positive cases identified during TAS should serve as an alert for programs to pay attention to possible transmission within an EU.
- It is important to consider how better EU formation could help prevent an area from passing TAS when transmission is still ongoing.
- There is a need to balance the importance of finding the positive cases with the pressure to stop MDA. Establishing realistic targets may be helpful.
- It is a priority to start this work as soon as possible to avoid having to restart programs in areas that have already been validated.
- A presentation from Haiti by Alain Javel shared how an EU was sub-divided based on evidence of ongoing transmission after following up positive cases from TAS 2 (part of an OR study). The two sub-EUs will both undergo TAS 3 and it is possible that the urban sub-EU, where some transmission appears to be ongoing, will fail and require additional rounds of MDA. This is a proactive program approach that was well-received by the group.



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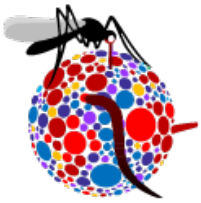
OR to prioritize PVS within a country

- Based on WHO consultations, programs should prioritize PVS activities to geographic areas or population groups at greatest risk of recrudescence. Four potential platforms have been identified for PVS: health facility screening, existing standardized surveys, targeted NTD surveys, and xenomonitoring.
- Prioritization for PVS may be based on epidemiological, programmatic, environmental, and demographic factors. Examples include:
    - Epidemiological: highest baseline endemicity, clusters of positive cases from TAS 1-3, zoonotic potential (*Brugia malayi*), and the vector species (*Aedes* or *Culex*)
    - Programmatic: low MDA coverage, missed or interrupted MDA rounds, large EUs, history of failed pre-TAS or TAS, and lowest bed net coverage
    - Environmental: elevation, mosquito density, abundance of vector larval habitat, rainfall, temperature, and vegetation cover
    - Socio-economic and demographic: least developed areas, population density, mobile/neglected population groups, inward migration from endemic countries, and systematic non-adherent individuals
- As demonstrated in the presentation by Hugh Sturrock, geostatistical methods can lead to better use of existing data (e.g., Monitoring & Evaluations [M&E] data and environmental covariates) to identify areas of greatest risk of ongoing transmission or recrudescence and may therefore aide programs in identifying priority areas for PVS implementation.
- Several PVS strategies have been proposed but field evaluations of PVS options are limited because they have not been adopted and implemented widely enough to generate data needed to inform guidelines.
- There is limited funding support for programmatic implementation of the available PVS options.

OR to guide hotspot response during PVS

- There is a need for practical PVS guidelines for countries to follow.
- Identification of positive children during TAS is likely to be a good indicator of a potential hotspot.
    - However, it does not follow that areas without positive children identified during TAS are not also potential hotspots.
    - There is no uniformity on country response to positive cases identified during TAS.
- It is possible to integrate LF PVS with other surveys. This can be cost-effective and provide actionable data.



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**KNOWLEDGE GAPS IDENTIFIED**

*What data and tools need to be generated to address the issues raised by the group?*

<u>OR to improve post-treatment surveillance</u>

- It is unclear how concerned we should be about areas classified as non-endemic for which old or limited data are available.
    - How should areas with little available data be taken into account? How much data do we need to collect in these areas to feel confident that they are/remain non-endemic?
- Although there is discussion about using Wb123 ELISA to detect exposure in children during LF PVS, it is unclear what seroprevalence threshold should be used.
    - This is especially important in the context of integrated surveillance where it is not feasible to conduct FTS.
    - There are also challenges with setting a positivity cut-off to classify individual results.
- It is not clear how concerned we should be about 'hotspot' villages with high prevalence in EUs that pass TAS.
    - This is related to the previous comment about goals of PVS. Are we concerned about any LF transmission or only transmission that puts an EU above the threshold for elimination as a public health problem?
- It is not clear which diagnostic test and which age group should be used for PVS.
    - Although mf provides the most reliable real-time information, its lack of sensitivity, coupled with a dearth of skilled microscopists, could lead this indicator to miss possible transmission in some cases.

<u>OR to improve EU formation during TAS</u>

- It is unclear what criteria should be used to trigger the division of an EU.
- Some programs are including purposive clusters, in addition to the 30+ random clusters, in TAS 2 or TAS 3 surveys, based on the identification of positive cases in a previous TAS. The utility and cost-effectiveness of this approach for identifying hotspots that merit program action is unclear and should be investigated.

<u>OR to prioritize PVS within a country</u>

- Clear guidelines for conducting PVS are urgently needed.
- Geostatistical models should be translated into user-friendly tools that countries can use.
- Program Managers should be engaged much more in ongoing discussions on PVS strategies.

OR to guide hotspot response during PVS

- Thresholds to use when defining/responding to hotspots have not been defined.
- It is unclear how to combine different diagnostics (e.g. mf, ag) into a single model.
- It is unclear how early we can/should respond to potential hotspots. More information is needed on the dynamics of resurgence and how fast and far transmission can spread.

**RECOMMENDED NEXT STEPS**

*What operational research and other actions need to be taken to address the knowledge gaps identified by the group?*

OR to improve post-treatment and post-validation surveillance

- What is the programmatic value of sampling in communities where positive cases were found during TAS? When is this recommended and what should be done with the information obtained?
- It will be important to focus on utilizing already-collected data, particularly those from large seroprevalence surveys. How can data from these surveys, which may not be optimally designed for NTD program needs, be used effectively?
- It would be useful to map out an overall multi-year OR surveillance strategy with WHO and programs for buy-in from USAID and other donors.
- OR should be conducted to determine the thresholds and other characteristics (e.g. hotspot size) below which a public health response is not needed. Longitudinal studies of, for example, hot spot areas within EUs that have passed TAS would be useful in determining this.
    - A related concern is how to balance the current goal of elimination as a public health problem with the potential future goal of elimination of transmission.
- If it is determined that additional MDAs should be conducted, what is the appropriate unit of response (should it be confined to the EU? IU? Sub-implementation unit [sub-IU]?)?
- OR should be conducted to compare the effectiveness of various PVS methods in a well-characterized population.
- Although models have the potential to be useful for answering some of the questions around PVS, the priority should be to focus on obtaining (either through new or existing data) high-quality inputs to inform models.
    - What factors are associated with ongoing transmission? Is there data that we could be collecting now to help feed into these models?
    - For current and newly available diagnostics, what is the most informative age group for PVS?
- Additional research is needed on the kinetics of available biological markers including antigen and antibody.

- Are our population-based surveys systematically missing non-adherent individuals? How do we measure this and how do we design surveys to capture these individuals?
- What are the appropriate entomological thresholds associated with elimination as a public health problem (and elimination of transmission)?
- How can we engage communities to generate demand for surveillance?
- An economic analysis, comparing the program savings and productivity gains of being LF-free with the cost of surveillance could help to garner country buy-in.

<u>OR to improve EU formation during TAS</u>

- OR focused on the criteria that should be used to trigger the division of an EU, as well as how to divide an EU, is needed.
    - What administrative boundaries should be used to sub-divide an EU (e.g., by IU, sub-IU)?
    - What if the residual prevalence is not geographically distributed but evenly distributed throughout the EU, is there any recourse?
- Will better EU formation prevent an evaluation area from passing TAS when transmission is ongoing?
- Is there a way to incorporate oversampling in potential at-risk communities (e.g., migrants, areas with known low coverage)? Would a pre-TAS 2 or pre-TAS 3 survey be useful?
- With some extra sampling during TAS, simulations could be run to compare what the results would have been if TAS had been conducted at the sub-EU level.

<u>OR to prioritize PVS within a country</u>

- Need to conduct more field trials of various PVS proposals/strategies to identify priority PVS strategies
- Determine the settings where various geostatistical models are applicable
- Can geostatistical models be standardized to be usable across all country settings?
- Can other health system surveillance platforms (e.g. passive screening of blood collected for other purposes) be used to detect LF signals of ongoing LF transmission?
- How do we leverage the health system to sustain long-term post-validation surveillance?

<u>OR to guide hotspot response during PVS</u>

- Are TAS data sufficient for identifying hotspots? If not the raw data, what about when combined with environmental covariates using geostatistical models? If not, should we be conducting community surveys focused on older age groups?

- What are the most effective tools and strategies to control and clear hotspots? Are targeted treatment approaches (e.g. family members, neighbors) sufficient? Empiric studies should be conducted to look at these approaches and the intervention should be compared with doing nothing.
- Will some hotspots die off on their own? Will they spread if left unchecked? Longitudinal monitoring in the absence of intervention would provide insight.
- A list of steps needed to identify hotspots should be defined.
    - Mathematical modelling can be used to define the threshold for action and the intervention that is needed at that point.