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

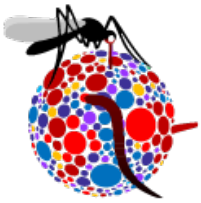
Tackling trachoma endgame challenges

Session Date: 11/13/20

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

Session Description: Global elimination of trachoma as a public health problem was targeted for 2020; however, only 10 countries had been validated by the beginning of 2020. Despite not meeting the ambitious 2020 elimination goals, many countries have made steady progress towards attainment of elimination. As programs gear towards the new 2030 NTD roadmap targets, innovative approaches are needed to enhance attainment of elimination and to sustain the elimination gains post-validation.

A number of end-game challenges that put country programs at risk of not attaining timely elimination of trachoma have been identified, including districts not attaining TF<5% following multiple cycles of MDA and trachoma impact surveys (TIS) and districts not sustaining TF<5% during trachoma surveillance surveys (TSS). In most endemic countries, the majority of districts attain and sustain TF<5% after one or two mass drug administration (MDA) cycles; however, some districts struggle to escape a repeating “MDA-TIS-MDA-TIS-MDA” cycle, and some districts experience a re-bound of TF (≥5%) at TSS and thus, per current guidance, have to restart another MDA cycle. Because of these “vicious cycles”, there may be a considerable time lag from when the first district in a given country attains elimination of TF<5% to the time (when the last district in the same country attains the TF elimination target. As a result, country programs may be caught up in a decade-long implementation of SAFE in just a few remaining districts. And, if these problematic “cycles” remain unbroken, countries risk missing the 2030 goals as they did to the 2020 goals.



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The participants of the breakout session will deliberate on operations research (OR) needed to support countries to enhance attainment of elimination and sustain gains. The broad discussion topics will focus on OR needed to enhance timely progression of districts through TIS and TSS milestones, including longer annual MDA cycles before TIS are done; enhanced MDA strategies; alternative survey strategies; and use of alternative indicators (such as TI, ocular chlamydial infection and serology) to inform attainment of elimination.

The session will include two pre-meetings that will comprise presentations and discussions on the broad topics to distil and prioritize OR questions. Finally, the third and final meeting will focus on review of the OR priorities distilled from the pre-meetings and packaging the agreed OR priorities into research "ready" topics.

Session Chairs: Jeremiah Ngondi and Stephanie Palmer

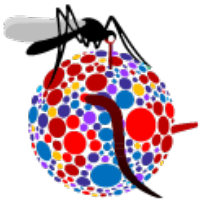
Session Rapporteurs: Laura Cane and Rosemary Pearson-Clarke

KEY DISCUSSION POINTS

- The standard SAFE strategy – Surgery for trichiasis, Antibiotics to clear ocular strains of chlamydia, Facial cleanliness, and Environmental improvements – is widely effective (e.g., 10 countries validated, 1.3 billion people no longer at risk for trachoma) but it is not working in all contexts. For example, 419 districts are still in MDA-TIS-MDA cycle, 159 districts have had trachomatous inflammation – follicular (TF) ≥5% during TIS at least twice, and 79 districts had TF ≥5% during TSS. While this represents a small proportion of the global program, in certain countries, just a few districts with "persistent" TF may prevent the entire country from reaching elimination.
- Independent risk factors associated with TF>5% at first TIS are higher baseline TF, lower access to water, and lower access to sanitation (data are few for WASH indicators). Independent risk factors associated with TF≥5% at TIS2 or greater are higher TF prevalence at previous TIS and lower access to water (data are few).
- Prior to COVID, in the previous 9 months, the estimated target date for validation of 4 countries in the USAID portfolio has been prolonged due to TIS and TSS with TF ≥5% (range of 1 to 4 years). There are implications of continuing MDA including: deferment of validation, prolonging

of program costs, loss of funding certainty, and loss of confidence in knowing the successful way forward.

- From a programmatic perspective, we need both to better understand the reasons for persistent TF via 1) a process that verifies quality of program delivery as a potential reason for repeat surveys where TF ≥5%; 2) a systematic, data driven predictive algorithm to assist in decision making in districts with persistent TF (based on clinical TF?); 3) established flexibility to MDA guidelines for districts with repeat survey where TF ≥5%; and 4) Established flexible access to the drug donation program
- There are four main categories of survey "failures": statistical, diagnostic, programmatic, and biological. Understanding the reason for a TIS/TSS with TF ≥5% and tailoring actions accordingly may result in a more favorable outcome.
- In some settings, there is a low correlation between TF and Ct infection. TF alone may not capture the whole picture of transmission, and other indicators may be necessary or useful to make more informed decisions. TI may indicate more recent/current infection and higher chlamydial loads and maintains a consistent relationship to Ct infection even in low TF prevalence areas. Serology and Ct infection may be used to confirm reemergence and Ct infection may be useful as a tool to confirm TF identified during field grading is actually due to trachoma. Serology measuring Ct antigens Pgp3 and CT694 may be helpful if used judiciously on a specific age group of interest or longitudinally on same age groups to trigger further investigation. Photography may be useful to use in low prevalence settings, where multiple reference graders can audit a selection of photographs to ensure they agree on the grading.
- Generally, it is more financially advantageous to undertake a planned TIS in all scheduled evaluation units (EUs) to determine whether or not to stop MDA rather than undertake an additional round of MDA in each EU and postpone the TIS for one year, except where the rate of TIS with TF ≥5% is high (>71%).
- Confidence intervals also may be useful for better understanding the results of TIS and TSS.
- Biannual (every 6 months) MDA did not result in significantly lower Ct infection prevalence compared to annual MDA. Quarterly MDA in children 1-10 has shown to be significantly better than annual MDA for Ct outcome in the target age group but not for the non-target group (people 11+). However, TANA and TANA II (TIRET) were not powered to detect a significant difference between annual and biannual treatment and it was suggested that these strategies may merit further investigation, though the conclusion of a Cochrane review in 2019 was that "there was no strong evidence to support any variation in the recommended annual mass treatment" and therefore, additional data will be needed to make a change in guidance. There are number of ongoing planned trials to help answer these outstanding questions, including TAITU, KETFO and TESFA.



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KNOWLEDGE GAPS IDENTIFIED

- Definition of persistence for deciding if enhanced strategies are needed. This may necessitate two definitions: one that defines persistence based on data from multiple surveys, encompassing "floating" persistence (wherein TF prevalence remains high/above a certain threshold), "bouncing" persistence (where TF prevalence falls <10% but not below 5%) and "rebounding" persistence (where TF falls below 5% at TIS and rebounds above 5% at TSS). The second definition is for areas that are just beginning treatment but are "hyper-endemic" and will likely require increased intensity of intervention.
- Methods/tools to identify districts likely to take longer to reach the TF elimination threshold, taking into consideration covariates such as baseline TF, MDA coverage, WASH variables, and spatial covariates.
- Methods to predict districts likely to show recrudescence (TSS TF≥5%)
- Tools/standardized "investigation" to facilitate the rule out quality of program delivery as a likely reason for repeat TIS with TF≥5%.
- A systematic, data-driven algorithm to assist in decision making in districts with persistent trachoma
- Established flexibility to MDA guidelines for districts with persistent trachoma
- Grader supervision methods to ensure grader proficiency is not contributing to diagnostic error
- Larger-scale, higher-powered data to determine which enhanced and/or targeted treatment strategies are more effective than annual MDA

RECOMMENDED NEXT STEPS

<u>Program Investigation</u>

1) What kind of metric can be developed to show that quality expectations for program implementation have been met?
2) What universally recognized quality control measures can be developed and implemented for the supervision of graders? (e.g., blinded evaluation using photography)
3) How do we contextually investigate unexpected or abnormal results – whether the TF survey result was <5% or ≥5%? (e.g., non-endemic districts surrounded by persistent districts)

<u>Program Monitoring (Supplemental Indicators)</u>

1) Should we include trachomatous inflammation (TI) in the decision making? Can we grade more accurately and efficiently? Can TI be consistently graded using photography? How do photos compare to field diagnosis of TI?
2) How can baseline TF be used as a part of the decision making and in what populations (age groups)? Is it possible to predict when threshold will be reached based on the trajectory of TF prevalence?
3) Do we need to approach different supplemental indicators for TIS vs TSS?

4) Can supplemental indicators be collected and analysed, at scale, in a timely fashion to facilitate program decision making?

Program Monitoring (Surveys)

1) Can we predict trachoma-persistent districts?
2) Could alternative evaluation designs cost effectively provide sufficient evidence to inform intervention strategies in trachoma-persistent districts?
3) How could confidence intervals help us understand impact and surveillance results?

Program Enhancement (MDA)

1) Should biannual treatment be considered and is it feasible (given cost, coverage)?
2) Is it possible that the number of rounds needed for each baseline category is not adequate? If so, what should the number of rounds be? What do modelling results say?
3) If F&E cannot be improved as quickly as desired, can the achievable level of F&E be factored into determining if the suggested number of MDA rounds is sufficient?
4) What is the most effective enhanced MDA strategy to use in areas that are not responding to traditional MDA?
5) How should persistence be defined in the context of deciding if a district requires an enhanced program?