Exploring the Potential of Integrated Serological Surveillance Platforms in Elimination Settings

Session Date & Time:	Tuesday, November 19; 1:00 PM to 4:00 PM
Session Location:	Bellagio 2
Session Description:	Multiplex serological assays present a potentially sensitive and cost-effective method for surveillance. However, there is no consensus on 1) analysis methods 2) how control programs can design and use serological surveys to support elimination efforts and monitor transmission post-certification and 3) interpretation of results into policy relevant outcomes
Session Chairs:	Chris Drakeley and Anthony Solomon
Session Rapporteur:	Sarah Sullivan, NTD Support Center

Multiplex serological assays can deliver a wealth of information from relatively small blood sample volumes, but questions remain about how to deploy this powerful tool in a way that would yield benefits across tropical and public health relevant diseases targeted for control and elimination. These challenges are seen in technical, operational, and policy domains and span the topics of analysis techniques, assay considerations, capacity building needs, financing, ethical issues, development of new policies to accommodate these methods, survey design considerations, and programmatic implementation and integration.

Dr. Espino's presentation addressed the potential for multiplex serological surveillance from the programmatic perspective, highlighting the implementation, ethical and financial considerations that would be necessary for rollout of multiplex serological surveillance on a programmatic level. Previous experience with multiplex assays for malaria (which are generally better characterized than for neglected tropical diseases, or NTDs) suggests value in using seroserveillance to target high burden areas. In malaria, many stakeholders anticipate using the tool to confirm the absence of transmission in elimination settings. There is also interest in applying serosurveillance models to the STH and schistosomiasis in order to target high burden areas, but this is complicated by gaps in the antigen library.

Presentations by Drs. Arnold, Fornace, and Pinsent approached the questions from an analytical perspective, delving into what kinds of analyses are possible based on multiplex sero-surveillance as well as characteristics of the data collection and laboratory analysis which would be necessary to produce interpretable results that would add value to programmatic decision-making. Dr. Arnold's presentation focused on using geostatistical modeling, continuous rather than binary serological response data, and adaptive sampling to perform population level inference and provide actionable information to programs. Dr. Pinsent focused on mathematical modeling approaches which utilize serosurveillance data to quantify transmission intensity through sero-catalytic models with a focus on trachoma. These models can be powerful tools, however, modeling data from across platforms, and with the different age groups sampled by different programs can be challenging. Dr. Fornace's presentation included methods for incorporating spatial and temporal elements into mapping transmission surfaces utilizing continuous antibody data, as well as methods for classification of seronegative and seropositive populations. This approach enables the targeting of areas with high seroprevalence or high uncertainty of prevalence for future surveys or interventions and could be expanded to integrate transmission models.

Based on these presentations and discussions in the group work portion of the session, the following gaps in knowledge and resources were identified. *(See table beginning on the next page.)*

Topic	Challenges	Proposed Solutions
Assay development, discovery and availability	• More sensitive and specific assays are needed for some diseases • Commercially available and well characterized tests are needed for multiplex platforms • Reference sera are often not available • International standards including quality assessment (QA) do not yet exist	• Centralize sources of purified antigens for coupling to beads or printing on arrays • Archive global reference sera or antibodies to standardize across labs and surveys • Learn lessons from: o other diseases with established reference sera including HIV and TB or Vaccine Preventable Diseases o Other initiatives such as PAHO: Destination Elimination and the Finland biodata program
Survey design	• Surveys currently conducted for specific diseases often target specific age groups or seasons which may not be relevant to across all diseases, limiting the value of integrated surveillance based on those surveys • Nationally representative samples may not have sufficient geographic resolution to identify the remaining foci of infection • Some powerful analytic tools require longitudinal data or data with multiple age cross sections which are not routinely collected in existing surveys	• Design new adaptations to existing surveys to ensure that data collected can be relevant to multiple diseases. • Target specific subsets of diseases for which combined surveillance could provide gains • Follow-up nationally representative sampling with spatially adaptive sampling
Analysis techniques	• Growing need for analytic capacity and tools to translate antibody data into actionable information • Measurement and modeling of low levels of transmission is a challenge across diseases • Using only binary data in low prevalence settings may introduce artificial information loss • Spatial models and transmission modeling are powerful tools for analyzing serological data but are not in widespread use	• Build capacity and develop networks across disciplines to ensure that the most robust tools can be utilized widely • Consider continuous analysis of output from multiplex serosurveillance, especially in low prevalence settings • Investigate creative modeling approaches, such as modeling multiple diseases with similar transmission dynamics or using multiple antigens • Develop and refine spatial modelling to allow for wealth of data on ecology and environmental change

Implementation	• Most country programs do not yet have the laboratory, analytical, and human resources capacity to conduct integrated serosurveillance • There is currently no established framework for how NTD multiplex data should be analyzed and how that will result in programmatic response • Integrated surveillance will require coordination between disease programs within ministries	• Integrate programs into the health system to ensure the longevity of projects and strengthen the health system • Establish antibody-based benchmarks for monitoring goals to drive program action • Build HR capacity in programs and local partner institutions • Harmonization of train laboratory and analysis techniques within and between areas • Transfer technology and QC to endemic countries/regions
Ethical consideratio	• Blood collection can be culturally sensitive, especially repeated collections • Specimens are often collected for a single disease survey but may retrospectively be assessed for multiple diseases	• Assess sensitivities around blood collection or other potentially difficult issues • Emphasize working with communities and getting buy-in for the work from those communities • Develop language that allows future analysis of bio-banked samples
Policy implications	• Integrated surveillance methods are not currently included in guidelines for disease control • There are not currently clear use-cases for these platforms and serology in general • Financing and business cases are not clear	• Develop international standards • Define use-case scenarios for integrated surveillance and their relative benefit over and relationship with other approaches • Undertake research on standards • Conduct policy dialogues • Review possible financing mechanisms
Financing	• Implementing integrated surveillance in country programs will not be without cost, especially when the broad scope of assays, laboratory equipment, consumables, maintenance and analysis is considered. • There is currently a lack of coordinated financing across global health groups • Ministries of Finance are important partners in ensuring the longevity of programs but may not be engaged	• Undertake health economics studies for field, lab, analytical and intervention elements to show ROI. Particularly in countries where centralized serological surveillance is proposed • Undertake studies of the cost effectiveness of multi-disease surveys to show the value of integrated surveillance • Undertake advocacy to generate buy-in from technical and non-technical people to encourage investment • Develop a cost effectiveness analysis method • Establish projects with longevity and broad remit so that human capital is not lost due to funding reductions