New Approaches to Integrating Molecular Surveillance into Malaria Control Programs

Grand Challenges Explorations Round 26
October 2020

THE OPPORTUNITY

At the Bill & Melinda Gates Foundation, we believe that malaria eradication within a generation is possible. We recognize that in order to achieve this, National Malaria Control Programs (NMCPs) must be empowered to use timely, high-quality data to inform their malaria strategic planning, decision-making, program implementation, and evaluation. As we work to sustain the decline in incidence rates that have marked the last fifteen years of malaria control, this concept of data-to-action has never been more important.

Our vision for data-to-action, recently endorsed by WHO's Malaria Policy Advisory Committee (MPAC), is one of stratification and sub-national tailoring. In the first step, multiple data sources – from geospatial to epidemiological data – are used to define district-level strata within a country. Next, additional data types are used as the input to mathematical models that output the optimal package of interventions that result in maximum malaria burden reduction within a given resource envelope. The success of stratification and sub-national tailoring is highly dependent on the underlying data, which may not always be complete, high-quality, and / or timely. We are therefore exploring new data streams that might improve our understanding of factors driving changes in malaria epidemiology or be used to optimize the choice of interventions modelled. One of these new data streams is serological, genetic, and / or genomic data which arises from malaria molecular surveillance.

Malaria Molecular Surveillance (MMS) is an umbrella term which describes the use of molecular biology approaches – from serology to genotyping to whole genome sequencing (WGS) – to interrogate parasite and / or vector populations in order to derive epidemiologically actionable information. MMS does *not* include research-oriented genetic and genomic investigations, such as studies using genomics to investigate parasite or mosquito biology. Rather, the emphasis is on analyses that can directly influence malaria control policy and practice. In addition to the laboratory techniques used, MMS also includes the bioinformatics tools and resources necessary to process, interpret, and share the resulting data.

THE CHALLENGE

Initial work in the MMS space focused on methods development and proof-of-concept pilot studies. Now, the tools and analyses are maturing, the infrastructure is in place, and the time-to-result is much shorter, meaning that MMS is beginning to influence program planning and execution. In elimination settings, genetics has been deployed in focused investigations of malaria importations. In higher-burden settings, MMS is being used to visualize the spatio-temporal spread of antimalarial drug resistance markers, influencing treatment guidelines, and to track the effect of different interventions on parasite genetic diversity as a surrogate measure of transmission intensity.

In June 2019, a WHO Technical Consultation on the role of parasite and vector genetic and genomic data in malaria surveillance ([workshop report](#)), stakeholders from MMS community – both on the research and programmatic sides – gathered with the goal of identifying those MMS use cases for which sufficient evidence exists to recommend routine use for malaria control and elimination, and those for which more upstream research is needed in order to generate a broader evidence base for future recommendations.

The list of use cases that are ready or near ready (marked with an asterisk*) for programmatic deployment includes:

- Detect drug resistance: monitor the prevalence/frequency of molecular markers of drug resistance to inform intervention selection, treatment guidelines, and surveillance
- Detect hrp2/3 deletions: monitor the prevalence/frequency of hrp2/3 deletion affecting RDT efficacy to inform diagnostic selection
- Assess drug resistance gene flow: determine the origins of drug resistance markers and monitor their spread within/among regions and parasite populations to inform containment strategies and regional policies around intervention selection, treatment guidelines, and surveillance*
- Predict emerging resistance: detect signatures of positive selection suggesting emerging resistance to inform intervention selection, treatment guidelines, and surveillance*
- Identify local transmission: identify focal areas of high transmission and clusters of infections to inform resource deployment*
- Distinguish local and imported cases: in elimination settings, classify cases as imported or otherwise for case investigation and elimination certification*
- Reconstruct transmission chains: elucidate contributing factors (e.g. seasonality, migrants, asymptomatic cases, and highly infectious individuals) to ongoing transmission patterns to inform intervention selection, resource deployment, surveillance, and case investigation*
- Determine connectivity of parasite populations: assess degree to which transmission is linked among regions due to linked parasite populations to inform program planning and resource deployment*
- Survey for allelic variation in target sites for gene drive: determine whether SNPs that would prevent CRISPR site recognition exist in wild populations to optimize gene drive release planning*

As MMS transitions from proof-of-concept work in academic institutions to operational reality in NMCPs, Ministries of Health, and National Public Health Institutes, the challenge lies in conducting the work in a way that engages country programs and malaria decision-makers and that empowers them to understand and use their data actively for programmatic decision-making.

The purpose of this call is therefore to identify new and innovative approaches to integrating malaria molecular surveillance into malaria surveillance and programmatic decision-making in malaria endemic countries.

What we are looking for:

We are looking for innovative proposals that will use MMS data to enable NMCPs to inform their national and sub-national surveillance efforts, national strategic planning, and/or intervention implementation. These may include proposals that: create or expand laboratory, bioinformatics, and data interpretation capacity within NMCPs or at institutions closely affiliated with an NMCP; create or implement tools for communicating and sharing parasite and/or vector molecular surveillance data; and/or build relationships

between groups with MMS capacity and NMCP partners. Proposals should target the use cases identified above that are ready or near-to-ready for programmatic deployment. We do not want respondents to be generating MMS data for research purposes; rather, the intent of this call is to support the application of MMS approaches to routine malaria surveillance and planning within NMCPs, Ministries of Health, or similar organizations.

While we welcome respondents from around the world, **we are particularly interested in proposals from respondents working in high-burden malaria settings. All proposals must include a principal investigator or co-investigator from a malaria-endemic country.**

Winning proposals should:

- Explain the rationale for and potential benefits of using MMS data in their setting
- Address one or more of the use cases outlined in the Challenge section above
- Include representation from the NMCP, Ministry of Health (MOH) representation, government agency or healthcare provider responsible for malaria control in the country / region
- Describe how MMS information arising from the project will be shared with the NMCP, MOH and other key stakeholders

A few examples of work that would be considered for funding:

- Implementing or scaling-up a laboratory assay for hrp2/3 deletion and / or antimalarial drug resistance marker surveillance in partnership with an NMCP
- Developing a web interface or reporting tool for communicating molecular data to stakeholders who do not have genomics / bioinformatics experience
- Creating a bioinformatics workflow for MMS data that goes from fastq file to a readable report summarizing the analysis results in a user-friendly way
- Developing and implementing a training program to familiarize NMCP staff with the use and interpretation of MMS data

We will not consider funding for:

- Proposals that do not include an investigator from a malaria-endemic country
- Proposals that do not include an explicit partnership with the NMCP, MOH or other authority responsible for malaria surveillance and control in the country / region
- Proposals that do not demonstrate how the results will immediately influence malaria decision-making by the relevant NMCP, MOH or other authority