Sero-epidemiology to support decision-making for malaria elimination

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Introduction

- Serology measures antibody responses which reflect previous exposure to pathogens
- Knowledge of malaria biomarker longevity allows **characterization of recent (6-12 months) and past (within 20 years) exposure** [1, 2]
- In comparison, **PCR/RDT diagnostics only detect concurrent infections** which are sparse at low-transmission
- In pre-elimination settings, surveys benefit from sensitive tools to detect residual transmission patterns [3]
- Population-level sero-epidemiology may provide added insight to support decision making in elimination

Aims & Objectives

Aimed to assess added benefit of including serology in population-level surveys to support decision making in pre-elimination settings

- Include serology as diagnostic end-point in a multi-country survey
- Describe the sero-epidemiological patterns and prevalences
- Compare serological findings to PCR/RDT diagnostics
- Examine serology as tool to identify high risk populations

Methods

Surveys in 5 pre-elimination settings
Lao PDR, Vietnam, Philippines, Cape Verde, Peru
19,411 individuals
RDT, PCR & dried blood spots

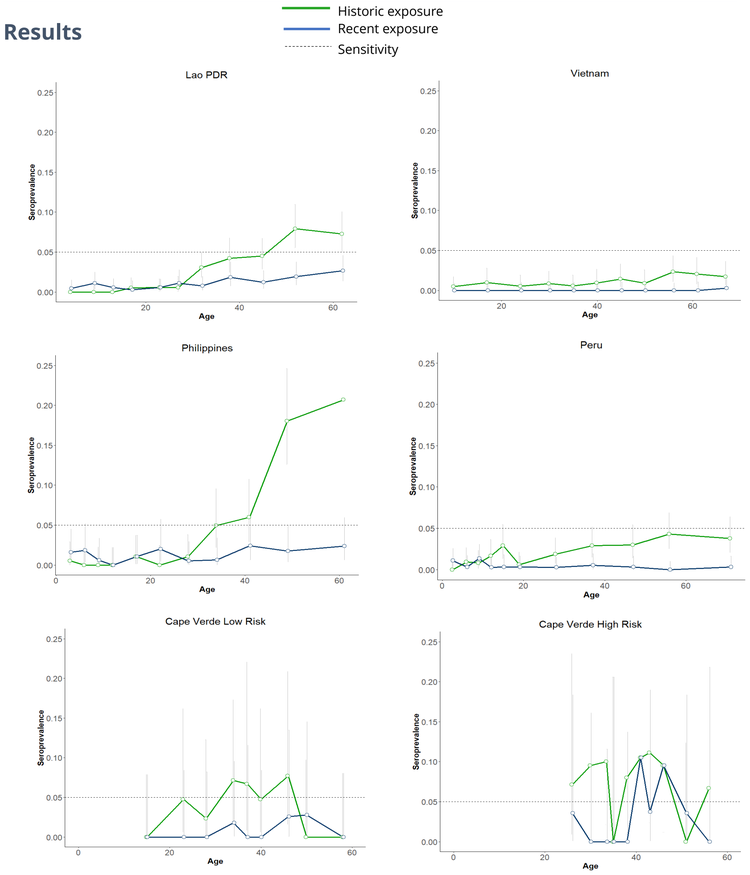
Serology: Luminex multiplex bead assays

Antigen	Exposure	Species
PfMSP119 PfAMA1	Historic	*Plasmodium falciparum*
Etramp5.Ag1	Recent	

Classification of sero-positivity
Unsupervised machine-learning approach **kmeans clustering** to define individuals as sero-positive
Sero-prevalence and PCR prevalence calculated

Case study: Cape Verde risk groups
Sampled high and low risk groups based on recent travel
Calculated relative risk for *P. falciparum* exposure between groups

Results



Figures 1-5 Age-stratified seroprevalence for recent exposure (6-12 months) and historic exposure (20 years) to *P. falciparum*.

Location	n	PCR		Serology			
		n	Prevalence (%)	n	Historic Exposure Prevalence (%)	n	Recent Exposure Prevalence (%)
Laos	4794	8	0.00 (0, 0)	117	0.02 (0.02, 0.03)	55	0.01 (0.01, 0.02)
Philippines	1919	0	0 (0, 0)	94	0.05 (0.04, 0.06)	27	0.01 (0.01, 0.02)
Peru	4000	0	0 (0, 0)	82	0.02 (0.02, 0.03)	19	0.004 (0.003, 0.006)
Vietnam	3982	0	0 (0, 0)	46	0.01 (0.01, 0.02)	1	0.000 (0, 0.001)
Cape Verde							
Low risk	256	0	0 (0, 0)	14	0.05 (0.03, 0.08)	4	0.01 (0.00, 0.03)
High risk	460	0	0 (0, 0)	19	0.04 (0.02, 0.06)	8	0.02 (0.01, 0.03)

Table 1 Number of individuals sampled per study site, PCR and sero-prevalence for recent and historic *P. falciparum* exposure

	Serology		PCR
	Historic	Recent	
Low risk	**2.2 (1.1, 4.2)**	0.4 (0.1, 1.2)	1 (1, 1)

Table 2: Results from Cape Verde case study: relative risk assessment comparing high risk traveller groups with "low risk" group

Results Summary

- At population-level, PCR diagnostics did not detect sufficient cases to inform knowledge of ongoing transmission
- Recent and historic exposure prevalences based on serology were higher than PCR prevalences
- Historic exposure was higher than recent in all settings
- Historic exposure increased with age in all settings
- Relative risk assessment found significantly higher risk of historic exposure by serology in high-risk group compared to low-risk group
- Relative risk assessment found no difference in risk by PCR in travelling group compared to low-risk group

Conclusions

- The results from the serological component of the surveys show that despite low levels of exposure**, serology gives added levels of insight into ongoing and historic transmission in pre-elimination settings**
- We have shown that serological results can be used to provide insight on transmission over a wider timeframe (6-12 months or up to 20 years) than PCR do
- Historic exposure was higher than recent exposure, and increased with age, which are consistent with knowledge of transmission in pre-elimination settings
- Case study findings demonstrate use of serology to identify higher risk groups or settings. In comparison, this was not possible using PCR data. Potential for targeted interventions or surveillance
- We highlight the **added information which can be extracted from active surveillance** samples with the **operationally feasible** addition of multiplex bead assay technology for serology.

1. Helb, D. A. et al. (2015) 'Novel serologic biomarkers provide accurate estimates of recent Plasmodium falciparum exposure for individuals and communities', Proceedings of the National Academy of Sciences of the United States of America, 112(32)
2. van den Hoogen, L. L. et al. (2020) 'Comparison of Commercial ELISA Kits to Confirm the Absence of Transmission in Malaria Elimination Settings', Frontiers in Public Health, 8, p. 480.
3. Surendra, H. et al. (2019) 'Analysis of serological data to investigate heterogeneity of malaria transmission: A community-based cross-sectional study in an area conducting elimination in Indonesia', Malaria Journal, 18(1)