Accelerating the elimination of *P. vivax* malaria through the implementation of *P. vivax* Serological Testing and Treatment (PvSeroTAT)

PhD Opportunities in
infectious disease epidemiology, statistical and mathematical modelling

About the Project

All countries in the Asia-Pacific and Latin American have committed themselves to eliminate malaria within the next 10-15 years. The major challenge in the elimination of malaria in these regions is the increasing proportion of malaria cases that are due to *Plasmodium vivax*, which is challenging to eradicate due to its unique biological features: the high burden of cryptic infections in spleen and bone marrow and rapid acquisition of clinical immunity result in a high prevalence of low-density, asymptomatic infections that are more difficult to detect with conventional diagnostics test. In addition, *P. vivax* has a dormant liver stage that can reactivate weeks to months after initial infection. These hypnozoites, which are undetectable with current diagnostics, are responsible for >80% of all blood-stage infections. Identifying and targeting these individuals with hypnozoites and/or cryptic spleen infection is essential for achieving *P. vivax* elimination. Given *P. vivax* infection rapidly induces a potent immune response that last for several months after clearance of the initial blood-stage infection, serological exposure markers (SEMs) can identify not only individuals with cryptic infection but also those with the highest probability of carrying hypnozoite and thus at highest risk of experiencing a future relapse.

Exploiting these immunological patterns, we have development of a serological assay and machine learning algorithm allows the identification of individuals at risk of relapse due to hypnozoites, enabling targeted application of treatment strategies such as *P. vivax* Serological Testing and Treatment (PvSeroTAT). In order to facilitate adoption of PvSeroTAT into national malaria elimination strategies, the Vivax Serology Partnership (VISPA) consortium is conducting a board program of research ranging from diagnostic test development, PvSeroTAT clinical trial, policy development to early implementation pilots and scale-up studies. Underpinning this program are studies aiming at gaining detailed understanding of anti-vivax antibody responses, the development improved sero-diagnostic algorithm as well as predicting the impact of different ways of implementing PvSeroTAT across different epidemiological setting and high-risk groups.

The aim of these PhD projects is to assist in the development and validate *P. vivax* sero-diagnostic tests across diverse transmission settings, evaluate pilot and scale-up studies to quantify epidemiological impact, and contribute to frameworks that enable national malaria programs and other parties to integrate PvSeroTaT into elimination strategies. The PhD student will work as part of the Vivax Serology Partnership (VISPA) consortium: Expanding Access to Vivax Serology Diagnostics),

which is across multiple institutes within Australia, Europe and throughout vivax endemic areas in the Asia-Pacific, Africa and Latin America.

PhD Opportunity 1: Developing targeted sero-diagnostic algorithms through an in-depth understanding of *Plasmodium vivax* sero-diagnostic signatures across different epidemiological setting and high-risk groups

Supervisors: Ivo Mueller, Dionne Argyropoulos, Lauren Smith

This PhD project will conduct in-depth analyses of anti-vivax antibody response in studies from all vivax endemic setting and use this knowledge to develop computational models to improve the adaptability of sero-diagnostic algorithms for *Plasmodium vivax* to diverse geographic and epidemiological settings. The student will design and implement models to understand how distributions of population-level characteristics such as transmission intensity, recent history of malaria control and individual-level characteristics such as age, gender etc affect immune response to create unique sero-diagnostic signatures. The models will inform the application of interventions such as *P. vivax* serological test and treat (PvSeroTaT) in alternative settings.

Essential: Masters (MSc) or BSc Honours degree in epidemiology, biostatistics, bioinformatics, data science, quantitative biology, or related field.

PhD Opportunity 2: Estimating the impact of *Plasmodium vivax* Serological Testing and Treatment (PvSeroTAT) in the context of programmatic implementation and scale-up studies

Supervisors: Ivo Mueller, Jen Flegg, Dionne Argyropoulos, Lauren Smith,

While cluster randomised clinical trials (CRTs) are the gold standard to determine the efficacy of novel public health interventions, these trials are generally very expensive and take many years from inception to final results. As a consequence, few of these trials are done. For PvSeroTAT a single large cluster randomised trial is being conducted. However, these are an increasing number of pilot implementation and scale-up studies being conducted in several countries. This PhD will develop and apply statistical and mathematical models to estimate the impact of PvSeroTAT and other malaria control interventions on malaria burden from both CRTs and non-CRT PvSeroTAT studies and extrapolate these results to other settings and PvSeroTAT implementation modes.

Essential: Masters (MSc) or BSc Honours degree in biostatistics, epidemiology, data science, applied mathematics or related field.

PhD Opportunity 3: Computational analysis of scenarios in *Plasmodium vivax* Serological Testing and Treatment (PvSeroTAT) implementation.

Supervisors: Nic Geard, Jen Flegg, Ivo Mueller

This PhD project will develop computational models to investigate optimal intervention measure to accelerate control and elimination of *Plasmodium vivax*. The student will design and implement models to compare interventions for *P. vivax*, including the impact of *P. vivax* serological test and treatment (PvSeroTaT), in diverse geographic and epidemiological settings. The models may explore a range of approaches to representing heterogeneity, for example in spatial population structure, vector ecology, and/or human mobility.

Essential: Honours/Masters degree in computer science, or related field.

PhD Opportunity 4: Mathematical modelling of *Plasmodium vivax* sero-diagnostics
Supervisors: Jen Flegg, Nic Geard, Ivo Mueller

This PhD project will develop mathematical models for transmission of *Plasmodium vivax*, and may draw upon agent-based models, multiscale systems, and both stochastic and deterministic model formulations. The student will design and analyse models that capture dynamics at the within host, individual, and/or population levels. The models will consider a range of transmission interventions, including the impact of *P. vivax* serological test and treatment (PvSeroTaT).

Essential: Honours/Masters degree in applied mathematics, or related field.

Candidate Requirements

We welcome applicants with strong backgrounds in either mathematics/statistics, computing science, epidemiology or biology who are keen to develop expertise in the complementary discipline, with projects focused on dry-lab, computational and quantitative approaches.

These positions are open to both domestic Australian and international students

Essential

- Honours/Masters degree with strong quantitative component.

Desirable

- Skills in R/Python or similar software
- Experience in quantitative data analysis, mathematics, statistics or computational biology

Training and Environment

- Opportunities to collaborate with international malaria research networks.
- Training in advanced statistical and computational methods.

- Supportive research environment, seminars, career development and grant opportunities within international malaria networks.
- Access to high-performance computing, excellent epidemiological datasets.

Funding and Support

- There are 2 fully funded VISPA scholarship available for students from vivax-endemic countries only.
- Additional scholarships are available through the University of Melbourne's Graduate Research Scholarships program.

Both types of scholarships are awarded on a competitive basis and cover a duration of 3 years.

How to apply

Please submit expressions of interest to vispaPhd@wehi.edu.au

EOIs should include:

- Cover letter explaining which project you are most interested in and why you think you are a good candidate for such a PhD
- Full CV
- Academic Transcripts from MSc or Honors and last two years of BSc studies.

Primary Supervisor Information:

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