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DEVELOPMENT OF A COMMUNITY-DELIVERED MALARIA ELIMINATION MODEL FOR MYANMAR

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The malaria program in Myanmar is currently transitioning from control to elimination phase in order to achieve its 2030 malaria elimination goal. As a consequence, malaria volunteers in Myanmar have been transforming into Integrated Community Malaria Volunteers (ICMVs) since 2017. This ICMV model was designed with no evidence base to include integrated services for malaria, lymphatic filariasis, dengue, tuberculosis (TB), HIV/AIDS and leprosy. To inform the evidence base, a series of studies aiming to develop an optimal and scientifically proven integrated community-delivered malaria elimination model for Myanmar was conducted. Firstly, a systematic review and meta-analysis of 28 studies investigating the impact of community-delivered models was undertaken to estimate the effectiveness of these community-delivered models. Secondly, inductive thematic analyses of qualitative data collected from focus group discussions (n=8), participatory workshops (n=2) and semi-structured interviews (n=19) were used to consolidate the perspectives of community leaders and members, and malaria stakeholders from Myanmar. In qualitative consultations, community leaders and members identified common health concerns in addition to malaria and included respiratory illness, childhood diarrhoea, skin infections and TB (in this order) and recommended incorporating preventive, and whenever possible curative, services for those diseases into the malaria volunteer model. Although stakeholders perceived that disease combination in ICMV model was optimal, community members perceived that more illnesses should be included. Stakeholders also suggested ways that volunteer recruitment, training, supervision and reporting in the current ICMV model could be optimized. Based on international evidence and recommendations from community consultations, a community-delivered malaria elimination model should consist of malaria, TB, dengue, respiratory illness and childhood diarrhoea. Providing a range of services together with malaria will ensure a positive advancement towards the malaria elimination goal.

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TREATMENT ALGORITHMS WITH RADICAL CURE OF VIVAX MALARIA BASED ON SEX: A COST-EFFECTIVENESS ANALYSIS TO SUPPORT ROLL OUT STRATEGIES

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The recent license of single-dose tafenoquine for radical cure of *Plasmodium vivax* has changed the landscape for malaria elimination. Tafenoquine will overcome the issue of poor adherence to a prolonged course of primaquine; however, its clinical use requires prior screening for glucose-6-phosphate-dehydrogenase (G6PD) deficiency to exclude patients at risk of drug-induced haemolysis. G6PD deficiency is a sex-linked disorder: whilst diagnosis at a 30% cut-off excludes hemizygous deficient males at risk of haemolysis, it will not accurately exclude heterozygous females with intermediate deficiency (30-70% activity). The diagnosis of intermediate deficiency requires a quantitative test, associated with increased logistical and infrastructure complexity as well as cost. To support a phased implementation and to bridge potential infrastructure gaps, we explored a treatment algorithm for tafenoquine stratified by sex. In this algorithm, after testing with the less costly qualitative test (which can diagnose G6PD deficiency at the 30% threshold), males who test normal will be prescribed tafenoquine. Females would be offered the choice of either primaquine or referral to a higher facility where quantitative testing (which can diagnose reliably at the 70% threshold) is available, enabling the use of tafenoquine after appropriate assessment of G6PD activity. The cost-effectiveness of this strategy was explored using a decision model for Afghanistan, Ethiopia, Indonesia and Vietnam. The model was parameterized for these countries using data on local costs, G6PD deficiency and hemoslysis from a large randomized controlled trial. In settings where quantitative testing is not readily available, this strategy would offer a cost-effective and easy to implement approach for enabling the safe and effective radical cure of vivax malaria, an essential step to achieving elimination.

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REFINING GLOBAL MAPS OF G6PD DEFICIENCY: HARNESSING NEW DATA AND ANALYTICAL METHODS

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Up to 2.5 billion people are at risk of *Plasmodium vivax* malaria. Clearance of dormant parasites in the liver ('radical cure') requires treatment with an 8-aminoquinoline, however this is associated with haemolysis in individuals with glucose-6-phosphate dehydrogenase deficiency (G6PDd). G6PDd is common, especially in malaria endemic regions. Understanding the spatial distribution of G6PDd, its prevalence, and local variants is essential to informing safe treatment policies. In order to refine global maps of G6PDd prevalence, we undertook a systematic literature review to update an existing global database of G6PDd prevalence surveys, identifying new studies published between 2010 and 2018. Surveys from the general population and among malaria patients were analysed separately. Surveys were georeferenced using published coordinates, information from authors or online mapping software (e.g. Google Maps). Global genomic datasets were explored to create a spatial covariate surface of broad-scale population relatedness. Final maps of G6PDd prevalence were produced via a Bayesian geostatistical model implemented using Integrated Nested Laplace Approximation (INLA). Of 7,447 papers screened, 813 were included. Population representative point prevalence data was extracted and added to the existing database of 1,734 spatially unique sites. Spatially continuous maps of G6PDd prevalence were produced at a resolution of approx. 5x5km, along with national estimates of the prevalence of G6PDd and number of affected individuals. Preliminary analysis demonstrated improved model performance and reduced uncertainty compared with previous research, particularly in areas where data coverage was previously poor. Improved input data, informative covariate data and computationally efficient methods have enhanced our ability to map G6PDd. The up-to-date maps of G6PDd synthesize our current knowledge on the local burden of G6PDd, while enabling informed inference where data are not yet available. These data will be critical for risk-benefit analysis of *P. vivax* radical cure and highlight priority areas for G6PD screening programs.

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IN SILICO PREDICTION OF THE STRUCTURE OF *PLASMODIUM FALCIPARUM* GAMETOCYTE DEVELOPMENT PROTEIN 1 AND ITS EVALUATION AS A DRUG TARGET

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Malaria transmission is a critical point in the disease cycle but the current drugs and vaccines target pre-erythrocytic and erythrocytic stages of malaria parasites. Therefore, transmission blocking strategies should be designed to target the sexual stage of the parasite. The exploration of transmission mechanism of the malaria parasite, *Plasmodium falciparum,* reveals that gametocytogenesis is critical in human host to mosquito vector transmission. Molecular studies demonstrate that gametocyte