Assessment of ultra-sensitive malaria diagnosis versus standard molecular diagnostics for malaria elimination : an in-depth molecular community cross-sectional study

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Submicroscopic malaria infections contribute to transmission in exposed populations but their extent is underestimated even by standard molecular diagnostics. Sophisticated sampling and ultra-sensitive molecular methods can maximise test sensitivity but are not feasible in routine surveillance. Here we investigate the gains achievable by using increasingly sensitive methods with the aim to understand what diagnostic sensitivity is necessary to guide malaria interventions.; Venous blood samples were collected from participants in a cross-sectional survey in two coastal medium-endemic villages in Madang province, Papua New Guinea. Using ultra-sensitive quantitative PCR (us-qPCR) on concentrated high-volume blood samples (2 mL) as reference, we quantified the proportion of Plasmodium falciparum and Plasmodium vivax infections and gametocyte carriers detectable in fingerprick blood volumes (200 μL) by standard 18S rRNA qPCR, us-qPCR, rapid diagnostic test (RDT), and ultra-sensitive P falciparum RDT. We further compared the epidemiological patterns observed with each diagnostic approach in the study population.; Venous blood samples were collected from 300 participants between Dec 5, 2016, and Feb 24, 2017 (ie, during peak rainy season). Standard qPCR identified 87 (54%) of 161 P falciparum infections and 73 (52%) of 141 P vivax infections detected by the reference method. us-qPCR identified an additional 11 (7%) P falciparum infections and 14 (10%) P vivax infections. 80 (86%) of 93 P falciparum gametocyte carriers and 75 (91%) of 82 P vivax gametocyte carriers were found among infections detectable by us-qPCR. Ultra-sensitive RDT missed half of P falciparum infections detected by standard qPCR, including high gametocytaemic infections. Epidemiological patterns corresponded well between standard qPCR and the reference method. As the prevalence of P vivax decreased with increasing age, the proportion of P vivax infections undetectable by standard qPCR increased.; Almost all potentially transmitting parasite carriers were identified with us-qPCR on fingerprick blood volumes. Analysing larger blood volumes revealed a large pool of ultra-low-density P falciparum and P vivax infections, which are unlikely to be transmitted. Therefore, current RDTs cannot replace molecular diagnostics for identifying potential P falciparum transmitters.; Swiss National Science Foundation.
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