

Estimating the hidden magnitude of the malaria community burden



The second push for global malaria eradication, launched more than a decade ago,¹ has motivated a renewed interest in the understanding of malaria transmission, and in the strategies required to interrupt it. In this respect, in order to eliminate malaria from a given geographical area, rapid detection and treatment of the clinical cases is rarely sufficient. In settings where transmission intensity is sufficiently high, populations exposed to continuous infective mosquito bites progressively develop a tolerance to malaria infections during the first few years of their life. This tolerance protects them against malaria disease, but not necessarily against the infection itself. This situation results in a varying frequency of asymptomatic carriage of malaria parasites. Indeed, the higher the transmission intensity, the earlier the acquisition of immunity and the larger the population capable of carrying malaria parasites in their blood without necessarily expressing clinical symptoms. To paraphrase the “iceberg” metaphor, some authors have described that the true burden of malaria infections lies “hidden beneath the surface”, and that clinical cases would only represent the so-called “ears of the hippopotamus”² of the total malaria burden. These symptomless infections, not motivating an active search for treatment, are invisible to the system, although they remain potentially transmissible to mosquitoes, thus acting as silent reservoirs of transmission.³ For this reason, estimating the true burden of malaria infections from the relatively small proportion of those that are clinically visible and detectable through the health system can provide an actionable idea of the magnitude of undercounting, and therefore of the efforts required to interrupt malaria transmission at the community level.

In *The Lancet Infectious Diseases*, Gillian Stresman and colleagues,⁴ representing a variety of malaria-endemic countries, propose a new approach to quantify, using a Bayesian model, the proportion of the total malaria infections in a given community detected through routine passive case surveillance. Such an indicator, termed P(Detect) and ranging from 0 to 100%, would use health system clinical data to derive an idea of the overall community transmission, by expressing the probability that an infection becomes symptomatic

and potentially detected by the health system. Thus, theoretically, a very high value of P(Detect)—ie, a value approaching 100%—would suggest that the vast majority of infections are clinically manifest and therefore detectable by the health system, whereas a low value would indicate that most of the parasite reservoir remains undetected by the health system. As the authors suggest, and for elimination purposes, such an indicator could have an enormous potential to help to identify “the critical point at which programmes could scale back control activities and rely on the health system to identify all infections”.⁴

The pooled analysis of paired health facility (passive case detection) and community survey data (household surveys) allows the study authors to explore the association between infection detection and transmission in malaria endemic areas. The analysis of such an impressive dataset (including 471 clusters in 13 countries for *Plasmodium falciparum* and 231 clusters in seven countries for *Plasmodium vivax*, for the period 2008–2017) shows low median estimated P(Detect) values (12.5% for *P falciparum* and 10.1% for *P vivax*). However, their more important finding is a negative association between the level of infection detection and the underlying intensity of transmission for both species (*P falciparum* adjusted odds ratio 0.63 [95% CI 0.57–0.69] and *P vivax* adjusted odds ratio 0.52 [0.47–0.57]).

As a plausible explanation for these findings, the authors suggest that as disease transmission and repeated exposure to malaria infection decrease, population immunity to this deadly infection will start to wane, rendering the population vulnerable again and gradually non-immune.⁵ As a result, the proportion of the infections that will become clinical (and as such, for which the affected individuals might seek health care and thus are detectable at the health system level) will also increase. Subgroup analyses done by the authors exploring the variability of P(Detect) according to age or seasonality further substantiate this hypothesis and help to validate their results, although such an association in the case of *P vivax* was less conclusive. In this respect, an important limitation of the work



5Stock-47894284-1

Lancet Infect Dis 2020

Published Online

April 8, 2020

[https://doi.org/10.1016/](https://doi.org/10.1016/S1473-3099(20)30142-0)

[S1473-3099\(20\)30142-0](https://doi.org/10.1016/S1473-3099(20)30142-0)

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[S1473-3099\(20\)30059-1](https://doi.org/10.1016/S1473-3099(20)30059-1)

presented relates to the absence of data in their analyses from highly malaria-endemic areas in the Pacific (eg, Papua-Indonesia and Papua New Guinea), where *P vivax* is a major cause of infection and disease, and where immunity to this species builds up even faster than it does for *P falciparum*.^{6,7} Generating estimates of P(Detect) in those regions could have further illustrated the association between transmission and clinical disease for a malaria species that clearly has its own particularities, and is extremely relevant if global eradication of malaria is to be achieved.

Despite the aforementioned limitations, the authors should be praised for their proposed approach to quantifying the degree of hidden malaria transmission, which is an important indicator of the likelihood of success of all malaria control and elimination strategies worldwide.

We declare no competing interests.

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