

# Contribution of Asymptomatic *Plasmodium* Infections to the Transmission of Malaria in Kayin State, Myanmar

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**Background.** The objective of mass antimalarial drug administration (MDA) is to eliminate malaria rapidly by eliminating the asymptomatic malaria parasite reservoirs and interrupting transmission. In the Greater Mekong Subregion, where artemisinin-resistant *Plasmodium falciparum* is now widespread, MDA has been proposed as an elimination accelerator, but the contribution of asymptomatic infections to malaria transmission has been questioned. The impact of MDA on entomological indices has not been characterized previously.

**Methods.** MDA was conducted in 4 villages in Kayin State (Myanmar). Malaria mosquito vectors were captured 3 months before, during, and 3 months after MDA, and their *Plasmodium* infections were detected by polymerase chain reaction (PCR) analysis. The relationship between the entomological inoculation rate, the malaria prevalence in humans determined by ultrasensitive PCR, and MDA was characterized by generalized estimating equation regression.

**Results.** Asymptomatic *P. falciparum* and *Plasmodium vivax* infections were cleared by MDA. The *P. vivax* entomological inoculation rate was reduced by 12.5-fold (95% confidence interval [CI], 1.6–100-fold), but the reservoir of asymptomatic *P. vivax* infections was reconstituted within 3 months, presumably because of relapses. This was coincident with a 5.3-fold (95% CI, 4.8–6.0-fold) increase in the vector infection rate.

**Conclusion.** Asymptomatic infections are a major source of malaria transmission in Southeast Asia.

**Keywords.** Mass drug administration; malaria; entomological inoculation rate; primaquine; *Plasmodium falciparum*; *Plasmodium vivax*; elimination; artemisinin resistance; Southeast Asia.

Artemisinin resistance in *Plasmodium falciparum* has emerged and spread in the Greater Mekong Subregion [1], leading to the failure of several artemisinin-based combination therapies (ACTs) [2]. Multidrug-resistant parasites spreading from western Cambodia are responsible for a recent resurgence of the disease across the eastern part of the Greater Mekong Subregion [3]. Meanwhile in Myanmar (in the western Greater Mekong Subregion), the incidence of clinical malaria cases has declined [4]. In this area, dihydroartemisinin-piperazine and artemether-lumefantrine remain effective against *P. falciparum*. It is

therefore urgent to eliminate falciparum malaria in Myanmar, the main gateway to India and Bangladesh, before parasites also develop resistance to these 2 ACTs.

Community-wide access to early diagnosis and treatment with an effective ACT is the most effective strategy to reduce the transmission of falciparum malaria [5]. In this region, insecticide-impregnated bed nets have only a marginal effect on the relevant anopheline mosquito vectors [6]. Early diagnosis and treatment limit the transmission that occurs from symptomatic individuals. However, prevalence surveys conducted with ultrasensitive diagnostic tools have revealed that infection with *Plasmodium* parasites is frequently asymptomatic in the Greater Mekong Subregion [7]. Thus, in this area of low endemicity and unstable transmission, healthy residents commonly harbor malaria parasites at low densities, below the detection threshold of microscopy or rapid diagnostic tests [8]. Over time, waves of higher density (although still asymptomatic) parasitemia occur with the sequential emergence of new antigenic variants, generating potentially transmissible densities of gametocytes [9]. Numerous studies have

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