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Received 14 January 2016; accepted 25 January 2016; published online 9 February 2016.
Correspondence: T. Boussama, Department of Medical Microbiology, Radboud University Medical Center, Geert Grooteplein Zuid 26-28, 6500 HB Nijmegen, The Netherlands (teun.boussama@radboudumc.nl).

The Journal of Infectious Diseases® 2016;213:1516–7 © The Author 2016. Published by Oxford University Press for the Infectious Diseases Society of America. All rights reserved. For permissions, e-mail journals.permissions@oup.com. DOI: 10.1093/infdis/jiw044

Reply to Goncalves et al

To the Editor—We agree with Goncalves et al that our study was restricted to treatment-seeking persons with symptomatic falciparum malaria. As such, the study did not assess the relative infectiousness of what may well be a larger, asymptomatic, and often submicroscopic malaria transmission reservoir. The absence of studies on the infectiousness of asymptomatic persons with submicroscopic malaria in low-transmission settings yields little evidence for or against targeting these populations as a strategy to accelerate malaria elimination; indeed, further evaluation is warranted.

It is important not to conflate asymptomatic malaria with submicroscopic malaria. Although the cited Thai study by Pethleart et al measured infectivity in the community, only those with slide-positive malaria were selected for mosquito feeding [1]. The 2 individuals identified in the community who were afebrile but infectious were readily detected by microscopy. We also did not sample those with submicroscopic malaria in our study, but we detected a substantial amount of submicroscopic gametocytaemia that made little contribution to human-mosquito transmission.

Those with submicroscopic malaria by definition harbor submicroscopic gametocytes at low densities, lower than those seen in asymptomatic but patent infections. In a large survey in Papua New Guinea that used both microscopic and molecular detection of malaria, symptomatic persons were more likely to be gametocytemic, and patent infections over-all showed a 6-fold increase in gametocyte density, as measured by quantitative polymerase chain reaction (PCR), compared with submicroscopic infections [2]. The large epidemiological study in Cambodia, Vietnam, and the Thailand-Myanmar border cited used high-volume ultrasensitive PCR to detect submicroscopic malaria: the 20% of individuals identified as harboring parasites averaged a parasite density of only 5 parasites/µL [3, 4]. Perhaps, then, it is not that surprising that among the 5000 residents sampled, not a single person had microscopic gametocytemia, the group that we identified as being >20-fold more infectious and infected >200 times more mosquitoes than their counterparts with either none or only submicroscopic gametocytes.

This latter cited study was unable to screen 28% of residents, many because they were away. As discussed by Goncalves et al, it is an open question whether the relative numbers of those with submicroscopic gametocytes and the potentially longer duration of their infection led to a substantial contribution to the infectious reservoir. Ultimately, it seems that the coverage of malaria-elimination interventions and access by hard-to-reach populations may be more important than the degree of sensitivity offered by advanced molecular detection methods.

Finally, we wholeheartedly agree that membrane feeding at a single time point cannot be the only measure of the infectious reservoir. In addition to sampling asymptomatic and submicroscopic infections, data on the duration of infectiousness and mosquito exposure in different populations are needed to better guide our understanding of the infectious reservoir [5].

Notes
Financial support. This work was supported by the Armed Forces Health Surveillance Center/Global Emerging Infections Surveillance and Response and the National Institute of Allergy and Infectious Diseases (grant K08 AI110651 to J. T. L.).

Potential conflicts of interest. All authors: No reported conflicts. All authors have submitted the ICME Form for Disclosure of Potential Conflicts of Interest. Conflicts that the editors consider relevant to the content of the manuscript have been disclosed.

Jessica T. Lin,1 Steven R. Meshnick,2 David L. Saunders,3 and Chanthap Loun4
1Division of Infectious Diseases, School of Medicine, and 2Department of Epidemiology, Gillings School of Global Public Health, University of North Carolina, Chapel Hill; 3Department of Immunology and Medicine, Armed Forces Research Institute of Medical Sciences, Bangkok, Thailand; and 4Armed Forces Research Institute of Medical Sciences, Phnom Penh, Cambodia

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Received and accepted 25 January 2016; published online 9 February 2016.
Correspondence: J. T. Lin, UNC Division of Infectious Disease, 130 Mason Farm Rd, Ste 2115, CB 7030, Chapel Hill, NC 27599-7030 (jessica_lin@med.unc.edu).

The Journal of Infectious Diseases® 2016;213:1517 © The Author 2016. Published by Oxford University Press for the Infectious Diseases Society of America. All rights reserved. For permissions, e-mail journals.permissions@oup.com. DOI: 10.1093/infdis/jiw045