Published in final edited form as:

Lancet Infect Dis. 2015 June ; 15(6): 630–631. doi:10.1016/S1473-3099(15)00018-3.

Authors' reply

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We appreciate the comments on our recent Article¹ that reports on the global extent of antimalarial drug resistance in *Plasmodium vivax*.

Wei Wang and colleagues raise concerns that our review ignores relevant literature documenting *P. vivax* chloroquine resistance in China. We constrained our analysis to articles published in English or from which data could be readily extracted, and hence did not identify the three reports in Chinese mentioned by Wang and colleagues. Two of these are case reports of possible chloroquine resistance, without confirmation of adequate blood concentrations. Wei and colleagues² report 21 patients who were not cured with a combination of chloroquine plus primaquine, several of whom had high-grade early treatment failure. The absolute risk of these events cannot be gauged because the total number of patients treated is not stated. We would be delighted to review the studies in more detail if the original articles can be provided. Our review included two clinical trials done in China, neither of which reported any patients not responding to antimalarial treatment, although in both studies the early administration of primaquine might have masked the presence of low-grade chloroquine resistance.

There have been two relevant articles since our review was published. A study by Liu and colleagues³ from the China–Myanmar border of Yunnan province, reported nine (1.5%) of 603 patients with late treatment failure. On the Myanmar side of the border, Yuan and colleagues⁴ report a study done in 2012 and 2013, in which ten (5.4%) of 401 patients did not respond to treatment. Although overall chloroquine efficacy was high in these studies, several patients had early high-grade treatment failure, and these occurred after chloroquine was given in combination with primaquine; the underlying efficacy of chloroquine monotherapy is likely to be substantially worse. There were no treatment failures in an unpublished study done in 2007 in the same region. These figures show the potential risk of emerging chloroquine resistance along the China–Myanmar border and emphasises the

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importance in maintaining vigilance for the spread of antimalarial drug resistance in this region.

Nathan Brendish questions whether our primary outcome of chloroquine efficacy at day 28 is compatible with table 1, which lists studies of shorter duration. Our review also aimed to document the diversity of clinical trial design and analysis that has been applied to *P vivax*, and hence all relevant studies were tabulated. However, in the four studies with less than 28 days follow-up and a further three with no available data at day 28, the day 28 efficacy outcome was uncategorised. Data were extracted by one of the authors, but the entire dataset is provided in a supplementary file available online at the Worldwide Antimalarial Resistance Network,⁵ in a form amenable to independent analysis and cross checking. The management of chloroquine-resistant *P vivax* has been discussed at length in a previous review⁶ and is presented comprehensively in the latest WHO antimalarial guidelines.⁷

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

RNP, KJB, NV, and NJW are members of the WHO steering committee for the Development of a Global Strategic Plan for *Plasmodium vivax* control and elimination. NJW is co-chairman of the WHO antimalarial treatment guidelines committee. RNP is a Wellcome Trust Senior Research Fellow in Clinical Science, NJW is a Wellcome Trust Principal Fellow, JKB is supported by a Wellcome Trust Project Grant B9RJIXO, and LvS is a member of the Asia Pacific Malaria Elimination Network.

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