Reviewer's report

Title: Time-to-infection by Plasmodium falciparum is largely determined by random factors.

Version: 3 Date: 22 September 2014

Reviewer: Richard Maude

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This was an interesting study which combined clinical data and modelling. However the methodology used some assumptions for which I could not find adequate justification. Additionally, the clinical data appeared to be somewhat under-powered and it is not clear that the conclusion was fully warranted in view of these limitations.

Major Compulsory Revisions

1. There were some inadequacies in the description of the method for determining PMR. Why assume a parasitaemia at the microscopy detection threshold at first PCR detection? Why assume PCR detection threshold 1 week prior? Why can only a maximum PMR be estimated for those who are PCR positive but don’t become microscopy positive? These should be clarified.

2. It was assumed that PMR is normally distributed. Why should this be the case? Did the authors have data to show this?

3. Time-to-detection and parasite growth rate appeared to be discussed as if they are independent measures but surely they are interdependent? Further explanation of this is needed.

4. The power of the clinical part of this study was limited by the number of patients and 1 week gaps between blood samples to determine time to infection. With a larger number of patients and smaller intervals between samples, the conclusions may have been different. The authors should acknowledge these limitations in the discussion. How was power calculated when planning this study? Out of the 197 individuals, how many were included? In the figures, there appear to be data from somewhat fewer than this? As children and adults were analysed separately, it should be stated how many individuals were in each group to give an indication of power to detect differences.

Minor Essential Revisions

1. Figure 4. What were the units for parasite multiplication rate?

2. There are some grammatical errors that should be corrected e.g. “Using the mode the sensitive…”

3. The thresholds for microscopy and PCR detection and their margin of error
should be stated early in the manuscript.

4. What was meant by “microscopy infection curves”?

Discretionary Revisions

None

**Quality of written English:** Acceptable

**Statistical review:** No, the manuscript does not need to be seen by a statistician.

**Declaration of competing interests:**

I declare that I have no competing interests