WHO Evidence Review Group on malaria submicroscopic infections, May 2017

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Background

In December 2013, WHO convened an Evidence Review Group (ERG) on the role of molecular-based diagnostic techniques for malaria in low transmission areas. The review focused on the different assays available at the time that had a diagnostic performance equivalent or superior to that of microscopy and rapid diagnostic tests (RDTs). On the basis of its review, the WHO recommended the continued use of malaria microscopy and antigen-detecting RDTs for the diagnosis of clinical malaria and routine malaria surveillance (of clinical cases). For epidemiological research and surveys aimed at mapping submicroscopic infections at low transmission intensity and identifying foci in elimination settings, WHO recommends the use of nucleic acid amplification (NAA)-based methods. Furthermore, WHO recommends that tests have a limit of detection of at least 2 parasites/µl. The 2013 ERG did not, however, conduct a detailed assessment of the clinical consequences of submicroscopic infections and their epidemiological contribution to transmission, nor did it provide recommendations on different detection/screening/surveillance approaches and how to utilize the information emerging from their use.

In recent years, the application of NAA-based diagnostic tools in epidemiological surveys and research has continued to expand; more recently, funding agencies, manufacturers and researchers have been working towards developing ultra-sensitive RDTs with limits of detection similar to those of NAA-based methods. Building on the findings and evidence gaps identified in 2013, WHO’s aim is to review new evidence on the role of submicroscopic infections in malaria transmission, as well as the case management and reporting of these infections once they have been detected, in order to provide clear guidance to national malaria control programmes. Where knowledge gaps still exist the group will identify research priorities and propose study designs to evaluate the public health importance of submicroscopic infections and the impact of detecting them using highly sensitive diagnostic tests.

Objectives

1. To review data on the natural history of submicroscopic *P. falciparum* and *P. vivax* infections in different epidemiological settings, to evaluate implications for detectability, duration of infection, and infectivity, and to assess the relationship with symptoms of clinical malaria.
2. To describe at population level the contribution of submicroscopic *P. falciparum* and *P. vivax* infections to transmission with respect to different levels of vectorial capacity and immunity in the population.

3. To define procedures for the case management and reporting of submicroscopic *P. falciparum* and *P. vivax* infections identified through multiple means, e.g., reactive case detection, surveys, research, etc.

4. To review and update the WHO recommendations on the diagnosis of *P. falciparum* and *P. vivax* malaria in low transmission settings, which were endorsed by the Malaria Policy Advisory Committee in March 2014, based on the report of the 2013 ERG meeting.

5. To establish a set of research priorities and study design characteristics to address knowledge gaps on the relative importance of submicroscopic infections and the public health impact of detecting them using highly sensitive diagnostic tests.

**Process**

The GMP/PDT unit will collaborate with Dr Teun Bousema, Radboud University Medical Center of The Netherlands, and Professor Chris Drakeley, London School of Tropical Medicine and Hygiene, in inviting relevant research groups to present reviews and original scientific papers addressing the specific objectives listed above. It is not anticipated that research consortia will be established at this time or that funding agencies will be required to sponsor the participation of the presenters and independent reviewers. The same Rapporteur who served for the previous ERG in December 2013 will be contracted to write the meeting report, if available.

The ERG meeting will involve approximately 25 participants and will require 3 days.

**A selection of proposed studies to review**

**Objective 1**

To review data on the natural history of submicroscopic *P. falciparum* and *P. vivax* infections in different epidemiological settings, to evaluate implications for detectability, duration of infection, and infectivity, and to assess the relationship with symptoms of clinical malaria:


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Objective 2

To describe at population level the contribution of submicroscopic *P. falciparum* and *P. vivax* infections to transmission with respect to different levels of vectorial capacity and immunity in the population:

**Objective 3**

To define procedures for the case management and reporting of submicroscopic *P. falciparum* and *P. vivax* infections identified through multiple means, e.g., reactive case detection, surveys, research, etc.
