

New evidence supports higher dose antimalarial to combat relapsing malaria

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Analysis of data from more than 6,800 patients located across 16 countries has supported the need to increase the dose of the antimalarial drug, primaquine, in malaria endemic countries.

This is detailed in 2 studies recently published in *The Lancet Infectious Diseases* which reviewed the efficacy and safety of primaquine doses used to prevent recurrence of *Plasmodium vivax* (*P. vivax*) malaria.

Led by Menzies School of Health Research (Menzies) Senior Research Fellow, Dr Rob Commons and The University of Melbourne Biostatistician, Dr Megha Rajasekhar, this research is part of an international collaboration of malaria experts from the [WorldWide Antimalarial Resistance Network](#) (WWARN).

The study measuring efficacy found that increasing the dose of primaquine from 3.5mg/kg to 7mg/kg halved malaria relapses, with limited impact on gastrointestinal symptoms. The second study examined the safety of this dosing, with similar risks found between different primaquine dose regimens.

Primaquine is a medication used for more than 60 years to target malaria parasites in the liver and prevents infection from continuing. The results of the combined studies significantly increase understanding of the best primaquine dose to prevent malaria relapses.

P. vivax malaria affects more than 7 million people each year, mainly throughout the Americas, Africa and the Asia-Pacific. It puts 40 per cent of the world's population at risk of the infection. Once infected, *P. vivax* can hide in the liver for long periods of time before reappearing and causing a malaria relapse.

The findings around the safety of the higher primaquine regimen have the potential to pave the way for the widespread implementation of effective malaria treatment. Increasing the dose of primaquine could have a significant impact on reducing *P. vivax* malaria relapses, as well as deaths and malaria transmission.

This research received funding from the Bill and Melinda Gates Foundation and Medicines for Malaria Venture.

Read the following studies in full:

- [Effect of primaquine dose on the risk of recurrence in patients with uncomplicated *Plasmodium vivax*: a systematic review and individual patient data meta-analysis](#)
- [Primaquine dose and the risk of haemolysis in patients with uncomplicated *Plasmodium vivax* malaria: a systematic review and individual patient data meta-analysis](#)

Quotes attributable to Menzies School of Health Research, Senior Research Fellow and lead co-author, [Dr Rob Commons](#):

“These important papers highlight that we have been using primaquine at a suboptimal dose for several decades.

“Our findings show that using a higher dose of primaquine can reduce malaria relapses by over 50 per cent.

“Most countries currently use a lower dose. Our results show the impact that increasing the dose could have on preventing people from getting recurrent malaria.

“This answers a question that the World Health Organization has highlighted as being a key research priority to resolve.”

Quotes attributable to The University of Melbourne, Biostatistician and lead co-author, [Dr Megha Rajasekhar](#):

“The second part of the study confirms that the increased dose is safe in patients at greatest risk of malaria relapses.

“We know that in patients with a genetic deficiency of the enzyme glucose-6-phosphate dehydrogenase – known as G6PD deficiency – the drug primaquine can cause haemolysis, or red blood cell destruction.

“Clinicians were worried that higher doses of the drug will cause side effects in people without this genetic deficiency, but our studies showed higher doses were safe for this group.

“New tests are now available to screen patients for G6PD deficiency, and this will allow higher doses to be prescribed safely, preventing malaria and speeding its elimination.”

Quotes attributable to the WorldWide Antimalarial Resistance Network (WWARN) Director, [Professor Philippe Guérin](#):

“The results of this study provide critical evidence supporting optimal dose of primaquine for radical cure of vivax malaria.

“This research is a great example of the malaria research community working together and demonstrates how data reuse can be at the forefront of generating new scientific knowledge.”

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Media contact:

Phone: (08) 8946 8658 | Email: media@menzies.edu.au

Menzies School of Health Research

Menzies is one of Australia’s leading medical research institutes dedicated to improving the health and wellbeing of Aboriginal and Torres Strait Islanders, and a leader in global and tropical research into life-threatening illnesses. Menzies continues to translate research into effective partnerships and programs in communities across Australia and the Asia-Pacific region.

WorldWide Antimalarial Resistance Network (WWARN)

Since 2009, the WorldWide Antimalarial Research Network ([WWARN](#)) has generated innovative tools and reliable evidence to inform the malaria community on the factors affecting the efficacy of antimalarial medicines. In the field of poverty-related infectious

diseases, data is scarce and scattered across institutions around the world. WWARN collates and standardises anonymised individual patient data (IPD) from many trials and studies conducted across endemic regions so that they can then be harmonised and analysed as a single dataset, increasing the statistical power needed to answer key questions in malaria research.

Part of the Infectious Diseases Data Observatory ([IDDO](#)), WWARN's repository holds over 200k IPD and shares the resulting evidence widely to inform both policymakers and future researchers globally to continually advance knowledge and build capacity for evidence-based practice. Find out more at info@wwarn.org