

Commentary

Bold measures to accelerate malaria elimination

Ric N. Price^{1,2}

¹ Global Health Division, Menzies School of Health Research, Charles Darwin University, Darwin, Australia

² Centre for Tropical Medicine and Global Health, Nuffield Department of Clinical Medicine, University of Oxford, Oxford, UK

Competing Interests: The author declares no competing conflict of interest.

Correspondence to: Professor Ric Price; Menzies School of Health Research, PO Box 41096, Casuarina, Darwin, NT 0811 Australia: email: ric.price@menzies.edu.au,
Tel: (61) 8 8922 8197, Fax: (61) 8 8922 8429.

In the Greater Mekong Subregion (GMS) intense drug pressure and indiscriminate use of poor quality antimalarial drugs, has led to the emergence of antimalarial resistance to all widely used drugs, including the artemisinin derivatives ¹. The malaria community remains divided as to the magnitude of this threat. Malaria cases in the GMS continue to fall, giving some authorities confidence that current activities will achieve elimination targets within the next few years. Counter arguments highlight the potential for parasites to evolve under prolonged, intense drug pressure and that this will result in widespread resistance to all available antimalarial drugs and the prospect of resurgent, untreatable malaria. Paradoxically the solution maybe promoting wider use of antimalarial drugs, to expedite parasite elimination before resistance evolves further.

Prompt diagnosis and treatment of patients presenting with clinical malaria can prevent progression to severe disease and reduce transmission. However ultrasensitive molecular diagnostics highlight a high burden of low density infections in asymptomatic individuals, below the threshold of detection of conventional diagnostic tests; this hidden reservoir undermines the effectiveness of mass screen and treat strategies ². An alternative approach is mass drug administration (MDA), in which antimalarial treatment is offered to high risk populations irrespective of confirmed parasitaemia ³.

In this edition of the Lancet Infectious Diseases, McLean and colleagues present a cluster-randomised control trial conducted in remote, rural Myanmar ⁴. Routine malaria case management was provided by community health workers (CHWs) who also distributed long-lasting insecticidal bed-nets (LLINs). In the intervention clusters, mass drug administration was provided on three consecutive months, involving treatment with 3-days supervised dihydroartemisinin-piperaquine and single low-dose primaquine. Enhanced access to basic malaria control activities in the control clusters reduced the prevalence of malaria, detected by ultrasensitive PCR, from 16.6% at baseline to 10.6% at 3 months. The results in the intervention clusters were more impressive, the prevalence of *P. falciparum* falling from 14.5% to 1.4% over the same period. MDA was well tolerated, safe and acceptable, with no evidence of the emergence of piperaquine resistant parasites. In the year following MDA, the incidence of *P. falciparum* malaria was 30% lower in the intervention arm, however

the benefits were transient. In the third year of follow up, the prevalence in the control arm fell to 2.7%, whereas in the intervention it rose to 2.8%.

The study confirms that in remote communities deployment of CHWs, early diagnosis and treatment of malaria and distribution of LLIN can reduce the burden of malaria substantially⁵. MDA accelerated the reduction in *P. falciparum* infections but the intervention was intense, involving extensive community engagement, three rounds of a supervised three day regimen, active case detection and screening of newcomers to the community. Was it worth it?

The overall effectiveness of MDA depends on both community coverage and preventing reintroduction of infection. Although 90% of the population in the intervention clusters completed at least one round of MDA, only 77% participated in all three rounds. This level of coverage may have been insufficient, with residual infections sustaining ongoing transmission. A significant limitation of the study was the relatively small sample size and the proximity of control and intervention clusters. Highly mobile populations of asymptomatic individuals will contaminate the magnitude of the effect of MDA, increasing re-importation of infection into the intervention clusters. Regional implementation of MDA with high levels of coverage have a more profound and longer lasting benefit, as has been demonstrated in Vanuatu, Comoros, and China⁶⁻⁸.

The key decision now is whether the results of recent large MDA trials, including the one by McLean and colleagues, warrant larger scale interventions^{9,10}. The approach may need to be tailored to specific settings, including targeting high risk populations and isolated communities, repeating MDA at regular intervals and inclusion of the radical cure of *P. vivax*. These decisions will require bold national and international leadership, as well as a sense of urgency if the spread of resistance is to be curtailed and elimination targets met.

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