Curbing malaria resistance with multiple therapies

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Credit: CDC

In order to preserve first-line drugs for treating malaria, multiple combination therapies should be deployed within a population to prevent resistance from developing, according to Maciej Boni from the Centre for Tropical Medicine and Global Health, University of Oxford, UK, and colleagues in a Policy Forum article published in this week's *PLOS Medicine*.

By treating individuals with a combination of drugs that have different mechanisms of action, the chances of a malaria parasite developing the multiple genetic mutations needed to survive exposure to a combination therapy is substantially decreased and the effectiveness of the therapy is prolonged.

Artemisinin combination therapies (ACTs) have been increasingly used to treat malaria since 2005, when they were recommended as first-line treatments for falciparum malaria by the World Health Organization (WHO). However, just two years later, in 2007, evidence of partial resistance to artemisinins appeared at the Thai-Cambodian border manifesting as a prolonged parasite clearance time in patients treated with a standard three-day course of ACT.

While it may be possible to increase the number of active drugs in a combination therapy given to an individual, doing so increases the potential for side effects and costs. An alternative strategy could be to deploy multiple different combination therapies to different individuals within a community. This approach would require malaria parasites to develop four or more mutations in order to survive across successive human hosts, without the need to develop new antimalarial drugs. In their article the authors argue that a policy of implementing multiple first-line combinations should be considered to preserve the drugs used to combat malaria.

The authors conclude, "[w]ith hundreds of millions of malaria cases per year globally, and challenging epidemiological, political, and economic situations in both African and Asian nations, global malaria policy should be looking thirty years into the future to ensure that our best efforts at elimination are not quickly undermined by strongly drug-resistant phenotypes... The conventional clinical focus on the parasites infecting a particular patient is inadequate to the problem of long-term resistance management. The authors emphasize "a need for a more

population-based approach to strategic drug resistance prevention in malaria," noting that "The patient is the community, and the community parasite biomass is the infection in need of an effective and well-managed therapy."

More information: Boni MF, White NJ, Baird JK (2016) The Community As the Patient in Malaria-Endemic Areas: Preempting Drug Resistance with Multiple First-Line Therapies. *PLoS Med* 13(3): e1001984. DOI: 10.1371/journal.pmed.1001984