Monitoring of antimalarial drug efficacy using routine data

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Introduction
Studies commonly used to determine antimalarial drug efficacy can be lengthy, resource-intensive and involve multiple sampling, leading to a high threshold for initiation. Less cumbersome approaches for monitoring drug efficacy are needed. Since 2014, MSF has been working in Cambodia to curtail the emergence of antimalarial resistance. We developed a novel approach for monitoring efficacy of *Plasmodium falciparum* (Pf) antimalarials using routine data.

Methods
MSF conducts passive case detection (PCD) in Preah Vihear province. Symptomatic individuals were tested using rapid diagnostic tests (RDT; SD Bioline Malaria Ag Pf/Pv) and polymerase chain reaction (PCR); monitoring of drug efficacy was only conducted for Pf malaria. Baseline data included initial PCR results, and treatment adherence with 3 day direct observed therapy, along with follow-up testing on day 28 (d28) using PCR. Further PCR follow-up on day 63 (d63) was added in Aug 2016 to evaluate if d28 results failed to capture late recrudescence. We report on PCD data collected between Oct 2015 and Jul 2017.

Ethics
This study was approved by the Cambodian National Ethics Committee for Health Research and the MSF Ethics Review Board.

Results
Between Oct 2015 and Jan 2016, when dihydroartemisinin-piperaquine was used as first-line treatment, 128 Pf cases were detected. Of these, 111 (87%) were traced for d28 follow-up. 40/111 (36%) tested positive for Pf on d28, of which 87% were due to recrudescence (20 of the 23 with sufficient genetic material). High failure rates contributed to a shift to artesunate-mefloquine as first-line treatment from Feb 2016. Between Feb 2016 and Jul 2017, 118 Pf cases were detected, with 92 traced at d28. Only 2% (2/92) of cases were positive at d28, one a recrudescence. After the addition of d63 follow-up from Aug 2016, 69 of 85 Pf cases (81%) were traced for d63 follow-up. However, only one individual at this timepoint (1.4%, 1/69) was Pf positive, for which there was insufficient genetic material to determine recrudescence. No adverse effects of our intervention were observed.

Conclusion
We demonstrated the feasibility of almost real-time efficacy monitoring using d28 follow-up. This endpoint may be sufficient to ascertain recrudescence, since follow-up at d63 identified only one further case. Our approach could be used to ascertain the need for change in first-line drugs, as was done here, or as an intermediate step towards full-scale efficacy studies. This strategy could be a valuable tool for MSF and others to combat drug resistant malaria. We are now continuing to evaluate whether d28 is a sufficient endpoint by gathering more data at d28 and d63.

Conflicts of interest
None declared.