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Mass testing and treatment on malaria in an area of western Kenya

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To the Editor—We appreciate the thoughtful commentary provided by Hamer and Miller [1] and are pleased that they arrived at many of the same conclusions that we did; however, we would like to clarify a few points.

First, we wish to correct the statement that, in our trial, mass testing and treatment (MTaT) was only implemented within the core areas of clusters. Rather, MTaT was implemented throughout intervention clusters, which included a core area ranging between 1 and 3 Km in diameter, and a 300-m buffer. As described, to limit contamination, inclusion criteria for the analytic sample required residence within the core area [2, 3].

Second, the 24–36% of circulating infections within the population estimated to have been missed included those missed due to the limit of detection (LoD) of the rapid diagnostic tests (RDT) used (12.6–19.6%) plus incomplete intervention coverage (5.7–25.0%) [2]. It would not have been feasible to use loop-mediated isothermal amplification (LAMP), as suggested by Hamer and Miller, or polymerase chain reaction (PCR), as both PCR and even the most "easy-to-perform" LAMP assays require a laboratory [4], and are thus impractical for MTaT occuring at the household. Further, even with the use of a more sensitive diagnostic test, up to 25% of infections might still have been missed in a round due to incomplete coverage. In a high transmission setting these infections likely would have been enough to seed a rebound to preintervention levels.

The MTaT trial in Zambia resulted in an approximate 50% statistically significant reduction in malaria prevalence [5]. We agree that larger intervention and buffer areas likely reduced parasite migration into core areas, decreasing bias toward the null. However, we also note that these trials used different analytic approaches. We accounted for differences from

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baseline in each arm in our final analyses rather than comparing ratios at each time point as was done in the Zambia trial [5]. Using this latter approach for our data, we calculate adjusted prevalence ratios of 0.92 (95% confidence interval [CI]: .78–1.08), 0.85 (95% CI: .76–.95) and 0.84 (95% CI: .72–.98) at baseline, year 1, and year 2, respectively. Although we considered this approach, we believe that baseline differences should be taken into account and chose the more conservative analysis. Additionally, the effect size in the Zambia trial was estimated using odds ratios, which for nonrare events overestimate relative risk [6]. Had their trial been designed to calculate prevalence ratios, they may have found an effect with a lesser magnitude.

Finally, we agree with Hamer and Miller that trials evaluating elimination packages should include high coverage of integrated vector control with highly efficacious insecticides, access to case management in the community and at the health facility, strong surveillance systems for defining areas for targeted interventions, and in appropriate settings, consideration of mass drug administration. These measures, along with standardized trial design and analytic methods may provide a road map toward evaluating malaria transmission reduction strategies.

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