

We recommend that in all reports of cluster-randomised trials, the range of cluster-level outcomes be presented by arm. In trials with fewer than 30 clusters, cluster-by-cluster data should be presented.

JB is an investigator on a trial of the effect of ivermectin on malaria transmission. LHM and RH receive royalties from sales of their textbook on cluster-randomised trials.

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- 1 Foy BD, Alout H, Seaman JA, et al. Efficacy and risk of harms of repeat ivermectin mass drug administrations for control of malaria (RIMDAMAL): a cluster-randomised trial. *Lancet* 2019; **393**: 1517–26.
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The results of the RIMDAMAL trial in Burkina Faso, reported by Brian Foy and colleagues,¹ show that repeated mass treatment with ivermectin can reduce the incidence of malaria in children aged 5 years or younger, with no serious adverse effects.

In the roadmap to deploy ivermectin as a malaria prevention tool, similar trials are ongoing or planned² but, as far as we know, none is targeting an onchocerciasis-endemic region with high ongoing *Onchocerca volvulus* transmission. Onchocerciasis is associated with frequent morbidity, including a high prevalence of onchocerciasis-associated epilepsy, in several endemic regions in Africa.^{3,4} Although biannual community-directed treatment with ivermectin is recommended in areas with high *O. volvulus* transmission, its implementation has been difficult in many onchocerciasis foci, mostly because of logistical challenges and cost.⁵

Therefore, as ivermectin is being considered as a tool to control malaria, efforts should be made to prioritise onchocerciasis-endemic areas in a bid to curb both malaria incidence and onchocerciasis-associated morbidity.

Moreover, while planning for future interventions, onsite qualitative research needs to be done to assess both the acceptability and potential endorsement by the local populations, as well as the programmatic feasibility of implementing mass drug administration of ivermectin several times a year.

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Authors' reply

We thank John Bradley and colleagues¹ for their inquiry into our results and conclusions. Our study design of a few clusters (a total of eight were randomly assigned to the control or intervention group) was necessitated by the RIMDAMAL trial being a modestly funded pilot trial on ivermectin efficacy and safety.² Furthermore, because we hypothesised that the ivermectin treatment would most affect clinical malaria incidence in this population living in a hyperendemic area, frequent measures of malaria incidence by study nurses were required. Practically, this meant that the clinical work was

intensive (ie, nurses visiting each child more than once per week in their remote village homes), much like other malaria studies with similar endpoints. Such work makes this type of research extremely difficult to do with the number of clusters recommended by Bradley and colleagues,¹ unless the study is generously funded.

We used a generalised estimating equation (GEE) method, which we provided to the *Lancet* reviewers, including the detailed statistical codes, during multiple stages of peer review. Upon further inspection prompted by Bradley and colleagues,¹ we discovered that correlation was induced among household clusters (n=233) rather than among villages (the unit of randomisation; n=8). We regret this error. When a GEE is reperformed with village as the cluster, the p value is 0.0083 rather than 0.0009 as we originally reported.² The GEE we used permitted analysis of individual-level data (and thus inclusion of important confounders) and incorporated differences in village size while not applying parametric assumptions to the random effect distribution.

Bradley and colleagues¹ write that generalised estimating equations and random effect models are inappropriate with so few clusters. We assume they say this because these models tend to inflate the probability of type 1 errors. However, the degree of inflation depends on the intraclass cluster coefficient, the coefficient of variation, and the number of individuals sampled per cluster.³ We believe that the cluster-level summary methods Bradley and colleagues¹ use to get p values of 0.34–0.38 on the RIMDAMAL I data are overly conservative because the aggregate counts result in a loss of information, namely individual-level confounders and other sources of correlation (such as housing cluster). The methods of Bradley and colleagues¹ might also be inappropriate because the assumptions of those tests are violated; the tests appear to be on the difference between the rates,