potential harm of IPTp-SP is particularly important given that many countries continue to use IPTp-SP despite the presence of high levels of SP resistance.

Harrington et al contrast our study in Malawi [3] and their study in Tanzania [2], in which SP was implicated as harmful. Notably, both of our retrospective studies agree that SP did not exacerbate clinical outcomes such as low birth weight or maternal anemia [3, 4]; their evidence of harm was limited to parasitologic and inflammatory measures [2] and, in a subsequent analysis, cord hemoglobin [4]. A key difference between studies—as discussed in detail in our report and echoed by Harrington et al—is the presence of the c581 mutation in *dhps*: In Malawi it remains nearly absent, whereas in Tanzania it is established [5] and has been associated with greater placental parasite density and inflammation. It seems plausible that their findings are specific to parasite strains harboring the c581 mutation, and are less generalizable to parasites harboring other resistance genotypes; this is supported by recent findings from Mozambique, where this mutation is also rare [6]. Furthermore, we have evidence from ongoing observational studies in southern Malawi that SP continues to protect from fetal growth restriction in first and second pregnancies, although protection is reduced compared to the 1990s. These are important observations because the c581 mutation still appears to be rare in much of sub-Saharan Africa [7], and our reported findings of SP safety and partial efficacy are likely generalizable to other African countries.

We expect that the durability of IPTp-SP will vary between epidemiologic contexts. Harrington et al call for "a more appropriate strategy [to] be deployed," and we agree this is needed now for areas such as described by them in northern Tanzania. Promising results have been reported for alternative strategies involving intermittent screening and treatment in pregnancy (ISTp) [8], and several multicenter trials are

Reply to Harrington et al

To the Editor—We agree with Harrington et al that the delivery of new interventions to reduce the effects of pregnancy-associated malaria is a pressing global priority for maternal and childhood health. The provision of intermittent preventive treatment in pregnancy (IPTp) with sulfadoxine-pyrimethamine (SP) to large populations of pregnant women in malaria-endemic areas deserves ongoing scrutiny.

To this end, a previous analysis of our overall cohort suggested waning efficacy of IPTp-SP in Malawi [1]. Because of the previous report by Harrington et al [2] showing potential for exacerbated placental parasite density and inflammation when SP is provided to women who are infected with highly resistant parasites, we determined whether a similar phenomenon occurred in Malawi. Assessing

evaluating ISTp or alternative drugs for IPTp. Nevertheless, several years will pass while those strategies are being tested, analyzed, and integrated into antenatal care programs. In the meantime, many countries are likely to continue using IPTp-SP. Continued monitoring of SP resistance and the corresponding effectiveness of IPTp-SP is clearly necessary, but IPTp appears to be appropriate where the c581 mutation is rare. Thus, our data indicate that, to protect mothers and newborns from the parasite populations that prevail across much of east, central, and southern Africa, IPTp-SP remains a safe intervention.

Notes

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