Table 1. Loss of Efficacy of Intermittent Preventive Therapy in Pregnancy at Multiple Sites in East Africa

Study	Placental Malaria	Maternal Anemia	Low Birth Weight
	OR (95% CI)[a]	OR (95% CI)[a]	OR (95% CI)[a]
Malawi			
1997–2001 (CS) [2]	0.79 (.68–.91)	0.81 (.73–.90)	0.63 (.53–.75)
2002–2006 (CS) [2]	0.95 (.82–1.10)	1.00 (.94–1.07)	0.90 (.78–1.03)
Mozambique			
2001–2002 (RCT) [10]	0.20 (.06–.67)[b]		0.74 (.42–1.29)[b]
2002–2006 (RCT) [3]	1.00 (.88–1.13)[b]	0.92 (.79–1.08)[b]	0.99 (.70–1.39)[b]
Tanzania			
2002–2005 (CS) [4]	0.93 (.51–1.72)	0.99 (.63–1.56)	0.71 (.33–1.54)

Abbreviations: CI, confidence interval; CS, cross-sectional; IPTp, intermittent preventive therapy in pregnancy; OR, odds ratio; RCT, randomized controlled trial.

[a] IPTp vs no IPTp.

[b] Relative risk.

Intermittent Preventive Treatment in Pregnancy With Sulfadoxine-Pyrimethamine: The Times They Are A-Changin'

To the Editor—The report from Malawi by Taylor et al [1] considering the effect of intermittent preventive treatment in pregnancy (IPTp) with sulfadoxine-pyrimethamine (SP) on pregnancy malaria outcomes is concerning. No benefit of IPTp-SP was observed in adjusted analyses, similar to recent observations from Malawi [2], Mozambique [3], and Tanzania [4] (Table 1). These concordant findings from distant sites in East Africa mandate an urgent reappraisal of IPTp-SP policy.

The report further concludes that "IPTp did not potentiate PAM morbidity despite the increasing prevalence and fixation of SP-resistant *P. falciparum* haplotypes" [1]. In contrast, in a recent report from Tanzania IPTp-SP was associated with increased drug-resistant alleles, higher parasite burdens, and more inflammation [5]. The Tanzania report proposed a mechanism of competitive facilitation for the observed exacerbation, wherein drug treatment of a mixed population of susceptible and resistant parasites can induce parasite overgrowth [6].

Several differences between the Malawi [1] and Tanzania [5] reports merit attention. The Malawi analysis excluded women who did not receive IPTp-SP and hence cannot consider whether IPTp-SP exacerbates infections relative to no drug. Only women with positive peripheral blood smears were studied, resulting in a skewed study population since many women with placental malaria have negative peripheral blood smears, primarily women with low-density, chronic placental infections [7]. The *dhps* c581 allele that was common in Tanzania is essentially absent at the Malawi site but may be key to the exacerbation previously observed [4]. More than one-third of women in the Malawi cohort versus none in the Tanzania cohort were known to be infected with human immunodeficiency virus (HIV), and the impact of HIV disease and treatment on competitive facilitation is unknown.

Competitive facilitation relies on key conditions [6], which are met by the Tanzania but not the Malawi study. First, multiple distinct parasite populations are assumed to compete within a niche (eg, the placenta), but the average number of *msp-2* alleles from peripheral blood was 1.8 in Malawi with 55% of women carrying single clones in the final year of the study [8]. Second, differential fitness between competing populations (drug susceptible and resistant) is assumed to vary with the absence or presence of selective pressure, but the Malawi study did not consider a true control group (no drug). Third, the selective effect of the drug is applied to a previously stable mix of parasite populations, most evident in chronic infections, but these may have been disproportionately removed from the Malawi study.

IPTp-SP had clear benefits when placental malaria rates were high and drug resistance levels were low [9]. However, malaria has decreased over recent years in many places including Malawi, and SP-resistant parasites are widespread throughout East Africa. Rather than expose all pregnant women and their offspring to a failing and possibly harmful drug, a more appropriate strategy should be deployed. IPTp-SP should

be discontinued where it offers no benefits, and research should emphasize alternative drugs, improved diagnostics, and vaccines for the prevention and treatment of pregnancy malaria.

Note

Potential conflicts of interest. All authors: No reported conflicts.

All authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Conflicts that the editors consider relevant to the content of the manuscript have been disclosed.

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