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Walker, PG; Cairns, M; (2015) Value of additional chemotherapy for malaria in pregnancy. *The Lancet Global health*, 3 (3). e116-7. ISSN 2214-109X DOI: [https://doi.org/10.1016/S2214-109X\(15\)70081-1](https://doi.org/10.1016/S2214-109X(15)70081-1)

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Value of additional chemotherapy for malaria in pregnancy



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In *The Lancet Global Health*, Silke Fernandes and colleagues¹ provide an important and timely assessment of the cost-effectiveness of increasing the doses of intermittent preventive treatment for malaria during pregnancy (IPTp) from two doses to three or more doses, as currently recommended by the WHO.

This analysis provides compelling evidence that the incremental reduction in low birthweight noted in women who receive additional doses of sulfadoxine pyrimethamine (SP) during pregnancy² will be highly cost-effective when included as part of standard antenatal care in most areas of sustained malaria transmission in Africa.

The demonstration that monthly IPTp-SP is cost-effective is important to both researchers and policymakers, and this result has clear implications for improving the health of both expectant mothers and their infants in this region. An estimated 32 million pregnancies occurred in such areas in 2010,³ which would have the potential to lead to an estimated 0.7 million low birthweight deliveries attributable to malaria if these women were not protected from infection.⁴

However, some key questions remain concerning how best to provide protection from malaria during pregnancy. Perhaps the most pressing is why, despite IPTp-SP having demonstrable cost-effectiveness with the previously recommended two doses⁵ and antenatal care coverage now being high across much of Africa, the proportion of women receiving even two courses of IPTp in many areas remains low.⁶

As the authors suggest, one contributing factor to this low uptake might be the emergence of resistance to SP, particularly in eastern Africa. SP is no longer efficacious for case management in such settings, and perception of SP as an ineffective drug might be undermining IPTp-SP. This factor has prompted researchers to look at alternatives to IPTp-SP such as the use of more efficacious or longer-lasting artemisinin combination therapies (ACTs), either on the basis of positive diagnosis from a rapid diagnostic test (RDT) at an antenatal care visit, or as an alternative presumptive therapy.⁷

It is reassuring that SP remains effective against low birthweight, the main determinant of cost-effectiveness in this analysis, in all but the most highly resistant areas (those with super-resistance conferred by six sequential

resistance mutations).² Although in these areas the efficacy of SP is now substantially inhibited,^{8,9} this constitutes a small proportion of east Africa. However, parasites with the preceding quintuple mutation are widespread throughout the region,¹⁰ highlighting the need to continually monitor the progress of resistance and its effect on IPTp-SP.

Estimates used in this analysis suggest that additional doses of SP have the same proportional effect on all-cause low birthweight in both moderate and low-resistance settings.⁷ This measure, however, depends on the proportion of all-cause low birthweight that is attributable to malaria. As a result, differences in SP effectiveness could feasibly be disguised if there is a higher proportion of malaria-attributable low birthweight in areas where SP is less effective. Similar arguments can be made about the potential limitations of using the impact of SP on all-cause low birthweight to compare effectiveness between higher and lower transmission settings.

The very fact that providing a greater number of doses of IPTp-SP is incrementally effective, even in settings where the parasite is sensitive,² also highlights the potential benefit of interventions using more effective drugs. This finding means there is either scope to improve clearance of existing infections or, if the gain from more IPTp-SP courses is due to longer prophylaxis, a longer-acting drug might achieve similar benefits with fewer administrations.

Data were also insufficient for Fernandes and colleagues¹ to extend their analysis to areas of low or unstable transmission, a situation that will hopefully become more common as malaria control progresses across Africa. In such situations, symptomatic disease during pregnancy is likely to cause an increased proportion of the overall burden,¹¹ and understanding how malaria-attributable risk of low birthweight and immunity to both placental infection and symptomatic disease change as transmission falls will become an increasingly important issue.

Any alternative strategy to IPTp-SP is likely to have its own challenges: concerns remain about providing ACTs during pregnancy to uninfected women; testing using RDTs is likely to be more costly, might miss some infections, and means that uninfected women

do not benefit from prophylaxis; and switching to case management of symptomatic women leaves many asymptomatic women unprotected from prolonged placental infection. The analysis by Fernandes and colleagues¹ is a clear benchmark by which to judge these various merits and limitations and thus is an important step towards ensuring a much higher proportion of women receive adequate care for malaria in pregnancy.

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PGTW and MC are supported by fellowships jointly funded by the UK Medical Research Council (MRC) and the UK Department for International Development (DFID) under the MRC/DFID Concordat agreement. We declare no competing interests.

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