

Additional File 2. Risk of bias assessment

Pregnancy outcomes analysed here were secondary outcomes in the analysis on treatment efficacy. Thus, there are some studies without PCR-corrected efficacy (i.e. studies with only PCR-uncorrected efficacy) that could be included if the primary objective is to assess pregnancy outcomes after different treatments. However, most of these excluded studies were conducted in the 1990s, and only three studies (totalling 271 women) used ultrasound to estimate gestational age.[26-28] In one of them, the proportion of LBW (birthweight <2,500 g) was more frequently observed after DP than ASAQ (13·2% [12/91] vs 4·2% [3/72], $p=0\cdot05$), although the mean birthweight and the proportion of PTB (<37.0 weeks) were not different.[28] In our meta-analysis, the risk of SGA was not different between DP and ASAQ, and inclusion of the three studies without PCR-corrected efficacy is unlikely to change our findings considering the relative size of this IPD meta-analysis.

To assess any influential studies, the final multivariable model was assessed for each outcome by excluding one study site at a time. This does not change our conclusions (data not shown).

Reference for additional files

1. McGready R, Brockman A, Cho T, Cho D, van Vugt M, Luxemburger C, Chongsuphajaisiddhi T, White NJ, Nosten F: Randomized comparison of mefloquine-artesunate versus quinine in the treatment of multidrug-resistant falciparum malaria in pregnancy. *Trans R Soc Trop Med Hyg* 2000, 94(6):689-693.
2. McGready R, Cho T, Samuel, Villegas L, Brockman A, van Vugt M, Looareesuwan S, White NJ, Nosten F: Randomized comparison of quinine-clindamycin versus artesunate in the treatment of falciparum malaria in pregnancy. *Trans R Soc Trop Med Hyg* 2001, 95(6):651-656.
3. McGready R, Ashley EA, Moo E, Cho T, Barends M, Hutagalung R, Looareesuwan S, White NJ, Nosten F: A randomized comparison of artesunate-atovaquone-proguanil versus quinine in treatment for uncomplicated falciparum malaria during pregnancy. *J Infect Dis* 2005, 192(5):846-853.
4. Kalilani L, Mofolo I, Chaponda M, Rogerson SJ, Alker AP, Kwiek JJ, Meshnick SR: A randomized controlled pilot trial of azithromycin or artesunate added to sulfadoxine-pyrimethamine as treatment for malaria in pregnant women. *PLoS One* 2007, 2(11):e1166.
5. McGready R, Tan SO, Ashley EA, Pimanpanarak M, Viladpai-Nguen J, Phaiphun L, Wüstefeld K, Barends M, Laochan N, Keereecharoen L *et al*: A randomised controlled trial of artemether-lumefantrine versus artesunate for uncomplicated Plasmodium falciparum treatment in pregnancy. *PLoS Med* 2008, 5(12):e253.
6. Piola P, Nabasumba C, Turyakira E, Dhorda M, Lindegardh N, Nyehangane D, Snounou G, Ashley Ea, McGready R, Nosten F *et al*: Efficacy and safety of artemether-lumefantrine compared with quinine in pregnant women with uncomplicated Plasmodium falciparum malaria: an open-label, randomised, non-inferiority trial. *Lancet Infect Dis* 2010, 10(11):762-769.
7. PREGACT Study Group, Pekyi D, Ampromfi AA, Tinto H, Traoré-Coulibaly M, Tahita MC, Valéa I, Mwapasa V, Kalilani-Phiri L, Kalanda G *et al*: Four artemisinin-based treatments in African pregnant women with malaria. *N Engl J Med* 2016, 374(10):913-927.
8. Nambozi M, Kabuya J-BB, Hachizovu S, Mwakazanga D, Mulenga J, Kasongo W, Buyze J, Mulenga M, Van Geertruyden J-P, D'Alessandro U: Artemisinin-based combination therapy in pregnant women in Zambia: efficacy, safety and risk of recurrent malaria. *Malar J* 2017, 16:199.
9. Anvikar AR, Kuepfer I, Mishra V, Bruce J, Arya T, Mishra DR, Mohanty S, Mohanty R, Srivastava B, Sharma S *et al*: Efficacy of two artemisinin-based combinations for the treatment of malaria in pregnancy in India: a randomized controlled trial. *Malar J* 2018, 17:246.
10. McGready R, Stepniewska K, Edstein MD, Cho T, Gilveray G, Looareesuwan S, White NJ, Nosten F: The pharmacokinetics of atovaquone and proguanil in pregnant women with acute falciparum malaria. *Eur J Clin Pharmacol* 2003, 59(7):545-552.
11. McGready R, Phy AP, Rijken MJ, Tarning J, Lindegardh N, Hanpitakpon W, Than HH, Hlaing N, Zin NT, Singhasivanon P *et al*: Artesunate/dihydroartemisinin pharmacokinetics in acute falciparum malaria in pregnancy: absorption, bioavailability, disposition and disease effects. *Br J Clin Pharmacol* 2012, 73(3):467-477.
12. Rijken MJ, McGready R, Phy AP, Lindegardh N, Tarning J, Laochan N, Than HH, Mu O, Win AK, Singhasivanon P *et al*: Pharmacokinetics of dihydroartemisinin and piperaquine in pregnant and nonpregnant women with uncomplicated falciparum malaria. *Antimicrob Agents Chemother* 2011, 55(12):5500-5506.
13. Valea I, Tinto H, Traore-Coulibaly M, Toe LC, Lindegardh N, Tarning J, Van Geertruyden J-P, D'Alessandro U, Davies GR, Ward SA: Pharmacokinetics of co-formulated mefloquine and artesunate in pregnant and non-pregnant women with uncomplicated Plasmodium falciparum infection in Burkina Faso. *J Antimicrob Chemother* 2014, 69(9):2499-2507.
14. Ndiaye JL, Ndiaye A, Faye B, Ba M, Tine R, Ndiaye D, Gaye A, Gaye O, Brasseur P: Open-label in vivo drug study to evaluate the safety and efficacy of artesunate plus amodiaquine

- combination in pregnant women with uncomplicated *P. falciparum* malaria in Senegal. *Trop Med Int Health* 2011, 16(Supplement 1):140.
- 15. McGready R, Keo NK, Villegas L, White NJ, Looareesuwan S, Nosten F: Artesunate-atovaquone-proguanil rescue treatment of multidrug-resistant *Plasmodium falciparum* malaria in pregnancy: a preliminary report. *Trans R Soc Trop Med Hyg* 2003, 97(5):592-594.
 - 16. Rijken MJ, McGready R, Boel ME, Barends M, Proux S, Pimanpanarak M, Singhasivanon P, Nosten F: Dihydroartemisinin-piperaquine rescue treatment of multidrug-resistant *Plasmodium falciparum* malaria in pregnancy: a preliminary report. *Am J Trop Med Hyg* 2008, 78(4):543-545.
 - 17. Cohee LM, Kalilani-Phiri L, Mawindo P, Joshi S, Adams M, Kenefic L, Jacob CG, Taylor TE, Laufer MK: Parasite dynamics in the peripheral blood and the placenta during pregnancy-associated malaria infection. *Malar J* 2016, 15:483.
 - 18. Kalilani-Phiri L, Thesing PC, Nyirenda OM, Mawindo P, Madanitsa M, Membe G, Wylie B, Masonbrink A, Makwakwa K, Kamiza S *et al*: Timing of malaria infection during pregnancy has characteristic maternal, infant and placental outcomes. *PLoS One* 2013, 8(9):e74643.
 - 19. Adam I, Ibrahim MH, A/elbasit IA, Elbashir MI: Low-dose quinine for treatment of chloroquine-resistant falciparum malaria in Sudanese pregnant women. *East Mediterr Health J* 2004, 10(4/5):554-559.
 - 20. Adam I, Elwasila E, Mohammed Ali DA, Elansari E, Elbashir MI: Artemether in the treatment of falciparum malaria during pregnancy in eastern Sudan. *Trans R Soc Trop Med Hyg* 2004, 98(9):509-513.
 - 21. Adam I, Ali DM, Abdalla MA: Artesunate plus sulfadoxine-pyrimethamine in the treatment of uncomplicated *Plasmodium falciparum* malaria during pregnancy in eastern Sudan. *Trans R Soc Trop Med Hyg* 2006, 100(7):632-635.
 - 22. Adam I, Tarning J, Lindegardh N, Mahgoub H, McGready R, Nosten F: Pharmacokinetics of piperaquine in pregnant women in Sudan with uncomplicated *Plasmodium falciparum* malaria. *Am J Trop Med Hyg* 2012, 87(1):35-40.
 - 23. Bounyasong S: Randomized trial of artesunate and mefloquine in comparison with quinine sulfate to treat *P. falciparum* malaria pregnant women. *J Med Assoc Thai* 2001, 84(9):1289-1299.
 - 24. Mutabingwa TK, Muze K, Ord R, Briceño M, Greenwood BM, Drakeley C, Whitty CJM: Randomized trial of artesunate+amodiaquine, sulfadoxine-pyrimethamine+amodiaquine, chlorproguanal-dapsone and SP for malaria in pregnancy in Tanzania. *PLoS One* 2009, 4(4):e5138.
 - 25. Boel ME, Rijken MJ, Leenstra T, Phyto AP, Pimanpanarak M, Keereecharoen NL, Proux S, Laochan N, Imwong M, Singhasivanon P *et al*: Malaria in the post-partum period; a prospective cohort study. *PLoS One* 2013, 8(3):e57890.
 - 26. Adam I, Idris HM, Elbashir MI: Quinine for chloroquine-resistant falciparum malaria in pregnant Sudanese women in the first trimester. *East Mediterr Health J* 2004, 10(4/5):560-565.
 - 27. Onyamboko MA, Meshnick SR, Fleckenstein L, Koch MA, Atibu J, Lokomba V, Douoguih M, Hemingway-Foday J, Wesche D, Ryder RW *et al*: Pharmacokinetics and pharmacodynamics of artesunate and dihydroartemisinin following oral treatment in pregnant women with asymptomatic *Plasmodium falciparum* infections in Kinshasa DRC. *Malar J* 2011, 10:49.
 - 28. Osarfo J, Tagbor H, Cairns M, Alifrangis M, Magnussen P: Dihydroartemisinin-piperaquine versus artesunate-amodiaquine for treatment of malaria infection in pregnancy in Ghana: an open-label, randomised, non-inferiority trial. *Trop Med Int Health* 2017, 22(8):1043-1052.