4.2.1. Intermittent preventive treatment of malaria in pregnancy (IPTp)

Clinical Question/ PICO

Population: Malaria-endemic areas
Intervention: Three or more doses of sulfadoxine–pyrimethamine
Comparator: Two doses of sulfadoxine–pyrimethamine

Outcome Timeframe	**Study results and measurements**	**Comparator** Sulfadoxine–pyrimethamine (2 doses)	**Intervention** Sulfadoxine–pyrimethamine (≥ 3 doses)	**Certainty of the Evidence** (Quality of evidence)	**Plain language summary**
Severe anaemia in 3rd trimester	Relative risk 0.73 (CI 95% 0.48 — 1.11) Based on data from 2,196 participants in 6 studies. (Randomized controlled)	34 per 1000 Difference:	25 per 1000 **9 fewer per 1000** (CI 95% 18 fewer — 4 more)	Low Due to serious risk of bias and serious imprecision [1]	
Anaemia in 3rd trimester	Relative risk 0.95 (CI 95% 0.9 — 1.01) Based on data from 2,088 participants in 7 studies. (Randomized controlled)	509 per 1000 Difference:	484 per 1000 **25 fewer per 1000** (CI 95% 51 fewer — 5 more)	Moderate Due to serious risk of bias [2]	
Parasitaemia at delivery	Relative risk 0.68 (CI 95% 0.52 — 0.89) Based on data from 2,096 participants in 7 studies. (Randomized controlled)	92 per 1000 Difference:	63 per 1000 **29 fewer per 1000** (CI 95% 44 fewer — 10 fewer)	Moderate Due to serious risk of bias [3]	

1. **Risk of Bias: serious.** The strongest effect was seen in a trial at high risk of selection bias; removal of this trial removes the statistical significance. None of the three trials was blinded, and all had a high attrition rate.. **Inconsistency: no serious.** Statistical heterogeneity is low. **Indirectness: no serious.** These three studies were conducted in Kenya (1996), Burkina Faso (2005) and Malawi (2005) in women in their first or second pregnancy. **Imprecision: serious.** These trials had inadequate power. To detect a 25% relative reduction in severe anaemia confidently would require a sample size of over 12 000.
2. **Risk of Bias: serious.** Two trials were at high risk of selection bias, three were unblinded and four had a high attrition rate. **Inconsistency: no serious.** Statistical heterogeneity is low. **Indirectness: no serious.** The four studies were conducted in Kenya (1996), Zambia (2004), Burkina Faso (2005) and Malawi (2005) in women in their first or second pregnancy. **Imprecision: no serious.** This meta-analysis has adequate power to detect an effect.
3. **Risk of Bias: serious.** Two of the three studies were at high risk of selection bias. All three had a high attrition rate. **Inconsistency: no serious.** A subgroup analysis suggests that the effect may be larger in women infected with HIV. **Indirectness: no serious.** These three trials were conducted in Kenya (1996), Zambia (2004) and Malawi (2005) in women in their first or second pregnancy. In two trials, the analysis was stratified by HIV status. **Imprecision: no serious.** This meta-analysis has adequate power to detect an effect.

Clinical Question/ PICO

Population: Malaria-endemic areas
Intervention: Three or more doses of sulfadoxine–pyrimethamine
Comparator: Two doses of sulfadoxine–pyrimethamine

Outcome Timeframe	**Study results and measurements**	**Comparator** Sulfadoxine–pyrimethamine (2 doses)	**Intervention** Sulfadoxine–pyrimethamine (≥ 3 doses)	**Certainty of the Evidence** (Quality of evidence)	**Plain language summary**
Miscarriage	Relative risk 1.43 (CI 95% 0.88 — 2.33) Based on data from 2,471 participants in 6 studies. (Randomized controlled)	0 per 1000 Difference:	0 per 1000 **0 fewer per 1000** (CI 95% 0 fewer — 0 fewer)	Very low Due to serious risk of bias and very serious imprecision [1]	
Stillbirth	Relative risk 1.14 (CI 95% 0.85 — 1.55) Based on data from 2,676 participants in 7 studies. (Randomized controlled)	30 per 1000 Difference:	34 per 1000 **4 more per 1000** (CI 95% 4 fewer — 17 more)	Very low Due to serious risk of bias and very serious imprecision [2]	
Neonatal mortality	Relative risk 0.88 (CI 95% 0.57 — 1.35) Based on data from 2,405 participants in 6 studies. (Randomized controlled)	21 per 1000 Difference:	18 per 1000 **3 fewer per 1000** (CI 95% 9 fewer — 7 more)	Very low Due to serious risk of bias and very serious imprecision [3]	
Preterm birth	Relative risk 1.28 (CI 95% 0.9 — 1.82) Based on data from 2,579 participants in 7 studies. (Randomized controlled)	122 per 1000 Difference:	116 per 1000 **6 fewer per 1000** CI 95%	Low Due to serious risk of bias and serious imprecision [4]	
Low birth weight	Relative risk 0.8 (CI 95% 0.69 — 0.94) Based on data from 2,190 participants in 7 studies. (Randomized controlled)	167 per 1000 Difference:	134 per 1000 **33 fewer per 1000** (CI 95% 52 fewer — 10 fewer)	High [5]	
Placental parasitaemia	Relative risk 0.51 (CI 95% 0.38 — 0.68) Based on data from 1,436 participants in 6 studies. (Randomized controlled)	63 per 1000 Difference:	32 per 1000 **31 fewer per 1000** (CI 95% 39 fewer — 20 fewer)	High [6]	
Cord blood haemoglobin	Relative risk		CI 95%		

Outcome Timeframe	**Study results and measurements**	**Comparator** Sulfadoxine–pyrimethamine (2 doses)	**Intervention** Sulfadoxine–pyrimethamine (≥ 3 doses)	**Certainty of the Evidence** (Quality of evidence)	**Plain language summary**
Mean birth weight	Based on data from: 2,190 participants in 7 studies. (Randomized controlled)	Sulfadoxine–pyrimethamine (2 doses): Mean birth weight in the control groups ranged from 2722 g to 3239 g. Sulfadoxine–pyrimethamine (≥ 3 doses): Mean birth weight in the intervention groups was 56 g higher (29 to 83 g higher).		High [7]	

1. **Risk of Bias: serious.** Two studies were at high risk of selection bias, and all three were unblinded and at high risk of attrition bias. **Inconsistency: no serious.** Statistical heterogeneity was low. **Indirectness: no serious.** The three studies were conducted in Kenya (1996), Malawi (2005) and Burkina Faso (2008) in women in their first or second pregnancy. **Imprecision: very serious.** The trials had inadequate power to detect an effect. Confident detection of a 25% reduction in mortality would require a sample size of over 25 000.
2. **Risk of Bias: serious.** Two studies were at high risk of selection bias, and all three were unblinded and at high risk of attrition bias. **Inconsistency: no serious.** Statistical heterogeneity was low. **Indirectness: no serious.** The three studies were conducted in Kenya (1996), Malawi (2005) and Burkina Faso (2008) in women in their first or second pregnancy. **Imprecision: very serious.** The trials had inadequate power to detect an effect. Confident detection of a 25% reduction in mortality would require a sample size of over 14 000.
3. **Risk of Bias: serious.** Two studies were at high risk of selection bias, and all three were unblinded and at high risk of attrition bias. **Inconsistency: no serious.** Statistical heterogeneity was low. **Indirectness: no serious.** The three studies were conducted in Kenya (1996), Malawi (2005) and Burkina Faso (2008) in women in their first or second pregnancy. **Imprecision: very serious.** The trials had inadequate power to detect an effect. Confident detection of a 25% reduction in mortality would require a sample size of over 14 000.
4. **Risk of Bias: serious.** Two of the four studies were at high risk of selection bias and three at high risk of attrition bias. **Inconsistency: no serious.** Statistical heterogeneity was low. **Indirectness: no serious.** These four studies were conducted in Kenya (1996), Zambia (2004), Malawi (2005) and Burkina Faso (2008) in women in their first or second pregnancy. **Imprecision: serious.** The 95% CI does not exclude what may be clinically important effects. Confident detection of a 25% reduction in pre-term birth would require a sample size of > 2500.
5. **Risk of Bias: no serious.** Two studies are at low risk of bias. Removal of the trials with high risk of bias did not influence the effect estimate. **Inconsistency: no serious.** Statistical heterogeneity was low. **Indirectness: no serious.** These studies were conducted in Kenya (1996), Zambia (2004), Malawi (2005 and 2006), Mali (2008) and Burkina Faso (2008) in women in their first or second pregnancy. **Imprecision: no serious.** The sample size is sufficiently large to detect a difference between the two drug regimens, and the result is statistically significant.
6. **Risk of Bias: no serious.** Two studies are at low risk of bias. Removal of the trials with high risk of bias did not influence the effect estimate. **Inconsistency: no serious.** Statistical heterogeneity was low. **Indirectness: no serious.** These studies were conducted in Kenya (1996), Zambia (2004), Malawi (2005) and Mali (2008) in women in their first or second pregnancy. **Imprecision: no serious.** The sample size is sufficiently large to detect a difference between the two drug regimens, and the result is statistically significant.
7. **Risk of Bias: no serious.** Two studies are at low risk of bias. Removal of the trials with high risk of bias did not influence the effect estimate. **Inconsistency: no serious.** Statistical heterogeneity was low. **Indirectness: no serious.** These studies were conducted in Kenya (1996), Zambia (2004), Malawi (2005 and 2006), Mali (2008) and Burkina Faso (2008) in women in their first or second pregnancy. **Imprecision: no serious.** The sample size is sufficiently large to detect a difference between the two drug regimens, and the result is statistically significant.