

4.2.3. Seasonal malaria chemoprevention (SMC)

Clinical Question/ PICO

Population: Children aged < 5 years (areas with seasonal transmission)
Intervention: Regular full treatment doses of antimalarial medicines (amodiaquine + sulfadoxine–pyrimethamine, artesunate + sulfadoxine–pyrimethamine or sulfadoxine–pyrimethamine alone) every 1–2 months during the malaria transmission season
Comparator: Placebo

Outcome Timeframe	Study results and measurements	Comparator Placebo	Intervention SMC	Certainty of the Evidence (Quality of evidence)	Plain language summary
Death from any cause (per 1000 per year)	Relative risk 0.66 (CI 95% 0.31 – 1.39) Based on data from 9,533 patients in 6 studies. (Randomized controlled)	3 per 1000 Difference:	2 per 1000 1 fewer per 1000 (CI 95% 2 fewer – 1 more)	Moderate Due to serious imprecision ¹	
Moderately severe anaemia (per 1000 per year)	Relative risk 0.71 (CI 95% 0.52 – 0.98) Based on data from 8,805 patients in 5 studies. (Randomized controlled)	67 per 1000 Difference:	48 per 1000 19 fewer per 1000 (CI 95% 32 fewer – 1 fewer)	Moderate Due to serious inconsistency ²	
Serious drug- related adverse events	Relative risk Based on data from 9,533 patients in 6 studies. (Randomized controlled)		CI 95%	Moderate Due to serious imprecision ³	
Non-serious adverse events	Relative risk Based on data from 9,533 patients in 6 studies. (Randomized controlled)		CI 95%	Moderate Due to serious risk of bias ⁴	
Clinical malaria	Based on data from: 9,321 patients in 6 studies. (Randomized controlled)	Placebo: 2.5 episodes per child per year (The incidence of malaria in the control groups was 2.88 episodes per child per year in Burkina Faso, 2.4 in Mali and 2.25 in Senegal). SMC: 0.7 episodes per child per year (0.4 to 1.0). Rate ratio: 0.26 (0.17 to 0.38).		High ⁵	
Severe malaria	Based on data from: 5,964 patients in 2 studies. (Randomized controlled)	Placebo: 35 episodes per 1000 children per year (The incidence of severe malaria in the control groups was 32 per 1000 children per year in Burkina Faso and 37 per 1000		High ⁶	

Outcome Timeframe	Study results and measurements	Comparator Placebo	Intervention SMC	Certainty of the Evidence (Quality of evidence)	Plain language summary
		children per year in Mali). SMC: 9 episodes per 1000 children per year (4 to 27). Rate ratio 0.27 (0.1 to 0.76).			

1. **Imprecision: serious.** There were very few deaths in these trials, and none of the trials had adequate power to detect an effect on mortality. Larger trials are necessary for this effect to be established confidently. A reduction in the number of deaths would be consistent with the high-quality evidence of a reduction in severe malaria..
2. **Risk of Bias: no serious.** There was no reason to downgrade for study limitations, directness or precision. **Inconsistency: serious.** There was substantial heterogeneity among these five trials, and the trials in the Gambia and Ghana did not show an effect. Downgraded by 1 for inconsistency. **Indirectness: no serious.** There was no reason to downgrade for study limitations, directness or precision. **Imprecision: no serious.** There was no reason to downgrade for study limitations, directness or precision.
3. **Imprecision: serious.** No drug-related serious adverse events were reported. Downgraded by 1 for precision, as trials of this size have inadequate power to fully detect or exclude rare, serious adverse events.
4. **Risk of Bias: serious.** Downgraded by 1 for study limitations. All seven trials reported observed adverse events; however, the adequacy of the methods used to collect these data is unclear in some trials. The only adverse event found to be statistically more common with SMC was vomiting after amodiaquine + sulfadoxine-pyrimethamine.
5. **Risk of Bias: no serious.** The trials were conducted in children aged < 5 years in Burkina Faso, the Gambia, Ghana, Mali (two) and Senegal. In three studies, amodiaquine + sulfadoxine-pyrimethamine administered monthly, in two studies sulfadoxine-pyrimethamine was given every 2 months, and in one study sulfadoxine-pyrimethamine + artesunate was given monthly. Two studies, in which insecticide-treated nets were also distributed, showed that the benefits remained even when use of mosquito nets was > 90%. There was no reason to downgrade for study limitations, inconsistency, indirectness or imprecision. **Inconsistency: no serious.** There was no reason to downgrade for study limitations, inconsistency, indirectness or imprecision. **Indirectness: no serious.** There was no reason to downgrade for study limitations, inconsistency, indirectness or imprecision. **Imprecision: no serious.** There was no reason to downgrade for study limitations, inconsistency, indirectness or imprecision.
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