5.2.5. Reducing the transmissibility of treated P. falciparum infections in areas of low-intensity transmission

Clinical Question/ PICO

Population: People with symptomatic malaria in malaria-endemic areas
Intervention: Short-course primaquine plus malaria treatment including an artemisinin derivative
Comparator: Malaria treatment with an artemisinin derivative alone

Outcome Timeframe	**Study results and measurements**	**Comparator** ACT	**Intervention** ACT + primaquine	**Certainty of the Evidence** (Quality of evidence)	**Plain language summary**
Malaria incidence, prevalence or entomological inoculation rate	Relative risk Based on data from 0 participants in 0 studies.		CI 95%		
People infectious to mosquitoes	Relative risk Based on data from 0 participants in 0 studies.		CI 95%		Limited observational data from mosquito feeding studies suggests that 0.25 mg/kg bw may rapidly reduce the infectivity of gametocytes to mosquitoes.

Outcome Timeframe	**Study results and measurements**	**Comparator** ACT	**Intervention** ACT + primaquine	**Certainty of the Evidence** (Quality of evidence)	**Plain language summary**
Participants with gametocytes on microscopy or PCR (day 8) (dose < 0.4 mg/kg bw) [1]	Relative risk 0.67 (CI 95% 0.44 — 1.02) Based on data from 223 participants in 1 studies. (Randomized controlled)	34 per 1000 Difference:	23 per 1000 **11 fewer per 1000** (CI 95% 19 fewer — 1 more)	**Low** Due to very serious imprecision [2]	
Participants with gametocytes on microscopy or PCR (day 8) (dose 0.4–0.6 mg/kg bw) [3]	Relative risk 0.3 (CI 95% 0.16 — 0.56) Based on data from 219 participants in 1 studies. (Randomized controlled)	35 per 1000 Difference:	11 per 1000 **24 fewer per 1000** (CI 95% 29 fewer — 15 fewer)	**Low** Due to serious imprecision and serious indirectness [4]	
Participants with gametocytes on microscopy or PCR (day 8) (dose > 0.6 mg/kg bw) [5]	Relative risk 0.29 (CI 95% 0.22 — 0.37) Based on data from 1,380 participants in 7 studies. (Randomized controlled)	30 per 1000 Difference:	9 per 1000 **21 fewer per 1000** (CI 95% 23 fewer — 19 fewer)	**High** [6]	
Mean percentage change in haemoglobin (Hb) [7]	Based on data from: 101 participants in 1 studies. (Randomized controlled)			**Low** Due to very serious indirectness [8]	ACT: 15% mean drop in Hb from baseline in the control group. ACT + primaquine: Mean drop in Hb from baseline in the intervention groups was 3% lower (10% lower to 4% higher).

1. AUC estimates (log10 AUC for days 1–43) are included as footnotes for each dosing stratum.
2. **Risk of Bias: no serious.** Includes one trial with no risk of bias detected. **Imprecision: very serious.** One small trial with CIs that include 50% reduction and no effect.
3. AUC estimates (log10 AUC for days 1–43) are included as footnotes for each dosing stratum.
4. **Risk of Bias: no serious.** Includes one trial with no risk of bias detected. **Indirectness: serious.** This is a single trial in a single setting. **Imprecision: serious.** A single trial with few events.
5. AUC estimates (log10 AUC for days 1–43) are included as footnotes for each dosing stratum.
6. **Indirectness: no serious.** While there is marked quantitative heterogeneity, the studies with no demonstrable effect had few events. Not downgraded.
7. One trial reported a relative decrease in haemoglobin against baseline in both groups on days 8, 15, 29 and 43 in all participants irrespective of G6PD status. No difference at any time between participants receiving primaquine and those that not did not. We present the data for day 43 in this table.
8. **Indirectness: very serious.** The percentage of people with large drops in haemoglobin, not the mean change in the

population, is the important safety outcome, and the estimates are averages in a small population (N = 99) that includes people with normal G6PD function. The study is therefore unlikely to detect effects in a small subgroup with a relatively uncommon adverse event.