Outcome Timeframe	Study results and measurements	Comparator No malaria vaccination	Intervention Malaria vaccination	Certainty of the evidence (Quality of evidence)	Summary
2017–2020 6 Important					
Female:male rate ratio of all-cause mortality; RTS,S/AS01 + SMC combination vs SMC alone [164] Phase 3b randomized study 2017–2020 6 Important	Rate ratio 0.35 (CI 95% 0.06 — 1.98) Based on data from 3,932 participants in 1 studies. [165] (Randomized controlled) Follow up: 3 years.			**Low** Due to very serious imprecision [166]	RTS,S/AS01 vaccination may result in little to no difference in all-cause mortality between girls and boys.
Female:male rate ratio of all-cause mortality in age-eligible and age-ineligible children in RTS,S/AS01 implementing vs. comparison areas (age-based vaccination) [167] Pilot implementation study 2019–2023 6 Important	1.04 (CI 95% 0.93 — 1.15) Based on data from 15,444 participants in 1 studies. [168] Follow up: month 0 to month 46.				There is probably no difference in all-cause mortality between girls and boys.

1. [Impact outcome] Protective efficacy (%) against clinical malaria episodes (modified intention-to-treat analysis). Per-protocol analysis protective efficacy 39.0% (95% CI 34.3 to 43.3). Clinical malaria assessed with: illness in a child brought to a study facility with a measured temperature of 37.5°C and P. falciparum asexual parasitaemia at a density of > 5000 parasites per cubic millimetre or a case of malaria meeting the primary case definition of severe malaria. Severe malaria primary case definition: P. falciparum asexual parasitaemia at a density of > 5000 parasites per cubic millimetre with one or more markers of disease severity and without diagnosis of a coexisting illness. Markers of severe disease were prostration, respiratory distress, a Blantyre coma score of 2 (on a scale of 0 to 5, with higher scores indicating a higher level of consciousness), two or more observed or reported seizures, hypoglycaemia, acidosis, elevated lactate level, or haemoglobin level of < 5 g per decilitre. Co-existing illnesses were defined as radiographically proven pneumonia, meningitis established by analysis of cerebrospinal fluid, bacteraemia, or gastroenteritis with severe dehydration). 4-dose intervention group (R3R) received 3 doses of RTS,S/AS01 at months 0, 1, and 2 and a 4th dose at month 20. The control group (R3C) received the comparator vaccine (Rabies vaccine) at months 0, 1, 2, and 20. Low transmission trial sites included Kilifi, Kenya and Korogwe, Tanzania. Moderate transmission trial sites included Lambarene, Gabon; Bagamoyo, Tanzania; Lilongwe, Malawi; and Manhica, Mozambique. High transmission trial sites included Siaya, Kenya; Nanoro, Burkina Faso; Kintampo, Burkina Faso; Kombewa, Kenya and Agogo, Ghana.
2. [174]. The number of cases averted over time was calculated as the sum of 3-monthly differences in the estimated number of cases between the control and the RTS,S/AS01 groups (R3R and R3C combined up to the time of 4th dose and R3R and R3C separately after the 4th dose) and expressed per 1000 participants vaccinated. In children, 1774 cases of clinical malaria were averted per 1000 children (95% CI 1387–2186) in the R3R group and 1363 per 1000 children (995–1797) in the R3C group. The numbers of cases averted per 1000 young infants were 983 (95% CI 592–1337) in the R3R group and 558 (158–926) in the R3C group. Among the older