Implementation questions and funding for evaluation and implementation research questions

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Credit: WHO/Neil Thomas.

Need for a learning agenda

- Many rich lessons learned from pilot introductions on safety in routine use, acceptability, feasibility, impact, and the use of remote tools for effective delivery during a pandemic
- Nonetheless, outstanding questions remain on vaccine delivery
    1. Programmatic optimization of delivery in different settings
    2. Increasing supply and reducing cost
    3. Optimizing impact, including combined use of vaccine and other malaria prevention measures
    4. Behavior Change and Communication, including optimal use of additional visits to catch up on other vaccines and child health measures
- Notably pilots were conducted in areas with functional EPI and NMCP programmes, in areas with perennial transmission through routine EPI (age-based administration throughout the year)
    - Areas introducing vaccine in initial phase (cat 1) may have weaker health systems
    - Some areas have high seasonality and may elect a seasonal delivery
- In addition, broader research agenda on malaria vaccines useful to guide priority research needs
    - Escape mutants, immunogenicity, co-administration studies

Processes to develop a research and learning agenda

- WHO and Gavi working with PMI Insights to develop a comprehensive and vetted research agenda with stakeholders, in particular those in endemic countries
- PMI Insights works with a research or public health institution within a malaria affected country to co-lead the process
- Broad and inclusive stakeholder consultation process to gather input
    - Ministries of health, research institutions and partners engaged in malaria vaccine introduction or research, CSO, regional and global bodies, global health funding agencies
- Rigorous evaluation process to prioritize and rank research topics and develop research agenda
    - Learning agenda will be drawn from the broader research agenda

Examples of potential questions for learning agenda or research agenda

- Define best schedule for introduction in highly seasonal settings for highest impact and operational feasibility (and optimal age range)*
- Monitoring of vaccine effectiveness and safety when introduced seasonally with new schedule*
- Acceptability of HWs/caregivers in seasonal malaria vaccination followed by SMC*
- Safety in campaign strategy where dose 4 may be given less than 12 months after dose 3*
- How best to leverage additional visits to increase uptake of other vaccines, ITN use, Vitamin A, deworming, other child health interventions
- Strategies to improve uptake of dose 4, in second year of life
- Document best practices from sub-national implementation in category 1 areas
- Assess strategies to reach zero dose and under reached children leveraging community demand for malaria vaccine
- Efficacy of a fractional dose of vaccine for dose sparing
- Added/synergistic effect of the malaria vaccine with Perennial Malaria Chemoprevention (PMC)
- Potential benefit of clearing malaria parasitemia prior to vaccination to increase vaccine efficacy
- Interchangeability of RTS,S and candidate malaria vaccine R21

* Mentioned in country presentations

Duration of protection from Phase III trial, 2009-2014: 11 sites, 7 countries

Vandoolaeghe *et al*, 2016, Expert Review of Vaccines https://doi.org/10.1080/14760584.2016.1236689

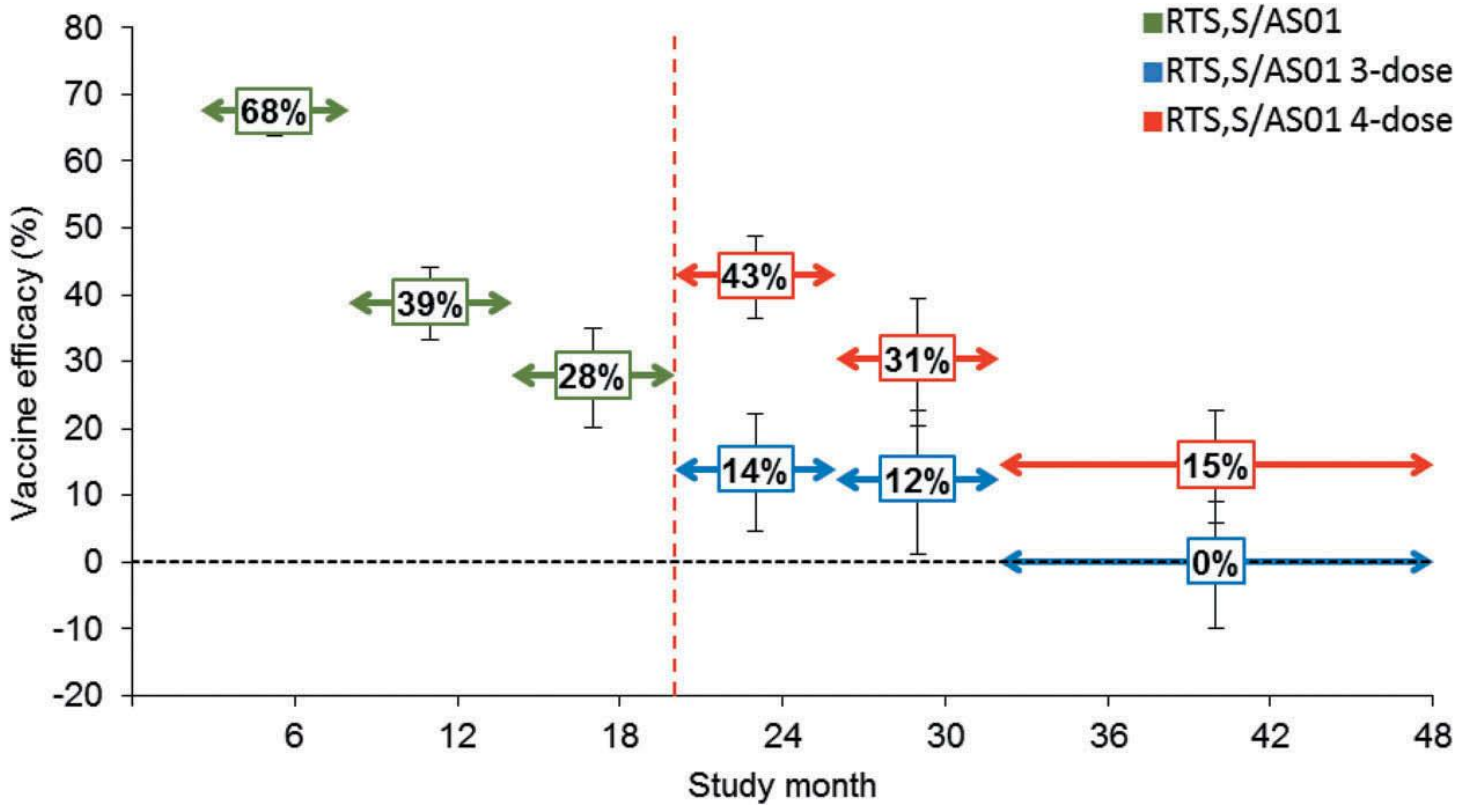


Figure 2. Vaccine efficacy against all episodes of clinical malaria, expressed as comparative clinical malaria incidence stratified by 6-monthly follow-up periods in the phase III efficacy trial, for children 5–17 months old (according-to-protocol cohort). RTS,S/AS01, pooled RTS,S/AS01 3-dose and 4-dose groups prior to administration of the 4th dose; RTS,S/AS01 3-dose, children receiving 3 doses of RTS,S/AS01 vaccine at months 0, 1, 2 and control vaccine at month 20; RTS,S/AS01 4-dose, children receiving 4 doses of RTS,S/AS01 vaccine at months 0, 1, 2 and 20. Double arrows indicate the follow-up period over which the respective vaccine efficacy estimates were calculated. Error bars indicate 95% confidence intervals. The dotted vertical line indicates the time of administration of the 4th dose.

Estimated impact over 48 months after vaccination with 3 or 4 doses, Phase III trial, 2009-2014

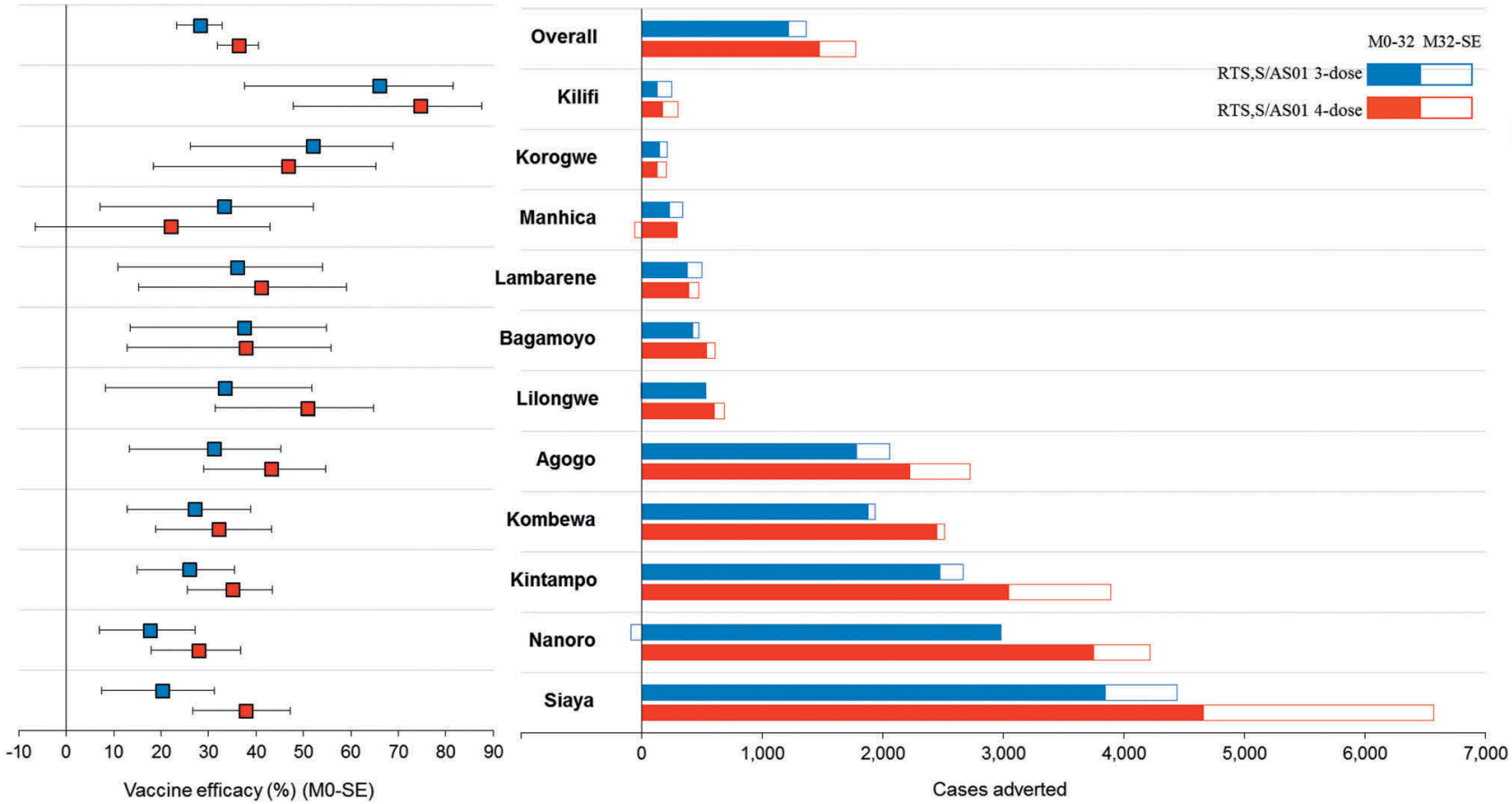
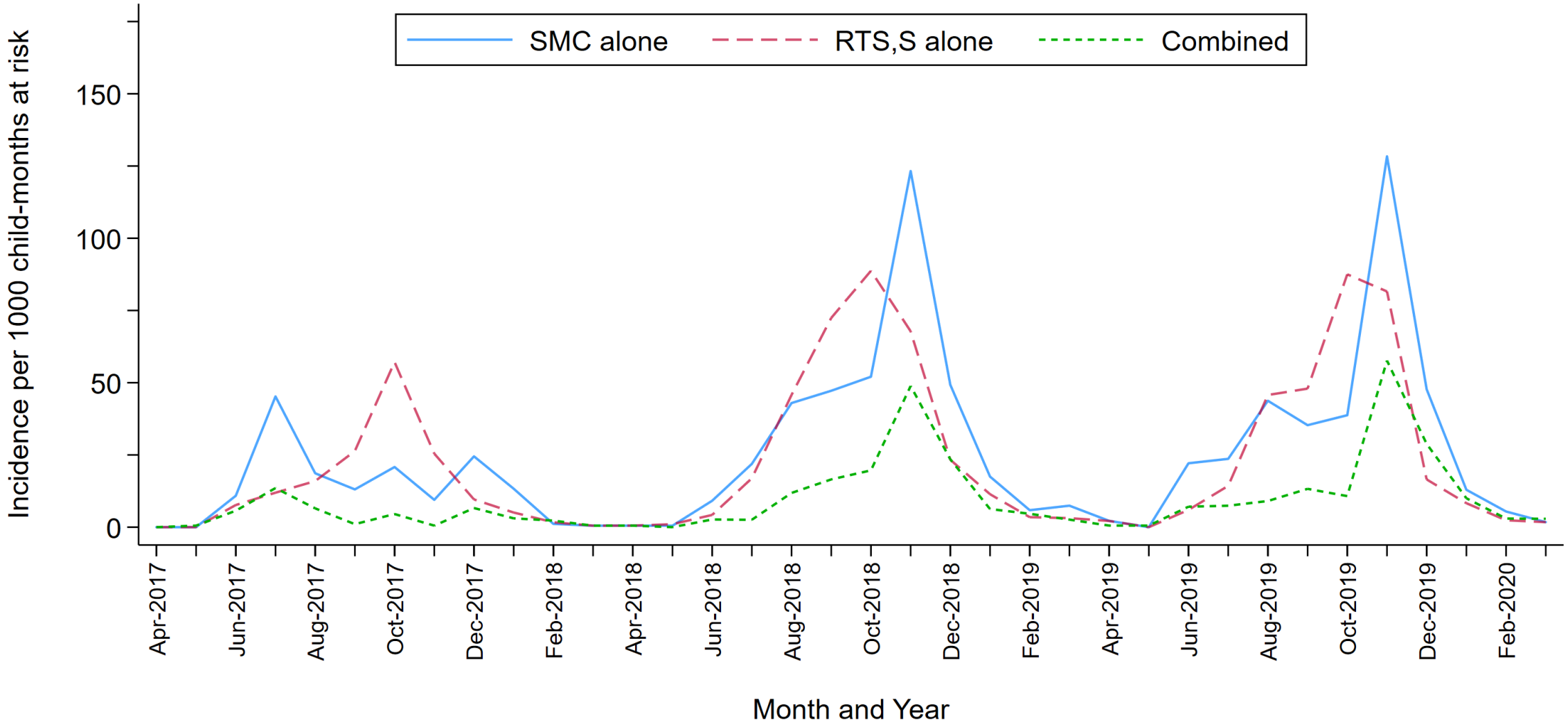


Figure 3. Vaccine efficacy over 48 months of follow-up on average, and cases of clinical malaria averted during the phase III efficacy trial, by center, for the 5–17 months age group (intention-to-treat cohort). RTS,S/AS01 3-dose, children receiving 3 doses of RTS,S/AS01 vaccine at months 0, 1, 2 and control vaccine at month 20; RTS,S/AS01 4-dose, children receiving 4 doses of RTS,S/AS01 vaccine at months 0, 1, 2 and 20; M, month; SE, study end (on average 48 months after dose 1). Error bars indicate 95% confidence intervals. Trial centers are ordered from the lowest (Kilifi) to the highest (Siaya) incidence of clinical malaria measured in the infant control group over the first 12 months of follow-up.

Monthly incidence of clinical malaria with seasonal delivery of RTS,S/AS01 with and without SMC, Phase III trial, Mali and Burkina Faso



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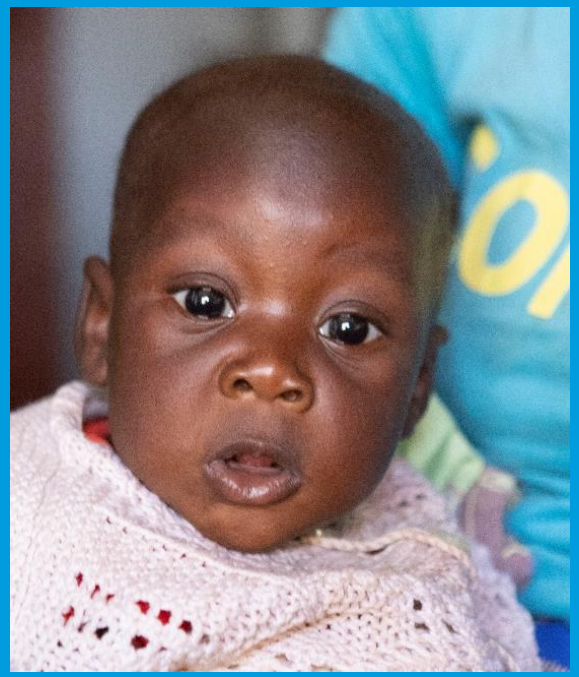
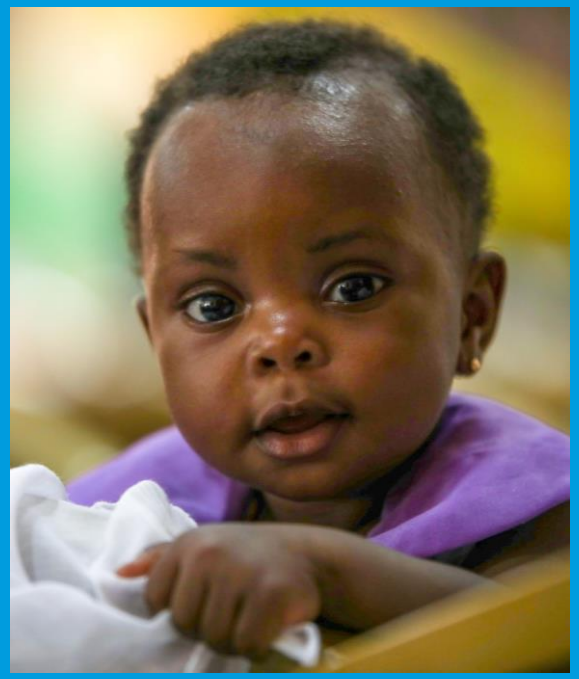
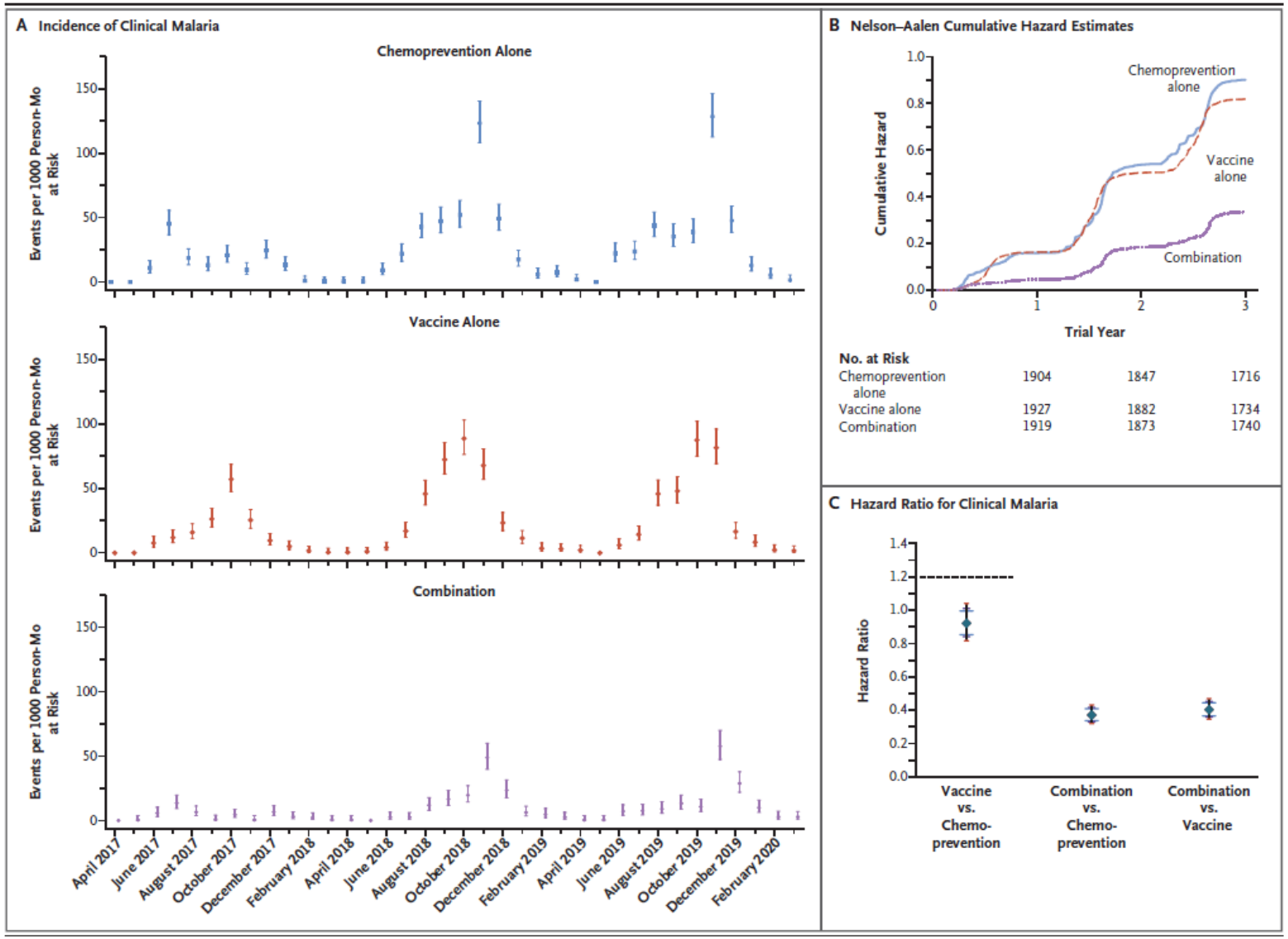




Temps pour des questions
Any questions?

Seasonal delivery of RTS,S/AS01 with and without SMC, Phase III trial, Mali and Burkina Faso



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