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Informing target product profiles for a second-generation childhood malaria vaccine: a modelling study

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INTRODUCTION

- The *P. falciparum* RTS,S/AS01 malaria vaccine demonstrated protection in phase 3 trials,[1] and will now be piloted in children in Ghana, Kenya and Malawi.
- Work is ongoing to enhance RTS,S vaccine impact, as recent evidence has indicated that dose timing and amount could impact efficacy.[2]
- Target Product Profiles (TPPs) are tools that help design and evaluate vaccine formulations. We used modelling to examine the TPP characteristics of efficacy, duration and dose timing, and considered the impact of an optimised malaria vaccine.

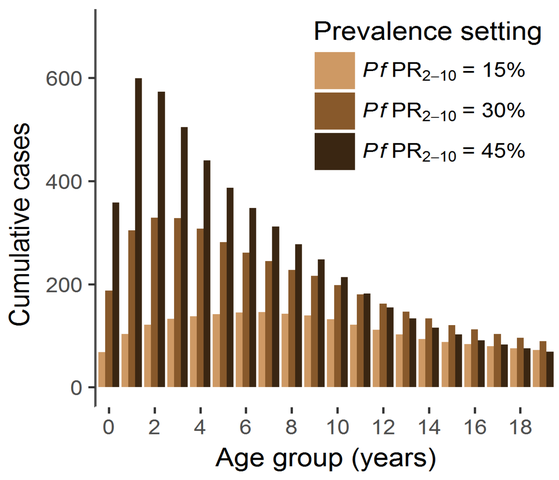


FIGURE 1
Cases over a 10-year period per 1,000 stratified by age and setting (no vaccine).

METHODS

- Individual-based mathematical model to simulate transmission,[3] coupled with antibody decay model to capture vaccine-derived protection.[4]
- Modelled a 3-dose vaccine for three vaccine efficacy profiles (Fig. 2), where the area under the efficacy curve was held constant.
- Compared current 4-dose RTS,S with a modified RTS,S,[3] and an intermediate scenario (Fig. 3).

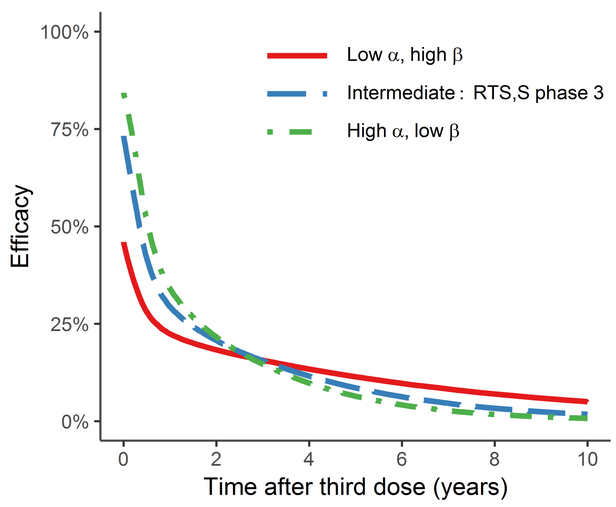
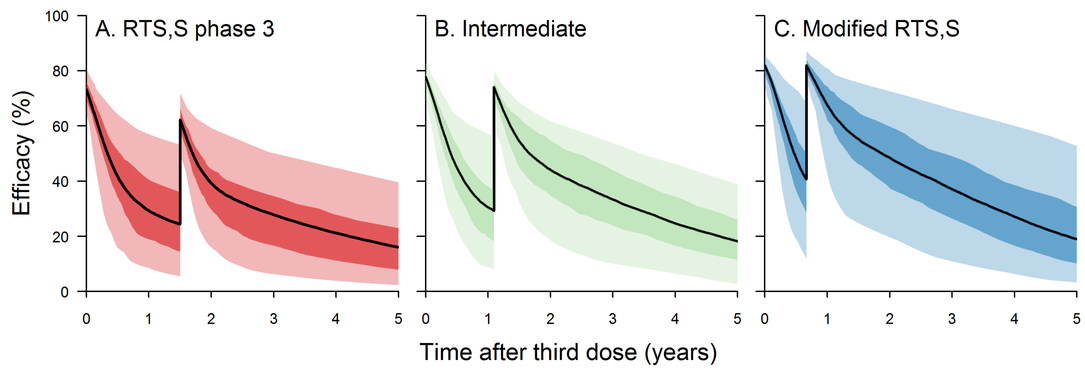


FIGURE 2
Three efficacy profiles for the 3-dose schedule, where the area under the efficacy curve

$$V(t) = V_{max}\left(1 - \frac{1}{1 + \left(\frac{CS(t)}{\beta}\right)^{\alpha}}\right)$$

is held constant. $CS(t)$ and $V_{\max}$ represent the antibody titre and maximum efficacy, and α and β approximate initial efficacy and duration.

FIGURE 3
Three vaccine efficacy scenarios for a 4-dose schedule.



RESULTS

- For a 3-dose schedule, initial efficacy was more important than duration for clinical cases averted (Fig. 4).
- This effect was more prominent in higher transmission settings, due to the concentration of malaria cases in younger age groups (Fig. 1), however there was also an age-shifting effect due to changing immunity dynamics.
- The modified vaccine was the most advantageous, but the age distribution of cases averted depended on fourth dose timing (Fig. 5).

FIGURE 4
Cumulative clinical cases (CCA) averted over 10 years per 1,000, for one-year age groups up to 20 years, for the efficacy profiles in Fig. 2.

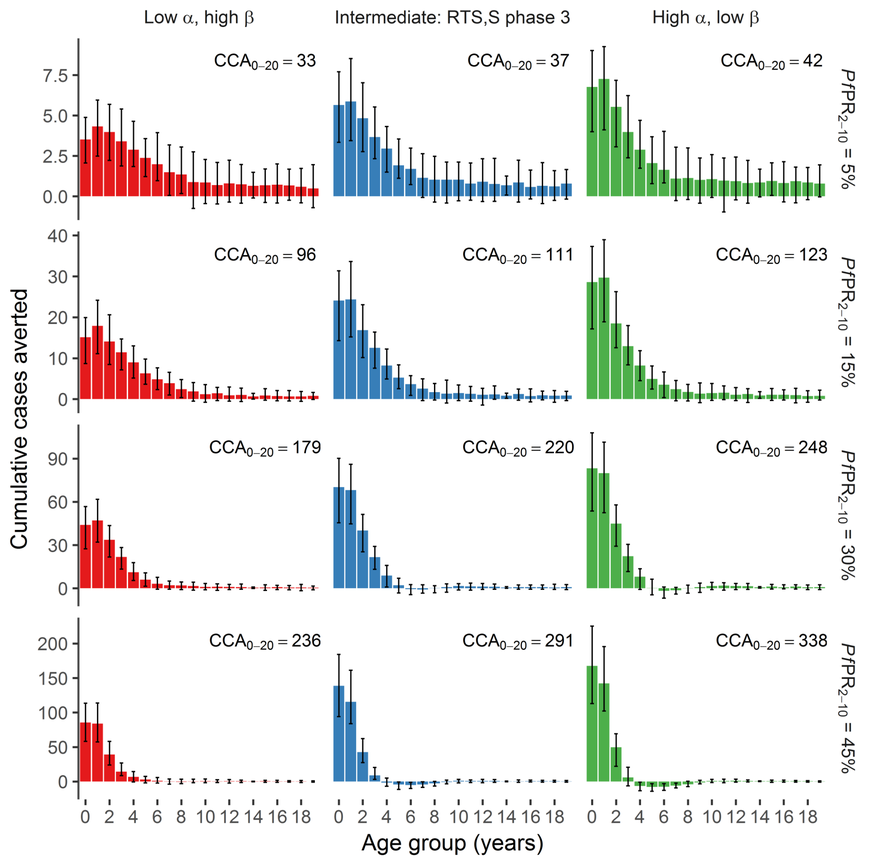
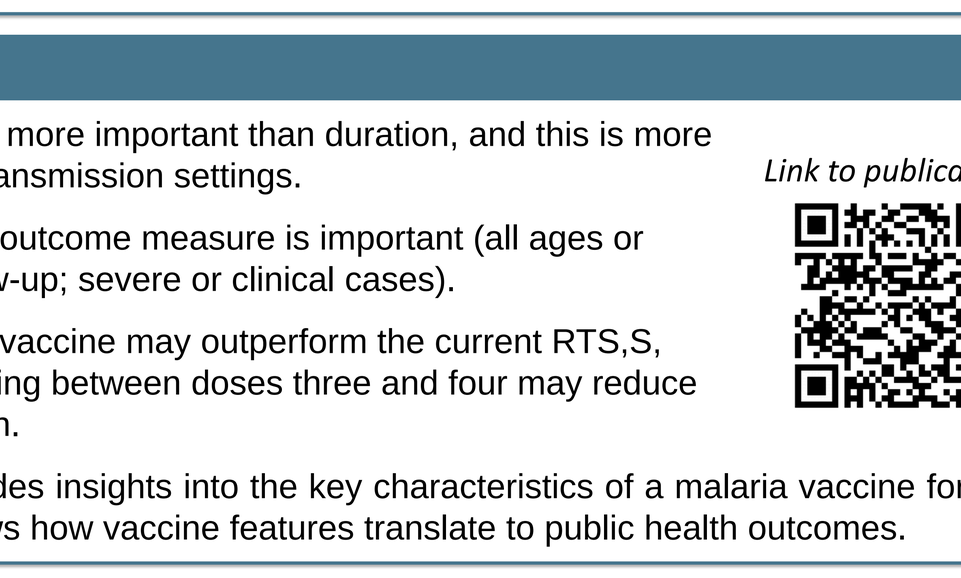


FIGURE 5
Cumulative clinical cases averted over a 10-year period per 1000, for the three efficacy profiles in Fig. 3 and four transmission settings.



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DISCUSSION

- Initial efficacy may be more important than duration, and this is more pronounced in high transmission settings.
- However, the chosen outcome measure is important (all ages or children; time of follow-up; severe or clinical cases).
- An optimised malaria vaccine may outperform the current RTS,S, but increasing the timing between doses three and four may reduce cases in older children.
- This TPP study provides insights into the key characteristics of a malaria vaccine for at-risk groups, and shows how vaccine features translate to public health outcomes.

Link to publication: