

Estimating the Spatiotemporally Heterogeneous Impact of Population and Environmental Factors on Malaria Vaccine Efficacy in Sub-Saharan Africa

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RTS,S/AS01 is the world's first malaria vaccine to be licensed and undergo pilot implementation. However, the efficacy of the vaccine in young children is variable, ranging from 22% in Mozambique to 75% in Kenya. Initial evidence suggests that vaccine efficacy is lower in sites with high-malaria incidence. Potential mechanisms include a "rebound" effect where vaccinated children may have higher cases of malaria compared to unvaccinated children over time. However, even within study sites, there may be substantial spatial heterogeneity in vaccine efficacy that is masked by overall efficacy estimates. Using data from a 5-year trial in Malawi, Ghana and Gabon, we evaluate the rebound malaria hypothesis and determine whether individual malaria incidence is modified by malaria transmission intensity in their surrounding area (MTI). We estimated MTI for each geocoded participant using remotely-sensed and survey-collected ecological variables from the natural, social and built environment using a random forest model. We then evaluated whether the relationship between vaccination and malaria incidence is modified by MTI over time. Results show substantial spatial heterogeneity within each site. Overall, while vaccinated children had lower malaria incidence within 1 year post-vaccination, estimated malaria incidence in vaccinated children increased to a rate higher than those in unvaccinated children at 4 years post-vaccination. In low-transmission settings, however, this effect is not observed. Results suggest that rebound malaria may contribute to reduced vaccine efficacy in high-transmission areas and future RTS,S vaccination campaigns should be spatially-tailored and paired with other interventions to reduce the rebound effect.

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