**Methods description for subnational tailoring of vaccine impact**

*Model*

To estimate vaccine impact, we utilised the Imperial College malaria model open-source R package [*malariasimulation*](https://mrc-ide.github.io/malariasimulation/index.html)version 2.0.1(1), a previously developed individual-based and age-stratified malaria transmission model. The model tracks several kinds of immunity, including pre-erythrocytic immunity which reduces the chance of infection upon receiving an infectious bite. Immunity to clinical disease depends on past exposure and, in infants, maternal antibodies. Immunity to severe malaria is dependent on both past exposure and age, as well as maternal antibodies. Immunity to blood stage parasitaemia reduces the chance an infection will be detected and increases with past exposure. Mortality is a fixed proportion of severe disease. *malariasimulation* incorporates input data to characterize malaria transmission in sub-Saharan Africa at the resolution of transmission intensity, demography, seasonality profiles, and coverage of non-vaccine interventions. Data on intervention coverages were sourced from the Malaria Atlas Project (MAP) and the World Malaria Report(2,3).

*Vaccine Efficacy*

We used a previously published R21 vaccine efficacy model from Schmit & Topazian(4), briefly summarized here. R21 induces an immune response to the central repeat amino acid region of the *P. falciparum* circumsporozoite protein (CSP), thereby reducing the probability of infection. First, the dynamic of CSP antibody titre over time was modelled assuming a boost upon the 3rd vaccine dose and booster dose up to peak levels, followed by a biphasic exponential decay. The R21 model was fit to Phase 2b trial data(5) from Burkina Faso over 3 years of follow up within a Bayesian framework. Vaccine efficacy beyond the 3 years of follow up in the trial is projected forwards assuming antibodies continue to decay at the same rate longer term and have the same relationship with efficacy against clinical infection.

*Modelling scenarios*

We modelled vaccine impact by running models with and without vaccination for each of the first administrative subnational units (admin-1s) in the malaria endemic countries of interest from 2000-2100. In the baseline scenario, vaccines were not introduced. These results include two vaccine scenarios where the vaccine is targeted subnationally according to the prevalence of infection in children aged 2-10:

* 10%: Vaccines were administered to children in all admin-1 units with moderate-to-high malaria transmission, defined as PFPR > 10% in 2019 according to MAP estimates(2).
* 35%: Vaccines were administered to children in all high-transmission admin-1 units, defined as PFPR > 35% in 2019 according to MAP estimates.

**Distribution of population by transmission intensity, 2019**

|  |  |  |
| --- | --- | --- |
| **Country** | **Proportion of population in vaccine implementation areas (10% PFPR threshold)** | **Proportion of population in vaccine implementation areas (35% PFPR threshold)** |
| **Nigeria** | 90% | 25% |
| **Cameroon** | 100% | 13% |
| **Democratic Republic of Congo** | 99% | 41% |

Vaccine coverage projections were sourced from Gavi scenario forecasts, which included estimated routine vaccine coverage for R21 for 31 malaria endemic countries from 2023 through 2100. We assumed that doses were delivered in an age-based strategy at 6, 7, 8, and 20 months of age.

For all modelled scenarios, we assumed constant coverage of non-malaria vaccine interventions from 2022 onwards, based on various data sources. These interventions include seasonal malaria chemoprevention (SMC), indoor residual spraying (IRS), insecticide-treated bed nets (ITNs), perennial malaria chemoprevention (PMC), and access to clinical treatment. Insecticide-treated net (ITN) usage follows a 3-year cyclical pattern based on administrated and time-based waning of net efficacy, and the pattern of the last 3-year cycle observed is carried out for the remainder of the simulation period, to capture this temporal trend.

Models were run with outputs recorded for single-year age groups up to age 20, followed by 10-year age groups from 20 to 100 years. Models were run on the admin 1 level, then aggregated up to the country level to estimate country-level cases and deaths. We applied bias correction to estimates based on World Malaria Report cases for each country, such that the average modelled number of cases from 2018-2020 approximated estimated malaria cases from the World Malaria Report in the same years. Central estimates were calculated as the average value across stochastic model runs using 50 random parameter draws each. 95% uncertainty intervals were constructed by pulling the 2.5% and 97.5% quantile values from 50 stochastic model runs. Cases and deaths averted were calculated by taking the difference between model outputs in the vaccine scenario and the no vaccination counterfactual.

**Example countries by administrative unit (admin-1) and transmission intensity**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Country** | **Admin-1** | **Urbanicity** | **PFPR (2019)** | **Transmission Intensity** |
| Democratic Republic of the Congo | Bas-Uele | rural | 0.532322 | High |
| Democratic Republic of the Congo | Haut-Katanga | rural | 0.324236 | Moderate |
| Democratic Republic of the Congo | Haut-Katanga | urban | 0.137504 | Moderate |
| Democratic Republic of the Congo | Haut-Lomami | both | 0.355668 | High |
| Democratic Republic of the Congo | Haut-Uele | both | 0.475098 | High |
| Democratic Republic of the Congo | Ituri | both | 0.366691 | High |
| Democratic Republic of the Congo | Kasai | both | 0.308079 | Moderate |
| Democratic Republic of the Congo | Kasai-Central | both | 0.419934 | High |
| Democratic Republic of the Congo | Kasai-Oriental | rural | 0.317409 | Moderate |
| Democratic Republic of the Congo | Kasai-Oriental | urban | 0.209559 | Moderate |
| Democratic Republic of the Congo | Kinshasa | both | 0.125918 | Moderate |
| Democratic Republic of the Congo | Kongo-Central | rural | 0.32279 | Moderate |
| Democratic Republic of the Congo | Kongo-Central | urban | 0.228956 | Moderate |
| Democratic Republic of the Congo | Kwango | rural | 0.382559 | High |
| Democratic Republic of the Congo | Kwilu | rural | 0.335712 | Moderate |
| Democratic Republic of the Congo | Kwilu | urban | 0.205687 | Moderate |
| Democratic Republic of the Congo | Lomami | both | 0.426975 | High |
| Democratic Republic of the Congo | Lualaba | rural | 0.449201 | High |
| Democratic Republic of the Congo | Mai-Ndombe | rural | 0.276662 | Moderate |
| Democratic Republic of the Congo | Maniema | rural | 0.289719 | Moderate |
| Democratic Republic of the Congo | Maniema | urban | 0.134748 | Moderate |
| Democratic Republic of the Congo | Mongala | both | 0.364867 | High |
| Democratic Republic of the Congo | Nord-Kivu | both | 0.169551 | Moderate |
| Democratic Republic of the Congo | Nord-Ubangi | both | 0.481297 | High |
| Democratic Republic of the Congo | Sankuru | rural | 0.242546 | Moderate |
| Democratic Republic of the Congo | Sud-Kivu | rural | 0.130273 | Moderate |
| Democratic Republic of the Congo | Sud-Kivu | urban | 0.066282 | Low |
| Democratic Republic of the Congo | Sud-Ubangi | both | 0.436878 | High |
| Democratic Republic of the Congo | Tanganyika | both | 0.342671 | Moderate |
| Democratic Republic of the Congo | Tshopo | rural | 0.537843 | High |
| Democratic Republic of the Congo | Tshopo | urban | 0.356808 | High |
| Democratic Republic of the Congo | Tshuapa | rural | 0.621827 | High |
| Democratic Republic of the Congo | Equateur | rural | 0.322495 | Moderate |
| Democratic Republic of the Congo | Equateur | urban | 0.132652 | Moderate |
| Cameroon | Adamaoua | rural | 0.265285 | High |
| Cameroon | Centre | rural | 0.354373 | Moderate |
| Cameroon | Centre | urban | 0.265726 | High |
| Cameroon | Est | rural | 0.363069 | Moderate |
| Cameroon | Extreme-Nord | both | 0.103182 | Moderate |
| Cameroon | Littoral | rural | 0.31535 | Moderate |
| Cameroon | Littoral | urban | 0.24104 | Moderate |
| Cameroon | Nord | both | 0.195777 | Moderate |
| Cameroon | Nord-Ouest | rural | 0.248696 | Moderate |
| Cameroon | Nord-Ouest | urban | 0.190259 | Moderate |
| Cameroon | Ouest | both | 0.228626 | High |
| Cameroon | Sud | rural | 0.43029 | Moderate |
| Cameroon | Sud-Ouest | both | 0.284795 | Moderate |
| Nigeria | Abia | rural | 0.502311 | High |
| Nigeria | Abia | urban | 0.429444 | High |
| Nigeria | Adamawa | both | 0.279808 | Moderate |
| Nigeria | Akwa Ibom | rural | 0.494907 | High |
| Nigeria | Akwa Ibom | urban | 0.441538 | High |
| Nigeria | Anambra | both | 0.23806 | Moderate |
| Nigeria | Bauchi | both | 0.139718 | Moderate |
| Nigeria | Bayelsa | rural | 0.314616 | Moderate |
| Nigeria | Bayelsa | urban | 0.229068 | Moderate |
| Nigeria | Benue | rural | 0.325421 | Moderate |
| Nigeria | Benue | urban | 0.252116 | Moderate |
| Nigeria | Borno | both | 0.144969 | Moderate |
| Nigeria | Cross River | both | 0.391381 | High |
| Nigeria | Delta | rural | 0.2282 | Moderate |
| Nigeria | Delta | urban | 0.171889 | Moderate |
| Nigeria | Ebonyi | both | 0.36519 | High |
| Nigeria | Edo | rural | 0.304134 | Moderate |
| Nigeria | Edo | urban | 0.214821 | Moderate |
| Nigeria | Ekiti | rural | 0.470331 | High |
| Nigeria | Ekiti | urban | 0.418433 | High |
| Nigeria | Enugu | rural | 0.220491 | Moderate |
| Nigeria | Enugu | urban | 0.168109 | Moderate |
| Nigeria | Federal Capital Territory | both | 0.247178 | Moderate |
| Nigeria | Gombe | both | 0.24779 | Moderate |
| Nigeria | Imo | both | 0.455755 | High |
| Nigeria | Jigawa | both | 0.095275 | Low |
| Nigeria | Kaduna | rural | 0.221747 | Moderate |
| Nigeria | Kaduna | urban | 0.171549 | Moderate |
| Nigeria | Kano | both | 0.08231 | Low |
| Nigeria | Katsina | both | 0.106946 | Moderate |
| Nigeria | Kebbi | both | 0.262783 | Moderate |
| Nigeria | Kogi | both | 0.242077 | Moderate |
| Nigeria | Kwara | rural | 0.439438 | High |
| Nigeria | Kwara | urban | 0.363361 | High |
| Nigeria | Lagos | both | 0.214255 | Moderate |
| Nigeria | Nassarawa | both | 0.28126 | Moderate |
| Nigeria | Niger | rural | 0.298385 | Moderate |
| Nigeria | Niger | urban | 0.232999 | Moderate |
| Nigeria | Ogun | rural | 0.436581 | High |
| Nigeria | Ogun | urban | 0.33048 | Moderate |
| Nigeria | Ondo | rural | 0.446564 | High |
| Nigeria | Ondo | urban | 0.368013 | High |
| Nigeria | Osun | rural | 0.517068 | High |
| Nigeria | Osun | urban | 0.428434 | High |
| Nigeria | Oyo | rural | 0.548649 | High |
| Nigeria | Oyo | urban | 0.392769 | High |
| Nigeria | Plateau | rural | 0.19576 | Moderate |
| Nigeria | Plateau | urban | 0.144794 | Moderate |
| Nigeria | Rivers | both | 0.294277 | Moderate |
| Nigeria | Sokoto | both | 0.21078 | Moderate |
| Nigeria | Taraba | both | 0.329687 | Moderate |
| Nigeria | Yobe | both | 0.14188 | Moderate |
| Nigeria | Zamfara | both | 0.198289 | Moderate |

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