AnophelesModel: An R package to interface mosquito bionomics, human exposure and intervention effects with models of malaria intervention impact

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Abstract

In recent decades, field and semi-field studies of malaria transmission have gathered geographic-specific information about mosquito ecology, behaviour and their sensitivity to interventions. Mathematical models of malaria transmission can incorporate such data to infer the likely impact of vector control interventions and hence guide malaria control strategies in various geographies. To facilitate this process and make model predictions of intervention impact available for different geographical regions, we developed AnophelesModel. AnophelesModel is an online, open-access, R package that directly allows incorporating generated entomological data for adjustment of models to assess intervention scenarios according to species and location-specific characteristics. In addition, it includes a previously published, comprehensive, curated database of field entomological data from over 50 *Anopheles* species, field data on mosquito and human behaviour, and on estimates of vector control effectiveness. Using the input data, the package parameterizes a discrete-time, state transition model of the mosquito oviposition cycle and infers species-specific impacts of various interventions on vectorial capacity. In addition, it offers formatted outputs ready to use in downstream analyses and by other models of malaria transmission for accurate representation of the vector-specific components. Using AnophelesModel, we show how the key implications for intervention impact change for various vectors and locations. The package facilitates quantitative comparisons of likely intervention impacts in different geographical settings varying in vector compositions, and can thus guide towards more robust and efficient malaria control recommendations. The AnophelesModel R package is available under a GPL-3.0 license at https://github.com/SwissTPH/AnophelesModel.

Introduction

Vector control targeting *Anopheles* (*An.*) mosquitoes and protecting people from their dangerous, malaria-infectious bites has been the predominant way of reducing the malaria burden worldwide (1). Over 220 million insecticide-treated nets (ITNs), the most common vector control tool, were distributed in 2021 (2), but the impact of these and other vector control interventions varies geographically depending on multiple factors. These factors include intra and inter-species heterogeneity in the characteristics of the vectors and geographical variation in vector species composition. *Anopheles* mosquitoes have a complex life-cycle, continuously adapting to and evolving with the surrounding environment. The species native to Africa can be very different to those found elsewhere (3). The interactions of circadian mosquito biting patterns and the behavioural patterns of humans are particularly relevant for the risk of human exposure to mosquitoes. Recent studies have emphasized the importance of considering these factors when estimating the geographic-specific impact of vector control interventions and for implementing vector control strategies (4-8). Additionally, the physical and chemical properties of the various interventions, such as the physical integrity and insecticide efficiency of ITNs and how each of these vary over time, also strongly impact the effectiveness of vector control (9-11).

Mathematical models of malaria transmission are frequently used to integrate quantitative evidence about the effects of malaria interventions to enhance prediction of impact and planning of interventions (12-14). This type of modelling has become an important part of decision-making, in particular for guiding national malaria strategic plans in malaria-endemic countries (15-17). For the models to accurately quantify the impacts of interventions, data from experimental hut trials and cluster-randomized control trials (9, 18-26) are generally used to parameterize their effects (12, 27-31). Nonetheless, model parameterizations should also consider local variations in human behaviour and thus human exposure to mosquito bites. Considering human behavioural data and setting-specific differences in mosquito biting and bionomics can improve model predictions of intervention effectiveness (5).

Integrating human activity, mosquito biting patterns and other entomological characteristics to adjust the estimated impact of vector control interventions comes with its challenges. Many independent studies with different experimental techniques and data recording approaches are involved. Comprehensive data are rarely collected at the same location and time. Several existing models and studies account for the life parameters of mosquitoes estimated from entomological data and have combined information on mosquito biting and human activity (7, 8, 30, 32-34). However, these are only a few studies and have been limited to a handful of locations. A comprehensive framework collating the different data types, allowing for direct data integration and interfacing with models to estimate location-specific intervention impact in a systematic way has been lacking.

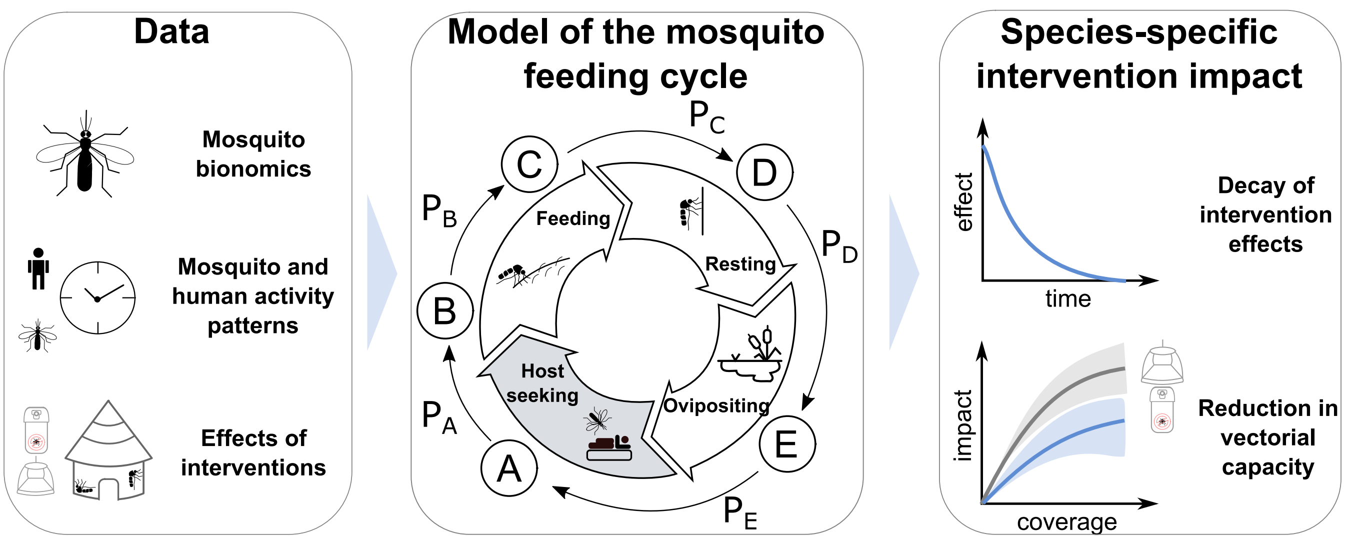

Figure 1: Overview of the AnophelesModel R package and its components. The package integrates several types of data (first panel) to estimate how vector control interventions affect transitions between the different states of the mosquito feeding cycle (states of the cycle denoted with letters A – E in the middle panel with transition probabilities P_A – P_E). Within the package, an entomological model is parameterised and used to infer the species-specific effects of vector control interventions, including their decay over time as well as their impact on the vectorial capacity (third panel).

Building on previous modelling of the mosquito feeding cycle (32) and of vector control impact (9, 28, 30), we have developed the AnophelesModel R package (Fig 1) to address these challenges. AnophelesModel estimates the species and geographic-specific impact of vector control interventions by allowing the user to directly integrate several layers of input data representing mosquito bionomic characteristics, mosquito and human activity patterns, human exposure to mosquitoes, and the effects of interventions.

Design and Implementation

AnophelesModel uses the data provided by the user to parameterize a mathematical model describing the mosquito feeding cycle (32) which infers how the state to state transitions within the feeding cycle are affected by different interventions, considering their decay over time. Thus, the model estimates the reduction in vectorial capacity for a given intervention. The package allows the user to run analyses for interventions and species-bionomics with self-provided data. It can compare multiple interventions in terms of their effect on vectorial capacity for various mosquito species across a range of geographical settings. Furthermore, it produces ready-to-use outputs which can be plugged into established models of malaria transmission dynamics such as OpenMalaria (35, 36).

Entomological model of the mosquito feeding cycle and vectorial capacity

Mosquito feeding dynamics are represented through a previously described state-transition model (Fig 1, middle panel) that simulates the feeding behaviour of female mosquitoes from a population (32).

Briefly, the model quantifies the probabilities of mosquito survival across five stages of the feeding cycle: host seeking, feeding, searching for a resting place, resting, and ovipositing. The total numbers of host seeking, infected and infectious (sporozoite positive) mosquitoes are modelled through a system of difference equations with one-day time steps. In the absence of intervention pressure, the stage-specific survival probabilities are assigned the values derived in *Chitnis et al.* (32). Intervention effects are modelled through reductions in these probabilities. The vectorial capacity, defined as the total number of subsequent infectious mosquito bites originating from each mosquito biting a human infected with malaria, is calculated analytically using the formulation derived in *Chitnis et al.* (32) and constitutes a proxy for the intervention impact.

Mosquito bionomics data

The feeding cycle model relies on quantified ecological and bionomic characteristics of the mosquitoes, including the parous rate, the human blood index, the sac rate, their endophily and endophagy. AnophelesModel allows the user to input their own data and tailor the entomological model to the vector species of interest. Additionally, it also harbours an extensive database of relevant parameters collated from published literature and publicly available sources. Using a Bayesian hierarchical model applied to previously-published entomological data (30, 37, 38), mosquito bionomic parameters were derived for *57 Anopheles* species and 17 complexes (groupings of sibling species) and included in the package.

Modelling the effects of vector control interventions on the mosquito feeding cycle

The protective effects of vector control interventions used in the AnophelesModel package are defined in terms of the reduction in the proportion of mosquitoes reaching each stage in the feeding cycle (Fig 1 middle panel). There are three main effects modelled:

- Deterrency: the reduction in the availability rate of humans to mosquitoes per day, estimated based on the proportion of mosquitoes that fail to reach a protected human or are deterred from biting due to intervention
- Pre-prandial killing: the proportion of mosquitoes that are killed before feeding
- Post-prandial killing: the proportion of mosquitoes that are killed after feeding

The user can directly input these effects and use the package to conduct impact analysis for the interventions of their choice. In addition, a couple of parameterisations for intervention effects are already available in the package for long-lasting insecticide-treated nets (LLINs), indoor residual spraying (IRS) and house screening. These effects have been estimated using previously published intervention models (Table S1). Accordingly, they have been parameterised with data generated from experimental hut trials and adjusted according to the intervention-specific temporal decay functions, measuring attrition, change in use, insecticide decay and physical deterioration for LLINs, and insecticide decay for IRS (9, 28, 30).

Each intervention is assigned a duration corresponding to the time between consecutive deployments (e.g., 3 years for LLINs and 0.5 years for IRS). The effects and the resulting reduction in vectorial capacity are calculated for a finite number of equally spaced time points throughout this duration (denoted as interpolation points in the package). All intervention effects are adjusted for the exposure of humans to mosquitoes as described in the section below.

Modelled effects of LLINs included in the package

A previously published system of logistic regression models (9, 30) can be used with the package to estimate the effects of LLINs deployments (cf. Supplementary Material). The decay of physical properties of mosquito nets in terms of attrition, use, physical and chemical integrity has been estimated using the data from the President Malaria Initiative (PMI) net durability studies (39), and on data from Morgan *et al.* (40) as described in *Briet et al.* (9) (cf. Supplementary Material). These datasets, containing properties of various net types in different countries, are also included in the package.

Modelled effects of IRS included in the package

The package includes several parameterisations of IRS effects for different insecticide and vector species combinations (cf. Supplementary Material) derived using experimental data from previous studies (23-26, 41).

Effects of house screening included in the package

The effect of house screening interventions available in the package is assumed to be a linear relationship with the availability of humans to mosquitoes, with a 59% reduction as estimated in (30) based on data from Belize (42) and Ghana (43).

Integrating mosquito and human activity patterns, estimating human exposure to mosquitoes

AnophelesModel implements a novel approach which allows using input data on biting rhythms and human activity to adjust the effects of vector control interventions depending on the exposure of humans to mosquito biting, endophily (the proportion of indoor resting mosquitoes) and endophagy (the proportion of indoor feeding mosquitoes). Precisely, the deterrency, pre-prandial and post-prandial killing effects of the interventions are adjusted by multiplying them by the corresponding setting-specific exposure coefficient. A detailed description of this approach is provided in the Supplementary Material. AnophelesModel also includes ready-to-use data on biting rhythms and human activity recently compiled by Sherrard-Smith *et al.* (7). In addition, the package database contains entries from a non-systematic sample of publications (44-53).

Interfacing with models of malaria transmission dynamics

In addition to providing estimates of intervention effects on vectorial capacity, the AnophelesModel package estimates the decay of intervention effects over time and generates parameterizations of vector control components which may be used for running simulations with the OpenMalaria model. OpenMalaria is an agent-based, stochastic model of malaria transmission dynamics and it has been extensively described in previous publications (13, 35, 36, 54). It can be used to simulate malaria transmission within a population of individuals, deploy interventions and estimate their impact on malaria burden over time.

OpenMalaria requires a configuration file in XML format which includes all the specifications of a simulation. The objects required for modelling vector characteristics and the effects of vector control interventions in OpenMalaria are XML snippets for inclusion in the scenario XML. Entomological characteristics are defined through an entomology XML snippet and intervention effects can be defined through the "*generic vector intervention*" (GVI) XML snippet (further information about OpenMalaria XML definitions is provided at https://github.com/SwissTPH/openmalaria/wiki). The GVI snippet includes the definition of decay and initial effect parameters for deterrency, pre- and post-prandial killing effects of interventions. In OpenMalaria, the intervention effects modelled through GVI components can be associated one of seven possible decay functions. AnophelesModel uses nonlinear least squares (R package minpack.lm version 1.2-2) to fit in turn each of the seven decay functions to the time series of estimated intervention effects and chooses the decay with the best fit (smallest residual sum of squares). The XML components needed for OpenMalaria simulation specifications can then be generated with the package.

Results

To illustrate the functionalities of the package, we provide examples using the data included in the package for two mosquito species, namely *Anopheles farauti* and *Anopheles gambiae* and compare the effects of LLINs deployments. All the code used in the analysis presented in this paper is included in the package GitHub repository (see section Availability and Future Directions).

Visualising human, mosquito and intervention characteristics

The AnophelesModel package can provide visualisations of the entomological characteristics of mosquito species at different locations and model how these impact various vector control interventions. One resource included in the package is a readily available database encompassing human activity patterns, mosquito biting patterns, mosquito entomological characteristics and intervention characteristics. The user can directly access the various data types through dedicated data objects. A detailed description of these data objects is provided in the package documentation.

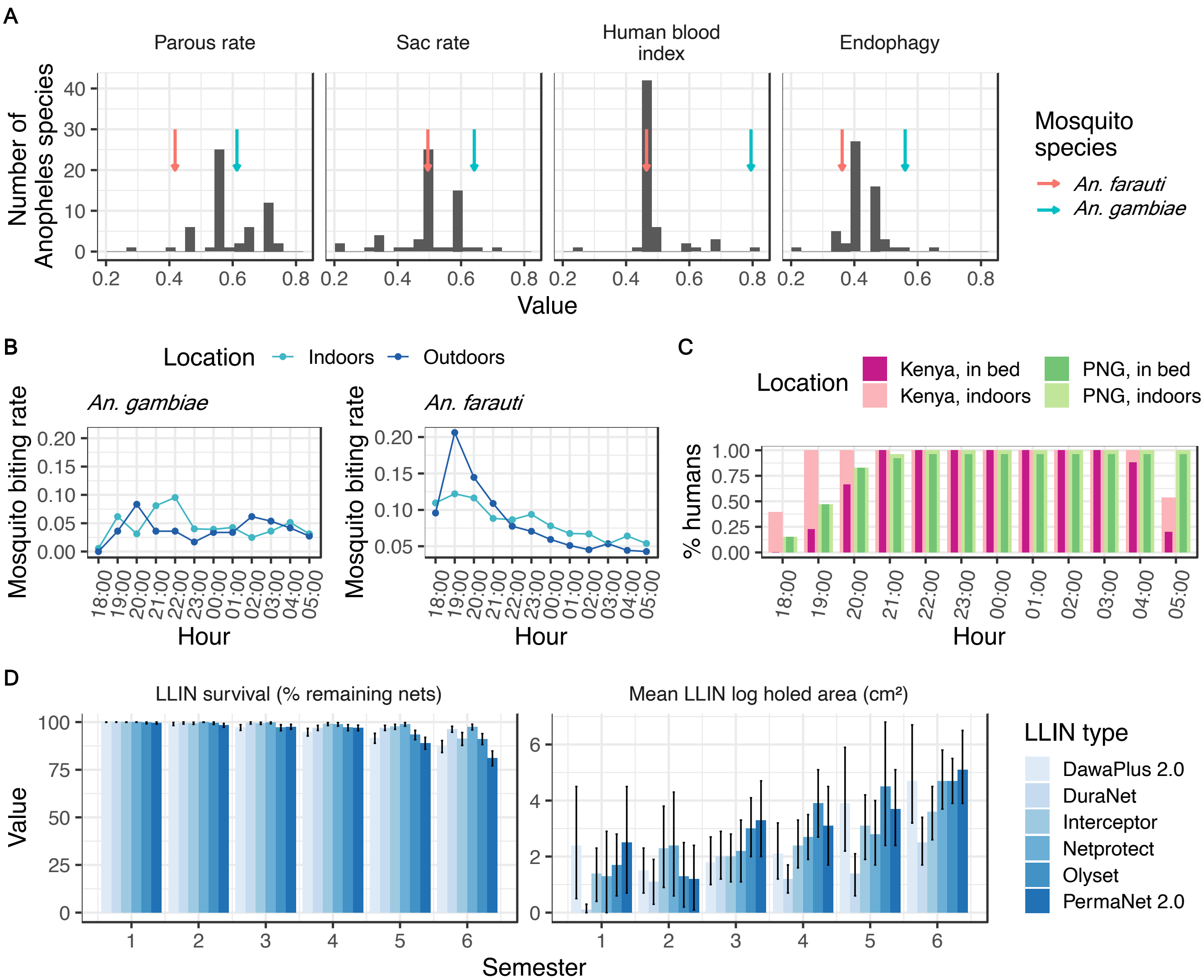

Figure 2: Examples of the key types of data available within the AnophelesModel database which can be used to estimate the impact of vector control interventions. In the package, entomological parameters **(A)**, mosquito biting patterns **(B)**, human activity patterns **(C)** and intervention properties **(D)** are provided and can be used to parameterise an entomological model of the mosquito feeding cycle. Examples are provided for *An. gambiae* and *An. farauti* in Kenya and Papua New Guinea (PNG) settings, respectively. In panel **(A)**, the arrows indicate the bars corresponding to the two mosquito species. In panel **(B)**, the grey area highlights the time when people sleep under a net. Panel **(D)** summarizes the observed variation in physical properties of LLINs in a Kenya-like setting (9). Data sources of all data types are specified in the "Design and Implementation" section.

The package database can be queried, for example to analyse how *An. gambiae*, among the dominant malaria vectors in sub-Saharan Africa (55), differs from *An. farauti*, a major vector in Papua New Guinea (PNG) (Fig 2). The two species are different not only in their bionomics, but also in terms of their biting patterns. *An. gambiae* has higher parous rates, sac rates, and human blood index, and is more endophagic than *An. farauti* (Fig 2A). Furthermore, *An. gambiae* preferentially bites indoors during the night, while *An. farauti* also bites outdoors, especially in the early evening (Fig 2B). These differences all affect the modelled impacts of interventions such as LLINs. In the following example, we demonstrate how AnophelesModel can be used to compare the impacts of LLINs for these two species in their respective settings mainly relying on the data present in the package database, and incorporating new, recently published data on human behaviour for a PNG-like setting (56) (Fig 2C).

Quantifying and comparing the species-specific impact of vector control interventions

We used AnophelesModel to incorporate the different mosquito, human and intervention data (Fig 2) and to model the effects of LLINs for the two species using distinct values for deterrency, pre- and post-prandial killing effects for the two settings. We estimated higher effects of LLINs for *An. gambiae* in the Kenyan-like setting compared to *An. farauti* in the PNG-like setting (Fig 3A), and a correspondingly higher reduction in vectorial capacity for *An. gambiae* in the Kenyan setting (Fig 3B).

The effectiveness of a vector control intervention is influenced by both its chemical and physical properties, and by the alignment of its temporal effects with the circadian rhythms of human behaviour and the mosquito biting patterns. With human presence indoors and in bed exhibiting the patterns shown in Fig 2C, a substantial proportion of the bites from *An. farauti* occur in the early evening when people are not yet sleeping under a net, in contrast to *An. gambiae*, which mostly bites at night. Thus, as found in previous analyses of the African data (7), the mosquito and human activity patterns strongly affect the estimated impact of vector control interventions, even when the physical and chemical durability of the mosquito nets are uniform (Fig 2D).

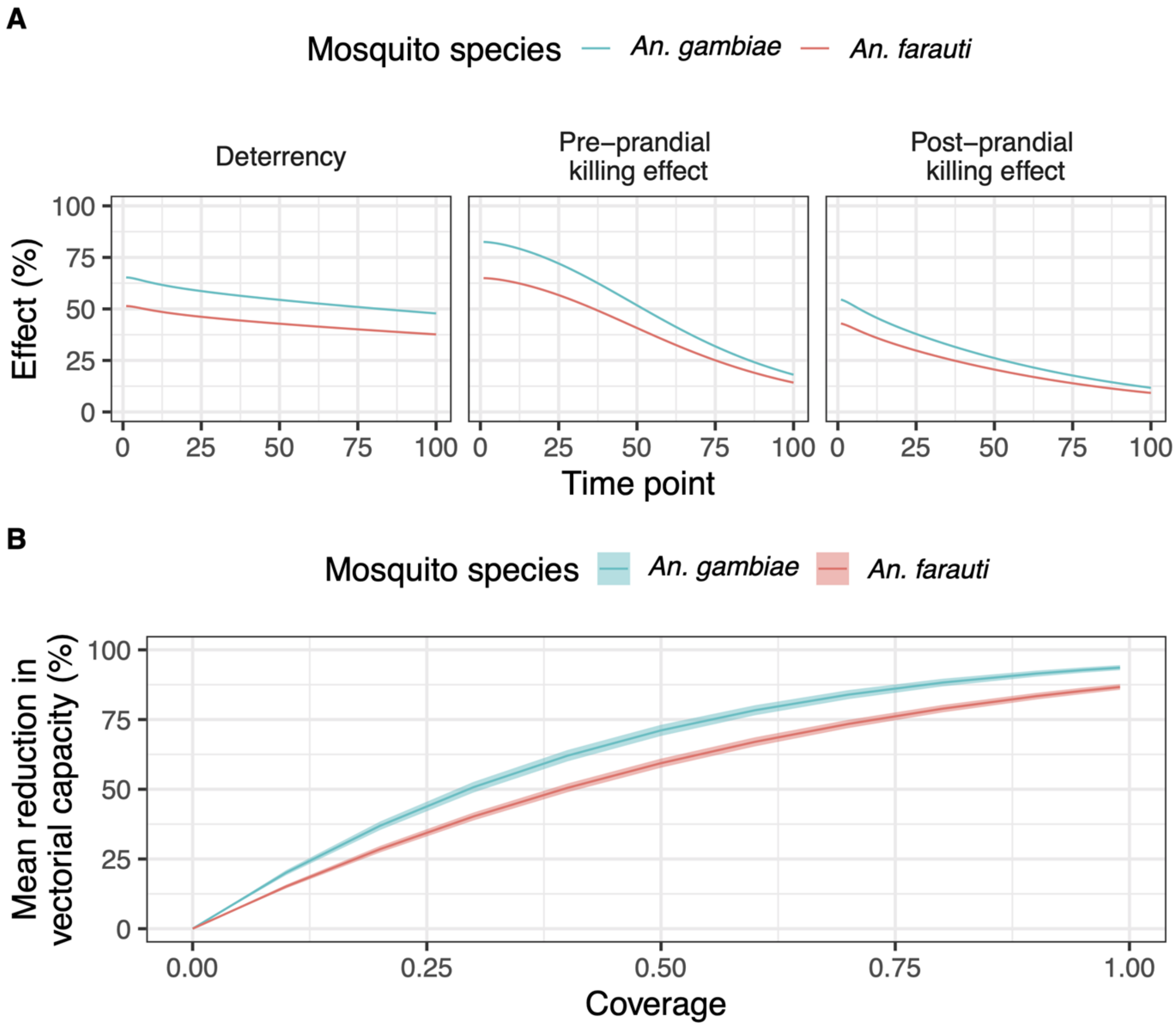

Figure 3: Estimated effects of LLINs deployment for *An. gambiae* and *An. farauti*. Mosquito, human and intervention data are combined in the AnophelesModel package to estimate the different types of intervention decay throughout time **(A)**, as well as the resulting mean reduction in vectorial capacity for varying LLINs deployment coverages (here equivalent to LLINs usage) **(B)**. The time units in panel **(A)** are defined by 100 equally distanced interpolation points across the duration of the interventions (i.e., 3 years for LLINs). The ribbons in panel **(B)** correspond to the variation of the vectorial capacity estimated

based on the confidence intervals of the mosquito bionomics parameters (details on uncertainty propagation provided in the Supplementary Material).

Similar to the examples provided for *An. gambiae* and *An. farauti*, the AnophelesModel package can be used to estimate and compare how the effects of interventions vary for other mosquito species and geographical locations. The user is not limited to the package database, but can input new data and use these in the modelling. The package documentation provides further examples illustrating the use of new data and also reproducing previously published analyses comparing *An. gambiae* and *An. albimanus* (30).

Interfacing AnophelesModel with models of intervention impact and malaria transmission

The estimated, exposure-adjusted effects of interventions (Fig 3) can be further incorporated in downstream analyses and models of malaria transmission dynamics. In particular, AnophelesModel contains functions for producing formatted entomology and intervention input for the OpenMalaria model.

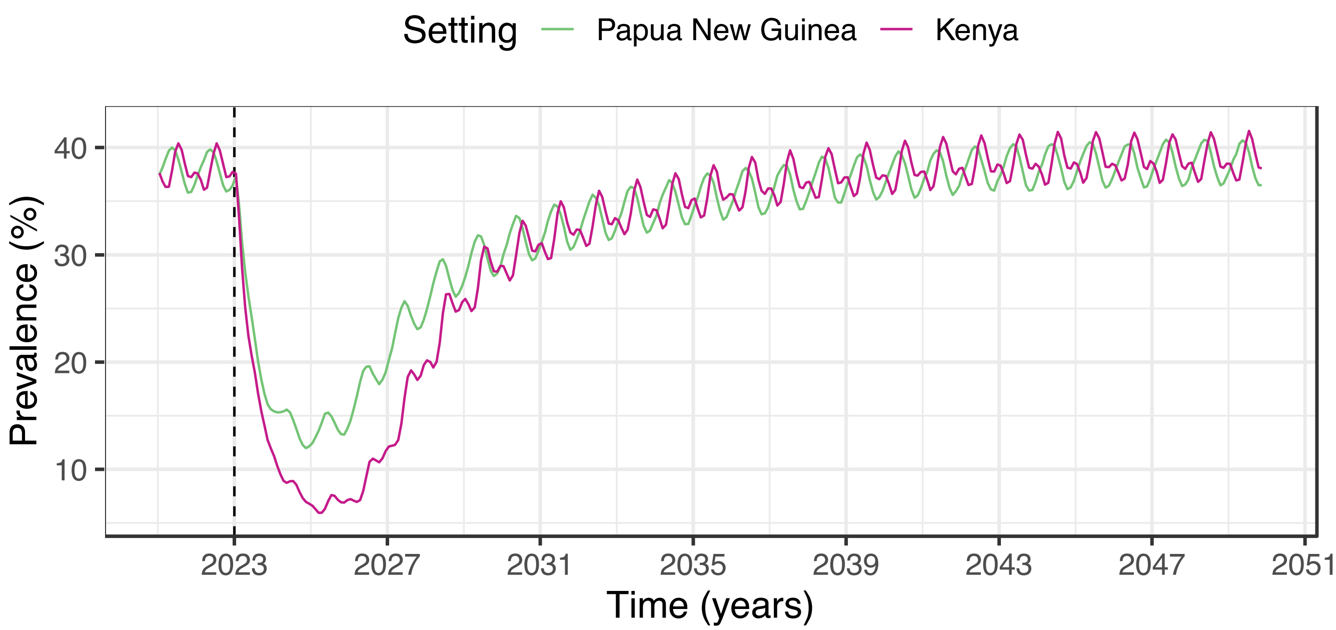

Figure 4: Simulation of the impact of LLINs deployment in OpenMalaria. XML snippets produced by AnophelesModel were used in OpenMalaria to model the entomology and effects of LLINs deployments in Kenyan-like and PNG-like settings and to simulate all-age prevalence. One deployment of LLINs was simulated in January 2023 (dashed line).

For illustrating using OpenMalaria the example considering the Kenyan-like and PNG-like settings described before (Fig 2-3), we informed the model parameters regarding seasonality of transmission, entomological, and vector control interventions with geographic-specific values. To do so, we estimated the geographic-specific entomological parameters (Fig 2A) and intervention effects decays (Fig 3A) of LLINs deployment using AnophelesModel and further incorporated them in OpenMalaria simulations of malaria dynamics. OpenMalaria version 44 was used for this analysis. Populations of 10,000 people in each setting were simulated starting January 1999, with a single LLINs deployment in January 2023 at 60% coverage. Case management was the only other intervention present in the simulation, deployed from the beginning, and was set to 50% effective coverage for both settings. Coverage of an intervention was defined as the proportion of people protected against malaria infection by that intervention.

For simplicity, in this simulation example, malaria transmission was treated as proportional to monthly rainfall, an assumption that is not implicit in real-world settings. Rainfall data was extracted from WorldClim (57) and shifted by a lag period of 30 days to consider the delay in mosquito density, emergence and infection. The Kenyan-like simulation used the rainfall profile of the Kisumu region, and the PNG-like simulation that of the Momase region. For the sake of comparison, the transmission intensity prior to start of the interventions deployment was considered similar in both settings by choosing an initial annual entomological inoculation rate of 15 infective bites per person per year for both simulated settings.

Plasmodium falciparum prevalence in all ages over time was simulated for the two settings (Fig 4). As expected, the impact in reducing prevalence by LLINs deployment was lower in the PNG-like setting compared to the Kenya-like setting. By allowing accurate incorporation of intervention effects in models of malaria transmission such as OpenMalaria, AnophelesModel facilitates exploring further, more complex intervention scenarios, such as combining vector control with drug interventions or supplementing the LLINs deployments with other interventions potentially targeting outdoor biting in PNG.

Availability and Future Directions

The AnophelesModel R package source code and data are publicly available online in a dedicated GitHub repository at https://github.com/SwissTPH/AnophelesModel. A user-friendly website available at https://swisstph.github.io/AnophelesModel/index.html provides package installation instructions, comprehensive descriptions of functions, parameters and data, and detailed examples of use-cases. A systematic tutorial and documentation of the different package functions are provided at https://swisstph.github.io/AnophelesModel/articles/AnophelesModel.html. Furthermore, all code used for the examples presented in this paper and for generating the corresponding figures is available at https://github.com/SwissTPH/AnophelesModel/tree/main/extdata. This include the XML files and scripts used for OpenMalaria simulations.

Patterns of human exposure to mosquitoes alongside mosquito bionomics should always be considered when using impact modelling to make decisions about vector control options in different geographical settings (4, 5, 7). For this purpose, the AnophelesModel package combines these different types of data to provide inputs into malaria models. In this paper, we have provided an example describing how to use the package outputs with the OpenMalaria model (35, 36). In the presented analysis, following inclusion of the exposure-adjusted intervention effects in OpenMalaria, we observed a clear difference in public health impact of LLINs deployment between the Kenya-like and PNG-like settings with similar pre-intervention transmission prevalence.

The value and usability of the package, as well as its interfacing with other models, have been already demonstrated in other published applications. For example, in a recently published study, AnophelesModel was used to inform the impact of vector control in a compartmental model of *Plasmodium vivax* malaria dynamics applied to identify malaria transmission hotspots in Panama (58). Furthermore, the package has been incorporated in a mathematical modelling framework to quantify the country-specific impact of interventions against *Plasmodium vivax* malaria (59).

The AnophelesModel package is flexible beyond the provided database, allowing the user to plug in new data and parameters and model intervention effects for a custom setting. The package database is not exhaustive and does not account for seasonal variation or variation by human age or occupational group. The package is a powerful tool for exploring how the impact of vector control interventions changes following the observed variation in input mosquito biting and human behaviour patterns.

Planned developments of the AnophelesModel package include extension of the database of mosquito, human behaviour and intervention characteristics through systematic reviews, including more recently-generated data and intervention models. Currently three interventions are modelled within the package, namely IRS, LLINs and house screening, but other interventions such as spatial repellents and attractive toxic sugar baits will be added in the future.

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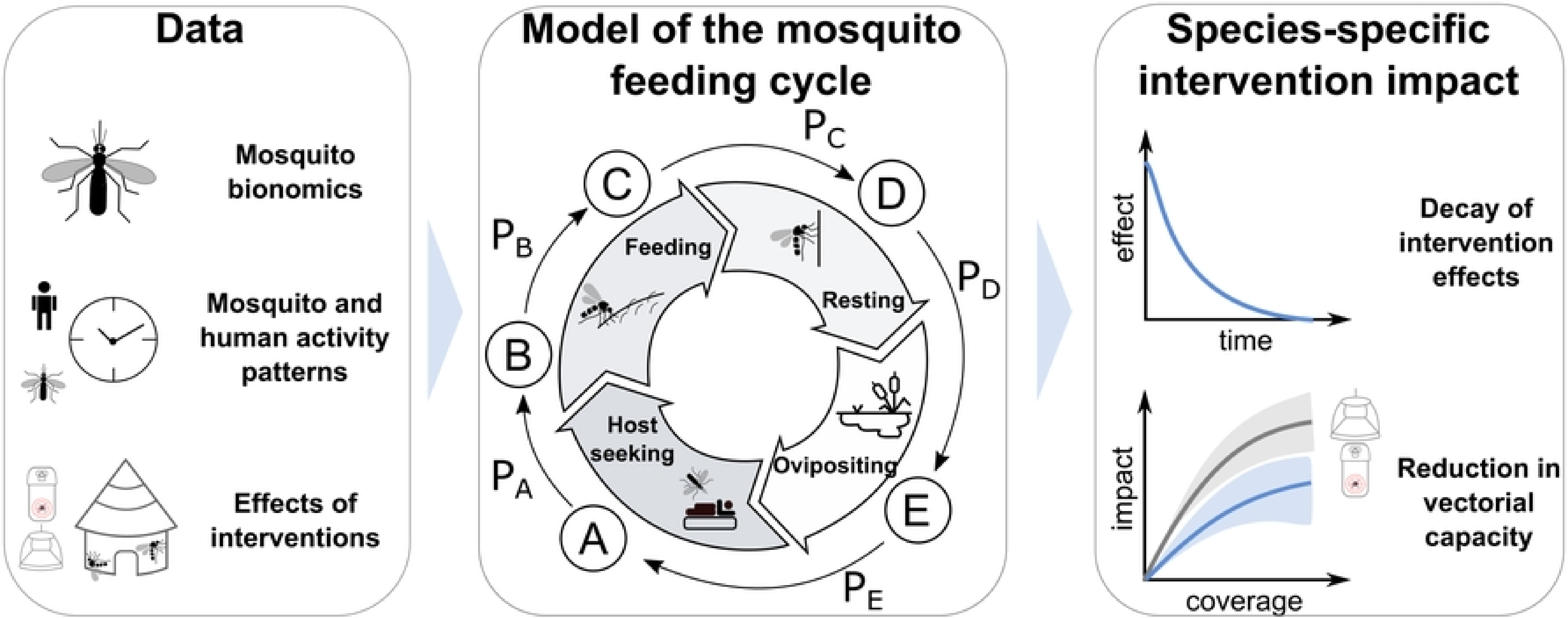

Data
Mosquito bionomics
Mosquito and human activity patterns
Effects of interventions
Model of the mosquito feeding cycle
P_C
P_B
P_D
P_A
P_E
A
B
C
D
E
Feeding
Resting
Host seeking
Ovipositing
Species-specific intervention impact
effect
time
Decay of intervention effects
impact
coverage
Reduction in vectorial capacity

Figure 1

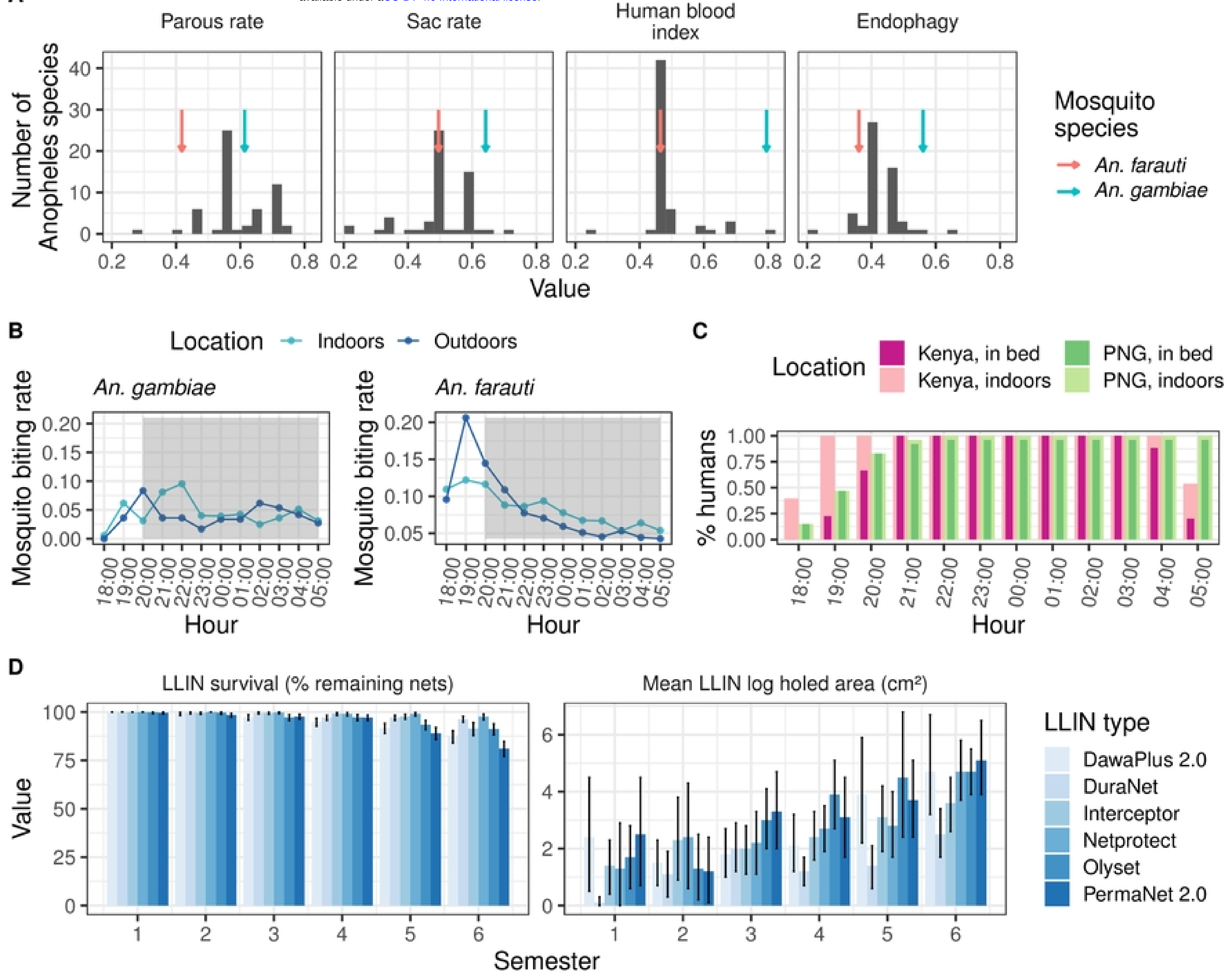
A
Parous rate
Sac rate
Human blood index
Endophagy
Number of Anopheles species
Value
Mosquito species
An. farauti
An. gambiae
B
Location
Indoors
Outdoors
An. gambiae
An. farauti
Mosquito biting rate
Hour
C
Location
Kenya, in bed
Kenya, indoors
PNG, in bed
PNG, indoors
% humans
Hour
D
LLIN survival (% remaining nets)
Mean LLIN log holed area (cm²)
Value
Semester
LLIN type
DawaPlus 2.0
DuraNet
Interceptor
Netprotect
Olyset
PermaNet 2.0

Figure 2

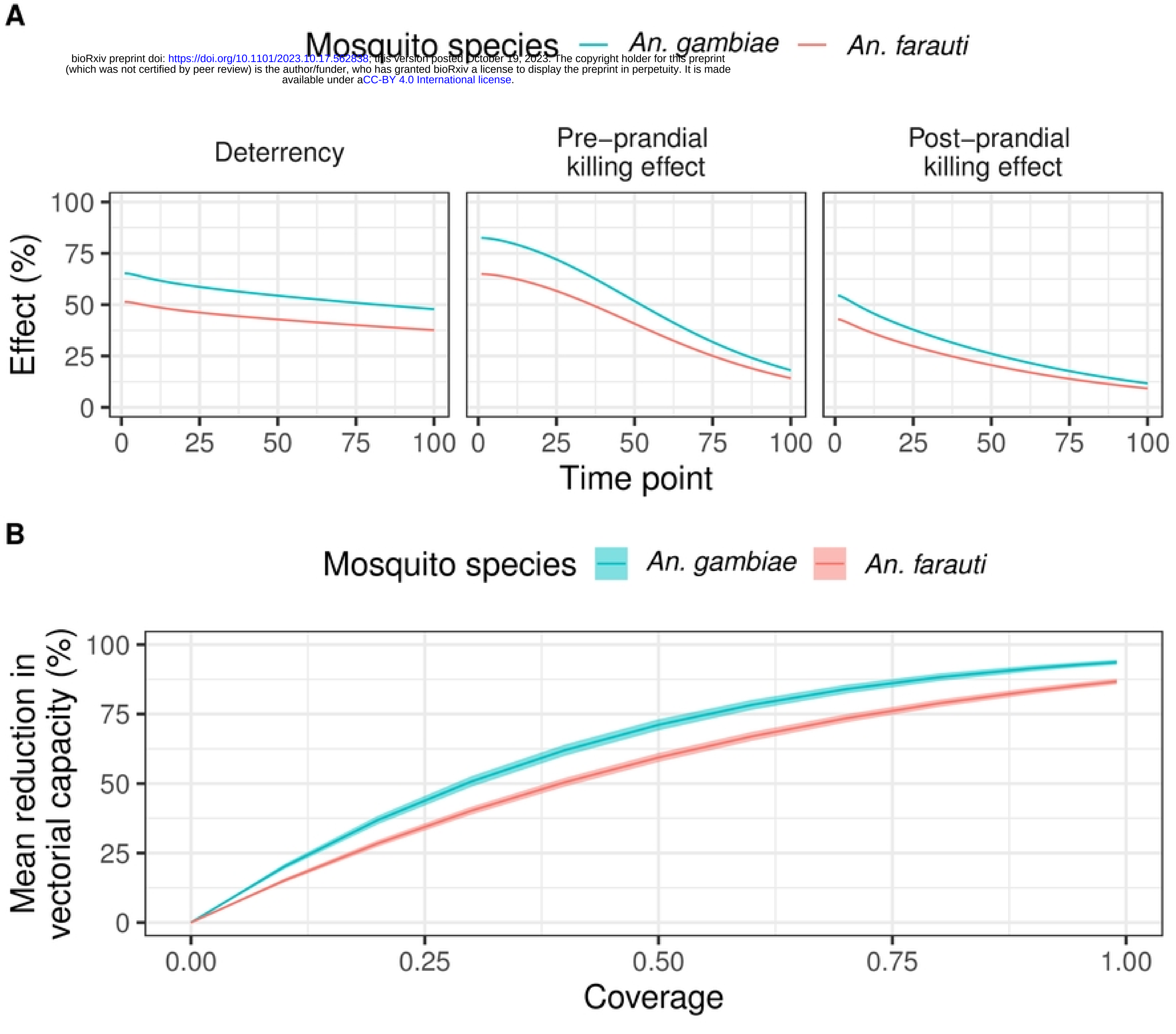
A
Mosquito species
An. gambiae
An. farauti
Deterrency
Pre−prandial killing effect
Post−prandial killing effect
Effect (%)
100
75
50
25
0
0
25
50
75
100
Time point
B
Mosquito species
An. gambiae
An. farauti
Mean reduction in vectorial capacity (%)
100
75
50
25
0
0.00
0.25
0.50
0.75
1.00
Coverage

Figure 3

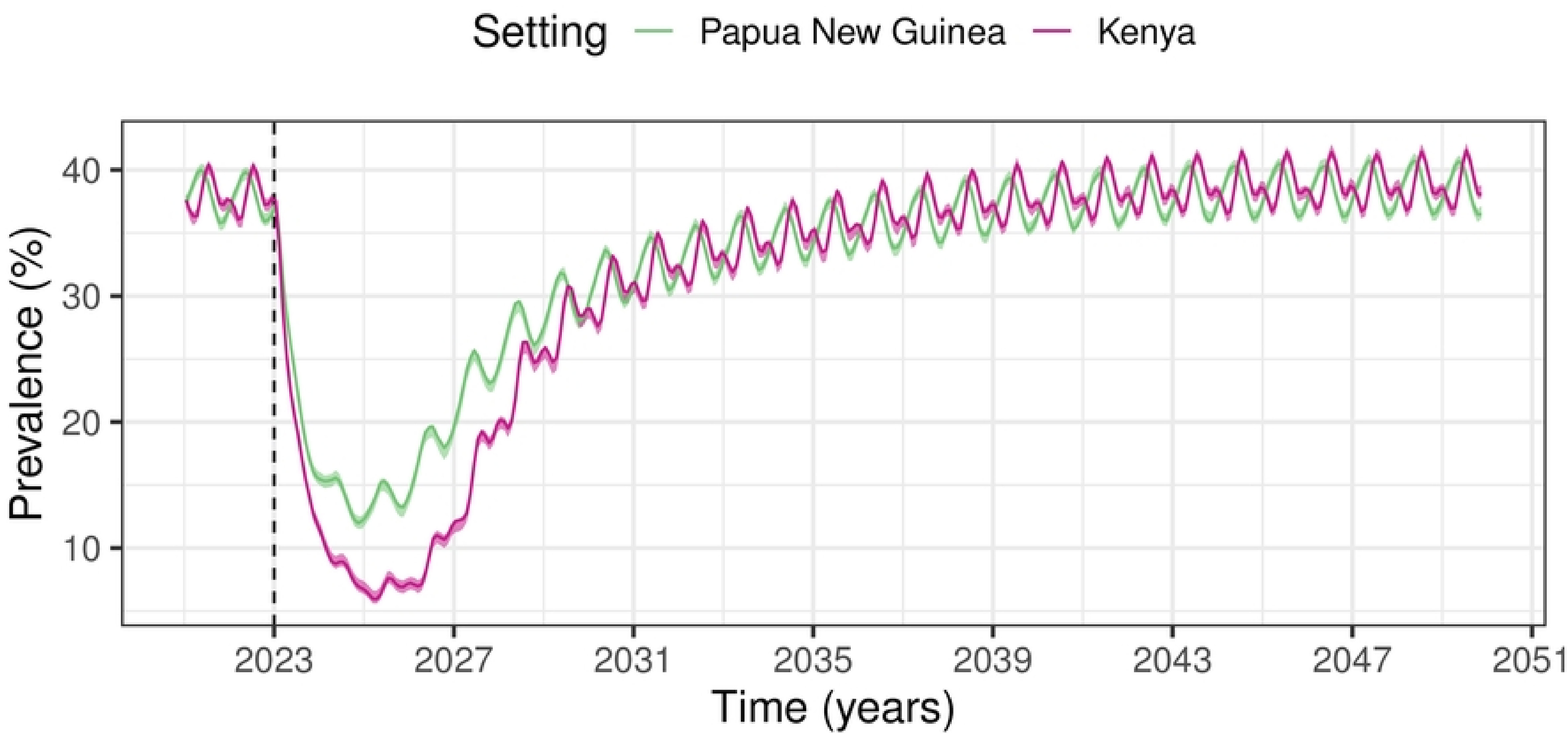
Setting
Papua New Guinea
Kenya
Prevalence (%)
40
30
20
10
2023
2027
2031
2035
2039
2043
2047
2051
Time (years)

Figure 4