A novel age-structured mosquito model for assessing the mechanisms behind vector control success: Additional File 1

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1. VECTOR MODEL PARAMETERISATION

In order to consider interventions in terms of coverage, we define the action of these three measures as described in Table S1. We consider coverage of LLINs to describe the percentage of indoor-sleeping individuals who sleep daily under bednets; coverage of IRS describes the percentage of people who have had their bedrooms sprayed in the previous 6 months; coverage of larvicides is taken to be the percentage coverage (by area) of larval sites with weekly larvicidal treatment.

An experimental hut trial in Benin tested the efficacy of LLIN and IRS interventions using a pyrethroid-impregnated polyester LLIN and chlorfenapyr IRS [1] against Anopheles gambiae and Culex quinquefasciatus. The bednets used were deliberately provided with either 6 holes (4cm^2 each) or 80 holes (2cm^2 each) to simulate different levels of integrity. The results for Anopheles gambiae vectors are shown in Table S2. LLINs were found to have the highest repelling effect, with only 12.1% of vectors successfully feeding in the presence of a bednet. However, they observed a 56.7% mortality in vectors that fed in huts treated with IRS, which was higher than the 49.5% of vectors that died when attempting to feed in huts where the individuals were protected by LLINs.

Use of the biological larvicide Bacillus thuringiensis israelensis (Bti) to treat Anopheles breeding sites has been tested in a study in Peru and Ecuador [2]. The larvicide was found to be effective, but due to the surface feeding habits of Anopheles larvae, it was found to be only effective for the first 7-10 days following spraying, after which it had sank sufficiently below the surface to have no further impact. The study saw an average adult density reduction (measured in bites per person per hour) of 50 - 70% in the 7 days following treatment across all identified larval breeding sites in a 2km radius.

Table S3 contains a summary of the vector-specific parameters, including feeding and biological parameters as well as vector control intervention assumptions.

2. DISEASE PARAMETERS

Table S4 shows the values used for disease-specific parameters, such as the intrinsic and extrinsic incubation periods and the mean human infection duration.

3. DERIVATIONS OF VECTOR CONTROL DEPENDENT TRANSMISSION MEASURES

Consider the age-structured gonotrophic cycle model at equilibrium, such that the number of blood-seeking vectors in generation n is $K^n B_0$, where

$$K = \frac{\pi_1\pi_2\pi_3\pi_4 q_1}{(\pi_2(q_1+q_2)+g)(\pi_3+g+q_3)(\pi_4+g)(\pi_1+g)} \tag{S1}$$

and

$$B_0 = \frac{\beta(1-\theta)}{\pi_2(q_1+q_2)+g}\,. \tag{S2}$$

It is sufficient to consider the blood-seeking class as this is the stage of the feeding cycle where vectors have potential to pick up or transmit disease through biting. If we define the binomial probability, $\kappa = xc$, of a successful feed leading to a new vector infection, then the probability a mosquito becomes exposed during generation n is $\kappa^{(n)} = (1-\kappa)^{n-1}\kappa$. Hence the probability a mosquito has been exposed before generation n is $[1-(1-\kappa)^n]$. Combining these gives the number of vectors in generation n that are already infected:

$$B_0 K^n [1-(1-\kappa)^n]\,. \tag{S3}$$

Table S1. Vector control coverage definitions

Control measure	50% coverage	100% coverage
LLINs	50% hosts sleep under nets	All hosts sleep under nets
IRS	50% bedrooms sprayed	All bedrooms sprayed
larvicides	50% larval sites treated	All larval sites treated

Table S2. Adult vector control: outcome probabilities from feeding attempt [1].

Control measure	Feed success	Death (pre-feed)	Death (post-feed)
LLINs (6 holes)	0.121 (0.054-0.188)	0.495 (0.392-0.597)	n/a
LLINs (80 holes)	0.318 (0.231,0.405)	0.373 (0.282-0.463)	n/a
IRS	0.894 (0.856-0.931)	n/a	0.567 (0.507-0.626)

The total number of diseased, D (exposed, Y, or infectious, Z), vectors is given by summation across the generations;

$$D = B_0 \sum_{n=0}^{\infty} [K^n - K^n(1-\kappa)^n] \quad \text{(S4)}$$

$$= \frac{\kappa K B_0}{(1-K)(1-K+\kappa K)}\,. \quad \text{(S5)}$$

If the incubation period is assumed to be equivalent to N generations (or cycles), then the probability of surviving until infectious is given by K^N and can be treated as a multiplicative factor when calculating the numbers of infectious and exposed vectors:

$$Z = K^N D\,, \quad \text{(S6)}$$

$$Y = D - Z\,. \quad \text{(S7)}$$

and hence directly calculate transmission measures as discussed in the main text.

In the absence of interventions the mean feeding cycle length is,

$$\delta = 1/\pi_1 + 1/\pi_2 + 1/\pi_3 + 1/\pi_4\,, \quad \text{(S8)}$$

where $1/\pi_2$ is the average time to hunt and take a blood meal. IRS and larvicides won't impact hunting time, but the repelling effect of bednets will result in some vectors taking longer to move from emerged to fed.

If we assume a repelled vector begins the hunting process from scratch, then the expected time taken to successfully feed will be equal to the time taken to feed given a successful first attempt plus the expected time taken to feed scaled by the proportion of vector that repeat on any given attempt.

$$\mathbb{E}[\text{Time to feed}] = \mathbb{E}[\text{Time} \mid \text{Successful attempt}] \quad \text{(S9)}$$

$$+\mathbb{P}[\text{Repeat}]\mathbb{E}[\text{Time to feed}] \quad \text{(S10)}$$

$$\mathbb{E}[\text{Time to feed}] = \frac{1}{\pi_2} + Q\omega(1-\sigma-\nu)\mathbb{E}[\text{T to feed}] \quad \text{(S11)}$$

$$\mathbb{E}[\text{Time to feed}] = \frac{1}{\pi_2(1-Q\omega(1-\sigma-\nu))} \quad \text{(S12)}$$

(S13)

Now we can express overall feeding cycle length, δ, in terms of bednet parameters:

$$\delta = \frac{1}{\pi_2(1-Q\omega(1-\sigma-\nu))} + \frac{1}{\pi_3} + \frac{1}{\pi_4} + \frac{1}{\pi_1} \quad \text{(S14)}$$

and the human blood feeding rate is given by:

$$a = Q\left(\frac{1}{\pi_2(1-Q\omega(1-\sigma-\nu))} + \frac{1}{\pi_3} + \frac{1}{\pi_4} + \frac{1}{\pi_1}\right)^{-1} \quad \text{(S15)}$$

The ratio of vectors to humans m, can be scaled by changes in the mosquito population ($m = M/H$), where

$$M = \sum_{i=0}^{\infty} B_0 K^i = \frac{B_0}{1-K} \quad \text{(S16)}$$

and K describes the probability of surviving each feeding cycle, with dependence on vector control parameters included in E_0 and K.

The death rate will depend on IRS and bednet usage. We can relate the probability of a vector surviving one feeding cycle, K, to a per cycle death rate $-ln(K)$, then we have

$$g = \frac{-ln(K)}{\delta} \quad \text{(S17)}$$

as the instanenous daily death rate.

Now that we have vector control dependent expressions for all relevant parameters, these can be substituted into our equations to calculate key transmission measures, such as R_0. In the presence of vector control measures, we relabel R_0 as the basic reproductive number under control, R_c.

Entomological inoculation rate

$$E = maK^N\left(\frac{\kappa K B_0}{(1-K)(1-K+\kappa K)}\right)\frac{1}{M}\,. \quad \text{(S18)}$$

Vectorial capacity

$$V = \frac{ma^2 p^v}{-\ln(p)} = \frac{ma^2}{g}e^{-gv}\,. \quad \text{(S19)}$$

Table S3. Parameters for mosquito biology and vector control (Anopheles gambiae)

	Definition	Value	Source
Q	Fraction of blood-meals indoors	0.9-0.95	[3]
π_2	Daily rate of feeding when blood-seeking	1/0.68	[3]
δ	Mean feeding cycle length	3	[3]
a	Daily rate of feeding on humans	Q/δ	[4]
g	Natural daily death rate	1/14	[5, 6]
σ_L	Probability of feeding in presence of LLINs	6 holes: 0.121 (0.054-0.188) 80 holes: 0.318 (0.231,0.405)	[1]
ν_L	Probability of pre-meal death in presence of LLINs	6 holes: 0.495 (0.392-0.597) 80 holes: 0.373 (0.282-0.463)	[1]
σ_I	Probability of feeding in presence of IRS	0.894 (0.856-0.931)	[1]
ν_I	Probability of post-meal death in presence of IRS	0.567 (50.7-62.6)	[1]
$\hat{\theta}$	Proportion of larvae that die from larvicidal treatment	0.6 (0.5-0.7)	[2]
β	Adult mosquito emergence rate from larval stages	1000-100000 (dependent on: disease and setting)	

Reproductive number under control

$$R_c = \frac{ma^2bc}{gr}e^{-gv} = \frac{ma^2bc}{-\ln(p)r}p^v = \frac{Vbc}{r}. \qquad \text{(S20)}$$

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Table S4. Disease parameters for malaria (Plasmodium falciparum)

	Definition	Value	Source
c	Proportion bites on infectious humans that result in mosquito infection	0.55 (0.47-0.63)	[7]
b	Proportion bites from infectious mosquitoes that result in human infection	0.037 (0.018-0.055)	[3]
u	Intrinsic incubation period in humans (days)	12 (8-23)	[8]
v	Extrinsic incubation period in vector (days)	10 (10-21)	[9]
$1/r$	Mean human infection duration (days)	14	[5]
x	Prevalence of infection in human population	varied	
κ	Probability vector infected after blood meal	cx	