

A model for malaria treatment evaluation in the presence of multiple species: Supplementary information

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This Supplementary document provides further details on the mathematical model and model parameters.

1 Human population dynamics

The model considers the human population in a stochastic, agent-based, framework that is coupled to a system of ordinary differential equations (ODEs) describing the mosquito population. The human dynamics are described in the main document, and in this document we supplement that description with the full table of stoichiometries for the human model dynamics in Table S1 with model parameters defined in Table S4. An individuals state with respect to *P. falciparum*, a_f , is in the set $\mathcal{F} := \{S_f, E_f, A_f, I_f, R_f, T_f, G_f\}$ and their state with respect to *P. vivax*, a_v , is in the set $\mathcal{V} := \{S_v, E_v, A_v, I_v, L_v, R_v, T_v, G_v\}$, thus their state in the multi-species model is $\mathbf{a} := (a_f, a_v)$, in the set $\mathcal{F} \times \mathcal{V}$.

The implementation of treatment entanglement in this paper assumes antimalarial treatment efficacy is the same against individual species in mixed infections as it is for mono-infections, but it does introduce new transitions. For example, an individual with mixed malaria may recover from both *Plasmodium falciparum* (*P. falciparum*) and *P. vivax* simultaneously. These modified rates and transitions are described in Table S3.

2 Mosquito population dynamics

The adult female mosquito population is based on standard SEI-type dynamics with births, deaths, seasonality and mosquitoes that can carry mixed malaria.

Let V , W_x and Y_x denote the number of mosquitoes that are susceptible to all species, exposed to species x and susceptible to other species, and, infectious with species x and susceptible to other species, respectively. Let Z_{Y_f, W_v} and Z_{W_f, Y_v} denote the number of mosquitoes that are infectious with

Table S1: Table of transitions and stoichiometry for the human agent based model, for species x . For *P. falciparum* there is no latent compartment. The total human population is $N = S_x + I_x + A_x + R_x + T_x + L_x + G_x$, and the infection rate of susceptible humans is $\lambda_x = b\epsilon_{M,x}(Y_x + Z_{Y_x,W_x} + Y_{fv})/N$. Rates which are affected by triggering and masking interactions in the model are highlighted in red and blue respectively (the interactions are defined in Table S3). Parameters are defined in Table S4.

From→to	Rate	Description
$S_x \rightarrow I_x$	$p_{c,x}\lambda_x$	Clinical infection of naive individual
$S_x \rightarrow A_x$	$(1 - p_{c,x})\lambda_x$	Asymptomatic infection of naive individual
$I_x \rightarrow \text{death}$	$p_{I_x,x}\sigma_x$	Death due to malaria
$I_x \rightarrow A_x$	$(1 - p_{I_x,x})\sigma_x$	Loss of clinical symptoms
$I_x \rightarrow T_x$	$\textcolor{blue}{p_{N,x}}c_x\tau_x + \textcolor{blue}{p_{M,x}}\eta_x(t)$	Standard treatment
$I_x \rightarrow G_x$	$(1 - \textcolor{blue}{p_{N,x}})c_x\tau_x + (1 - \textcolor{blue}{p_{M,x}})\eta_x(t)$	Treatment including radical cure
$A_x \rightarrow L_x$	$p_{h,x}\alpha_x$	Recovered with hypnozoites
$A_x \rightarrow R_x$	$(1 - p_{h,x})\alpha_x$	Recovered with no hypnozoites
$A_x \rightarrow T_x$	$\textcolor{blue}{p_{M,x}}\eta_x(t)$	Standard treatment via MDA
$A_x \rightarrow G_x$	$(1 - \textcolor{blue}{p_{M,x}})\eta_x(t)$	Radical cure treatment via MDA
$R_x \rightarrow I_x$	$p_{R_x,x}r_x\lambda_x$	Clinical infection of semi-immune
$R_x \rightarrow A_x$	$(1 - p_{R_x,x})r_x\lambda_x$	Asymptomatic infection of semi-immune
$R_x \rightarrow S_x$	ω_x	Waning immunity
$L_x \rightarrow I_x$	$p_{R_x,x}r_x\lambda_x$	Clinical infection of hypnozoite carrier
$L_x \rightarrow A_x$	$(1 - p_{R_x,x})r_x\lambda_x$	Asymptomatic infection of hypnozoite carrier
$L_x \rightarrow I_x$	$p_{L_x,x}\textcolor{red}{\nu}_x$	Relapse to clinical infection
$L_x \rightarrow A_x$	$(1 - p_{L_x,x})\textcolor{red}{\nu}_x$	Relapse to asymptomatic infection
$L_x \rightarrow S_x$	κ_x	Hypnozoite “death”
$T_x \rightarrow \text{death}$	$p_{T_x,x}\rho_x$	Standard treatment outcome is death
$T_x \rightarrow A_x$	$p_{TfA}(1 - p_{T_x,x})\rho_x$	Treatment completed but fails to fully clear blood-stage parasites
$T_x \rightarrow R_x$	$(1 - p_{A_x,x})(1 - p_{TfA})(1 - p_{T_x,x})\rho_x$	Treatment successfully completed
$T_x \rightarrow L_x$	$p_{A_x,x}(1 - p_{TfA})(1 - p_{T_x,x})\rho_x$	Treatment completed but hypnozoites remain
$G_x \rightarrow \text{death}$	$p_{G_x,x}\psi_x$	Radical cure treatment outcome is death
$G_x \rightarrow A_x$	$(1 - p_{G_x,x})p_{TfP}\psi_x$	Treatment with radical cure completed but blood-stage parasites remain
$G_x \rightarrow R_x$	$(1 - p_{P,x})(1 - p_{TfP})(1 - p_{G_x,x})\psi_x$	Treatment with radical cure completed and successful
$G_x \rightarrow L_x$	$p_{P,x}(1 - p_{TfP})(1 - p_{G_x,x})\psi_x$	Treatment with radical cure completed but hypnozoites remain

P. falciparum and exposed to *P. vivax* and vice versa. Let the force of infection from species x on the mosquito population be denoted by $\lambda_{M,x}$; the equations for $\lambda_{M,x}$ are given by Equations (13)-(15). The mosquito population is modelled by the following system of ordinary differential equations (ODEs):

$$\frac{dV}{dt} = \delta_0 M - (\lambda_{M,f} + \lambda_{M,v} + \lambda_{M,fv})V - \delta(t)V, \quad (1)$$

$$\frac{dW_f}{dt} = \lambda_{M,f}V - (\gamma_f + \delta(t))W_f, \quad (2)$$

$$\frac{dW_v}{dt} = \lambda_{M,v}V - (\gamma_v + \delta(t))W_v, \quad (3)$$

$$\frac{dW_{fv}}{dt} = \lambda_{M,fv}[V + W_f + W_v] + \lambda_{M,f}W_v + \lambda_{M,v}W_f - (\gamma_f + \gamma_v + \delta(t))W_{fv}, \quad (4)$$

$$\frac{dY_f}{dt} = \gamma_f W_f - \delta(t)Y_f, \quad (5)$$

$$\frac{dY_v}{dt} = \gamma_v W_v - \delta(t)Y_v, \quad (6)$$

$$\frac{dZ_{Y_f,W_v}}{dt} = \gamma_f W_{fv} + (\lambda_{M,v} + \lambda_{M,fv})Y_f - (\gamma_v + \delta(t))Z_{Y_f,W_v}, \quad (7)$$

$$\frac{dZ_{W_f,Y_v}}{dt} = \gamma_v W_{fv} + (\lambda_{M,f} + \lambda_{M,fv})Y_v - (\gamma_f + \delta(t))Z_{W_f,Y_v}, \quad (8)$$

$$\frac{dY_{fv}}{dt} = \gamma_f Z_{W_f,Y_v} + \gamma_v Z_{Y_f,W_v} - \delta(t)Y_{fv}, \quad (9)$$

where (10)

$$\delta(t) = \delta_0 \left(1 - \xi \cos \left(\frac{2\pi(t - \phi)}{365} + \pi/2 \right) \right), \quad (11)$$

$$M = V + W_f + Y_f + W_v + Y_v + W_{fv} + Z_{Y_f,W_v} + Z_{W_f,Y_v} + Y_{fv}, \quad (12)$$

and parameters are described in Table S4. The mosquito dynamics are depicted in Figure S1.

Here we derive the force of infection equations for the mosquito population. The force of infection equations are presented in terms of a force of infection for *P. falciparum* ($\lambda_{M,f}$), for *P. vivax* ($\lambda_{M,v}$) and for mixed infections ($\lambda_{M,fv}$). The mono-infection terms need to consider successful infection from single species infectious individuals and a partially-successful infection from individuals with mixed infection, whereas, the mixed force of infection accounts for successful infection by both species.

First, let \mathcal{A}_x be the set of infectious states in the single species model for species x , that is, $\mathcal{A}_x = \{I_x, A_x, T_x, G_x\}$, and let \mathcal{A}_x^c be the complement, that is $\mathcal{A}_f^c = \{S_f, R_f\}$ and $\mathcal{A}_v^c = \{S_v, R_v, L_v\}$. Thus, an individual in state $\mathbf{a} := (a_f, a_v)$ is infectious with a *P. falciparum* mono-infection if $\mathbf{a} \in \mathcal{A}_f \times \mathcal{A}_v^c$, a *P. vivax* mono-infection if $\mathbf{a} \in \mathcal{A}_f^c \times \mathcal{A}_v$, or a mixed infection if $\mathbf{a} \in \mathcal{A}_f \times \mathcal{A}_v$. We define $f(\mathbf{a})$ to be a function which takes a state, \mathbf{a} , and returns the number of individuals in that state. Lastly, let the probability of transmission of species x from a human, in state a , be $\epsilon_{H,a_x} = \zeta_{a_x} \epsilon_{H,x}$ (the relative infectiousness of

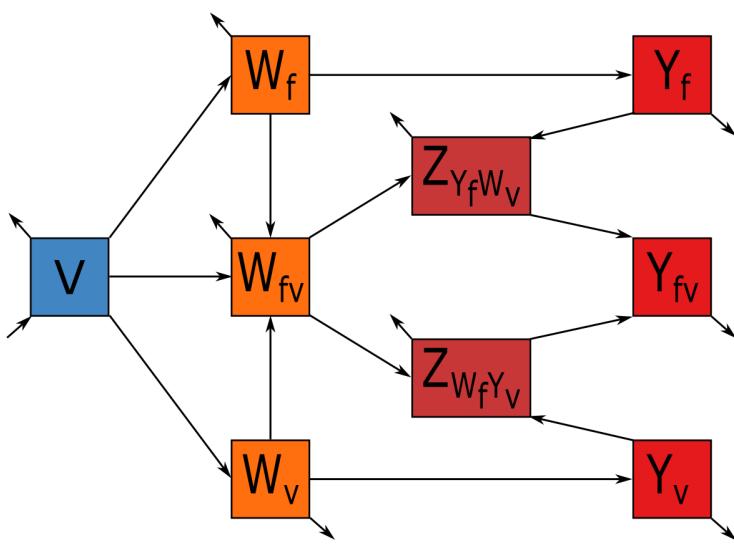


Figure S1: Schematic of the mosquito portion of the transmission model, where V are the susceptible mosquitoes, W are those exposed but not yet infectious, Y are those infectious, Z are for those in combinations of W and Y , and the subscripts are defined as $f=P. falciparum$ and $v=P. vivax$. This is also colour coded as blue=susceptible, red=infectious, orange=latent. The system is fully described by Equations (1)-(15). Despite appearances, this is a simple susceptible-exposed-infectious mosquito model, just with all possible combinations of those for the two parasite species.

an individual in state a multiplied by the probability of transmission from an infectious bite).

Infectious humans with mixed infections in state $(a_f, a_v) \in \mathcal{A}_f \times \mathcal{A}_v$ pass on the mixed infection to each susceptible mosquito at rate $\frac{b}{N} \epsilon_{H,a_f} \epsilon_{H,a_v} f(a)$, pass on *P. falciparum* only at rate $\frac{b}{N} \epsilon_{H,a_f} (1 - \epsilon_{H,a_v}) f(a)$ and pass on *P. vivax* only at rate $\frac{b}{N} (1 - \epsilon_{H,a_f}) \epsilon_{H,a_v} f(a)$. Therefore, the force of infection resulting in mosquitoes being infected by *P. falciparum*, *P. vivax* and mixed malaria are:

$$\lambda_{M,f} = \frac{b}{N} \left[\sum_{\mathbf{a} \in \mathcal{A}_f \times \mathcal{A}_v^c} \epsilon_{H,a_f} f(a) + \sum_{\mathbf{a} \in \mathcal{A}_f \times \mathcal{A}_v} \epsilon_{H,a_f} (1 - \epsilon_{H,a_v}) f(a) \right], \quad (13)$$

$$\lambda_{M,v} = \frac{b}{N} \left[\sum_{\mathbf{a} \in \mathcal{A}_f^c \times \mathcal{A}_v} \epsilon_{H,a_v} f(a) + \sum_{\mathbf{a} \in \mathcal{A}_f \times \mathcal{A}_v} (1 - \epsilon_{H,a_f}) \epsilon_{H,a_v} f(a) \right], \quad (14)$$

and

$$\lambda_{M,fv} = \frac{b}{N} \sum_{\mathbf{a} \in \mathcal{A}_f \times \mathcal{A}_v} \epsilon_{H,a_f} \epsilon_{H,a_v} f(a). \quad (15)$$

3 Radical cure coverage and outcomes

This section outlines calculations relating to coverage of radical cure in the accelerated radical cure and unified radical cure scenarios, based on eligibility, glucose-6-phosphate dehydrogenase (G6PD) status and rapid diagnostic test (RDT) accuracy. The parameters related to , RDT accuracy, G6PD and haemolysis are given in Table S2.

Table S2: Table of parameters related to RDTs, G6PD status and haemolysis.

Symbol	Description	Value	Source
p_{inel}	Proportion of cases ineligible for radical cure	0.04	Assumed
p_{g6pd}	Proportion of eligible cases with G6PD < 30%	0.06	Assumed
p_{sens}	Sensitivity of RDT	0.94	[1]
p_{spec}	Specificity of RDT	0.91	[1]
p_{haem}	Probability of haemolysis if G6PD < 30% and treated with radical cure	0.109	[2]
$p_{untreated}$	Probability unable to be treated for haemolysis	0.1	[3]
p_{death}	Probability of death if untreated for haemolysis	0.1	[3]

Let p_{inel} , p_{g6pd} , p_{sens} and p_{spec} be the probabilities that individuals are ineligible for treatment (<6 months, pregnant or lactating), have G6PD < 30% given eligibility, the probability of a true positive test (sensitivity) and the probability of a true negative test (specificity), respectively. The probability a patient detected with a *Plasmodium vivax* (*P. vivax*) infection is not given radical cure, p_{norc} , is

$$p_{norc} = p_{inel} + (1 - p_{inel})(p_{g6pd}p_{sens} + (1 - p_{g6pd})(1 - p_{spec})).$$

Table S3: Table delineating how the interaction parameters affect transmission. All interaction parameters are dimensionless.

Symbol	Explanation	Modifies	Transitions affected	Value(s)	Reference(s)	Notes
Treatment Entanglement						
-	Simultaneous treatment for mixed infections.	New flows.	Simultaneous treatment: $(I_f, I_v) \rightarrow (T_f, T_v)$, $(I_f, A_v) \rightarrow (T_f, T_v)$, $(A_f, I_v) \rightarrow (T_f, T_v)$, $(A_f, A_v) \rightarrow (T_f, T_v)$, $(I_f, L_v) \rightarrow (T_f, T_v)$, $(A_f, L_v) \rightarrow (T_f, T_v)$.	[4–6]	Whenever an individual with a mixed infection would enter a state with treatment, they will instead be treated with respect to both species.	
-	Simultaneous end of treatment for mixed infections.	New flows.	The flows are changed similarly for radical cure. $(T_f, T_v) \rightarrow (A_f, R_v)$, $(T_f, T_v) \rightarrow (R_f, A_v)$, $(T_f, T_v) \rightarrow (A_f, A_v)$, $(T_f, T_v) \rightarrow (A_f, L_v)$, $(T_f, T_v) \rightarrow (R_f, R_v)$, $(T_f, T_v) \rightarrow (R_f, L_v)$.	-	The efficacy of treatments for each strain are assumed equal to those of mono infections. That is, the probability of each treatment outcome is equal to the product of the two transition probabilities for mono infections.	

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Table S3 – *Continued from previous page*

Symbol	Description	Modifies	Transitions affected	Value(s)	Reference(s)	Notes
-	Infection during treatment.	New flows.	$(T_f, S_v) \rightarrow (T_f, T_v)$, $(S_f, T_v) \rightarrow (T_f, T_v)$, $(T_f, R_v) \rightarrow (T_f, T_v)$, $(R_f, T_v) \rightarrow (T_f, T_v)$.	-		If, while an individual with monoinfection is undergoing treatment, they are infected by the other species of malaria, they will be treated for both.
Masking						
h_v	Probability that masking occurs	The probability of receiving standard treatment for mixed infection, given treated, $p_{N,fv} = h_v p_{N,f} + (1 - h_v) p_{N,v}$, and $p_{M,fv} = h_v p_{M,f} + (1 - h_v) p_{M,v}$.	$(I_f, I_v) \rightarrow (T_f, T_v)$, $(I_f, A_v) \rightarrow (T_f, T_v)$, $(A_f, I_v) \rightarrow (T_f, T_v)$, $(A_f, A_v) \rightarrow (T_f, T_v)$.	0.5 (0.2, 0.8)	Informed by expert elicitation.	This is the probability that a mixed infection is treated as though it were a <i>P. falciparum</i> infection, either through only <i>P. falciparum</i> being detected, or health workers not adhering to radical cure guidelines. The transition probabilities for radical cure, given treated, are also modified to stay complimentary to the probability of standard cure, given treated.
Triggering						

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Table S3 – *Continued from previous page*

Symbol	Description	Modifies	Transitions affected	Value(s)	Reference(s)	Notes
z_f	Increase in <i>P. vivax</i> relapse rate due to triggering.	The rate of $\hat{\nu}_v = z_f \nu_v$	$(R_f, L_v) \rightarrow (R_f, I_v)$, $(R_f, L_v) \rightarrow (R_f, A_v)$.	3.5 (2.0, 6.0)	[7]	Increased rate of <i>P. vivax</i> relapse following <i>P. falciparum</i> infection.

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Table S4: Table of parameters.

Symbol	Description	<i>P. falciparum</i>	<i>P. vivax</i>	Units	Source Location	Notes
Initial Conditions (Humans)						
N_0	Population size	100,000	100,000	people		Assumed.
I_0/N_0	Clinical (proportion)	0.01	0.005	per capita		We initialise with mixed terms set to zero for mosquitoes and humans (these terms are not presented in this table). Assumed.
A_0/N_0	Asymptomatic (proportion)	0.25	0.05	per capita		Assumed.
R_0/N_0	Immunity (proportion)	0.7	0.4	per capita		Chosen to give smooth dynamics.
L_0/N_0	Liver-stage (proportion)	-	0.03	per capita		Assumed
T_0/N_0	Undergoing ACT Treatment (proportion)	0.01	0.005	per capita		Assumed.
G_0/N_0	Undergoing radical cure (proportion)	0	0	per capita		Assumed.
Initial Conditions (Mosquitoes)						
M/N	Ratio of mosquitoes to humans	1/3	1/3	unitless		Assumed.
W	Exposed (proportion)	0.1	0.1	per capita	Mondul Kiri	Assumed.

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Table S4 – *Continued from previous page*

Symbol	Description	<i>P. falciparum</i>	<i>P. vivax</i>	Units	Source Location	Notes
Y	Infectious (proportion)	0.1	0.1	per capita		Assumed.
Species-independent parameters						
ξ	Amplitude of seasonality	0.05	0.05	unitless	Asia-Pacific region	Assumed.
b	Number of mosquito bites per human per day	0.38 (0.1, 0.5)	0.38 (0.1, 0.5)	per day		Assumed. Ranges from [6].
ϕ	Day of peak transmission from mosquitos	300.0 (1.0, 365.25)	300.0 (1.0, 365.25)	day	Cambodia	Calibrated so that incidence peaks in October.
δ	Inverse of average life expectancy of mosquitoes	0.0714 (0.028, 0.125)	0.0714 (0.028, 0.125)	per day	Mount Cameroon region, Indonesia	Average life expectancy of 14 days [6, 8, 9].
μ	Inverse of average human life expectancy	4.053072e-05 (3.933693e-05, 4.680086e-05)	4.053072e-05 (3.933693e-05, 4.680086e-05)	per day	Cambodia	Average life expectancy is 67.5 years [10].
Simplifying assumption of species-independent parameters						
p_{TfA}	Probability standard treatment fails to clear gametocytes	0.03 (0.0, 1.0)	0.03 (0.0, 1.0)	unitless	Gambia and Kenya	Assuming 3 day course of ACT [11].

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Table S4 – *Continued from previous page*

Symbol	Description	<i>P. falciparum</i>	<i>P. vivax</i>	Units	Source Location	Notes
p_{TfP}	Probability radical cure fails to clear gametocytes.	0.03 (0.001, 0.1)	0.03 (0.001, 0.1)	unitless	Gambia and Kenya	Assuming 14 day primaquine with three days of ACT has the same efficacy against blood-stage malaria as the standard 3 day treatment of ACT.
α	Inverse of average asymptomatic infectious period	0.0167 (0.05, 0.15)	0.0167 (0.05, 0.15)	per day	Northern Ghana	Average asymptomatic infectious period of 130 days [6].
ω	Inverse of average duration of natural immunity	0.00038 (0.0, 0.005)	0.00038 (0.0, 0.005)	per day	Tanzania and The Gambia	Calculated from 5 year half-life from [12].
r	Relative susceptibility of those with some immunity to this species compared to those without	1.0 (0.0, 1.0)	1.0 (0.0, 1.0)	unitless		Assume no anti-parasite immunity with respect to susceptibility to infection. Anti-parasite immunity is captured via a reduction in infectiousness in asymptomatic carriers.
ζ_A	Relative infectiousness of asymptomatic cases compared to clinical	0.1 (0.05, 0.8)	0.1 (0.05, 0.8)	unitless		Informed by expert elicitation.

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Table S4 – *Continued from previous page*

Symbol	Description	<i>P. falciparum</i>	<i>P. vivax</i>	Units	Source Location	Notes
ζ_G	Relative infectiousness of cases undergoing radical cure (primaquine-based treatment) compared to clinical	0.0 (0.0, 0.1)	0.0 (0.0, 0.1)	unitless		Assumed.
ζ_I	Relative infectiousness of clinical cases compared to clinical with a <i>P. falciparum</i> -only	1.0 (1.0, 1.0)	1.0 (1.0, 1.0)	unitless		Assumed.
ζ_T	Relative infectiousness of cases undergoing standard treatment compared to clinical cases with no treatment	0.0 (0.0, 0.33)	0.0 (0.0, 0.33)	unitless		Assumed.
c	Treatment coverage level	0.3 (0.0, 1.0)	0.3 (0.0, 1.0)	unitless		Assumed.
Species-dependent parameters						

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Table S4 – *Continued from previous page*

Symbol	Description	<i>P. falciparum</i>	<i>P. vivax</i>	Units	Source Location	Notes
γ	Inverse of duration of latent period in mosquitoes (AKA the extrinsic incubation period)	0.1 (0.028, 0.2)	0.0833 (0.028, 0.33)	per day	Mixture, South and South-East Asia	Average latent period of 10 days for <i>P. falciparum</i> and 12 for <i>P. vivax</i> [6, 13] for all, [14] for <i>P. vivax</i> , all ranges from [15].
p_c	Proportion of non-immune expected to develop clinical malaria	0.95 (0.8, 1.0)	0.8 (0.8, 1.0)	unitless	USA, sub-Saharan Africa, Columbia	[6, 16, 17] for all, [18] for <i>P. vivax</i> .
p_R	Proportion immune expected to develop clinical malaria upon reinfection	0.5 (0.0, 0.77)	0.2 (0.0, 0.66)	unitless		Assumed. Informed by Columbian experiment [18] which had 0.66 for <i>P. vivax</i> in a small population of young healthy volunteers, Cambodian data [19, 20] and ranges from [6].
ρ	Inverse of average duration for regular treatment	0.33 (0.125, 0.33)	0.33 (0.125, 0.33)	per day	Gambia and Kenya	Assume a 3 day course of ACT. [6, 11].
ϵ_M	Transmission probability: mosquito to human (per bite from an infectious mosquito)	0.5 (0.0, 0.8)	0.3 (0.0, 0.8)	unitless		Informed by expert elicitation. Partially informed by [6, 21, 22] for all, [23, 24] for <i>P. vivax</i> .

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Table S4 – *Continued from previous page*

Symbol	Description	<i>P. falciparum</i>	<i>P. vivax</i>	Units	Source Location	Notes
ϵ_H	Transmission probability: human to mosquito (per bite on an infectious human)	0.1 (0.0, 0.5)	0.1 (0.0, 0.5)	unitless		Informed by expert elicitation. [6, 25] for <i>P. falciparum</i> , [23, 26] for <i>P. vivax</i> , ranges from [15].
κ_v	Inverse of average time until hypnozoites die naturally	-	0.0025 (0.002, 0.003)	per day	South East Asia	On average, hypnozoites die out after 400 days [6, 27]. The 1/500 day limit is from [23].
$p_{A,v}$	Probability of recovering with hypnozoites after standard treatment	-	0.68 (0.5, 0.8)	unitless	Global	[6, 14]
$p_{h,v}$	Probability of naturally recovering with hypnozoites	-	0.5 (0.2, 0.8)	unitless		Assumed.
$p_{L,v}$	Probability a relapse results in clinical malaria	-	0.2 (0.0, 0.66)	unitless		Assuming $p_{L,v} = p_{R,v}$.

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Table S4 – *Continued from previous page*

Symbol	Description	<i>P. falciparum</i>	<i>P. vivax</i>	Units	Source Location	Notes
$p_{P,v}$	Probability of recovering with hypnozoites after radical cure	-	0.217 (0.0, 0.43)	unitless	Mixed, global	[6, 28]. We assume that there is a higher rate of failure for increased radical cure scenarios ($p_{P,v} = 0.2204$) which accounts for the probability an individual stops treatment because of haemolysis.
ψ	Inverse of average duration infectious after treatment that includes radical cure has begun	0.142 (0.07, 0.5)	0.142 (0.07, 0.5)	per day		Assuming a 14 day course of primaquine.
σ	Inverse of average duration of symptoms in untreated clinical malaria	0.07143 (0.01, 0.2)	0.05 (0.01, 0.5)	per day	<i>P. falciparum</i> from Africa/West Africa and USA data	A 14 day and 20 day average for <i>P. falciparum</i> and <i>P. vivax</i> , respectively [17, 29]. Ranges from [6].
$\eta(t)$	Inverse of average time until treatment from MDA or MSAT.	-	-	per day		This function is scenario specific.
ν	Inverse of average time to relapse	- (-, -)	0.022 (0.00667, 0.04762)	per day	South East Asia and Melanesia	Average time to relapse is 45 days [6, 23, 30, 31].

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Table S4 – *Continued from previous page*

Symbol	Description	<i>P. falciparum</i>	<i>P. vivax</i>	Units	Source Location	Notes
p_I	Probability that untreated clinical malaria results in death	0.021 (0.02, 0.2)	0.001 (0.0015, 0.2)	unitless	Africa and Asia	Informed by expert elicitation for pv. [6, 32] for pf.
p_N	Probability of receiving radical-cure based treatment	-	-	unitless		This parameter is scenario specific.
p_M	Probability of receiving radical-cure based treatment from MDA or MSAT	-	-	unitless		This parameter is scenario specific.
p_T	Probability that an individual undergoing standard treatment dies from malaria	0.0066 (0.0, 0.075)	0.000001 (0.0, 0.001)	unitless		[6]

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Table S4 – *Continued from previous page*

Symbol	Description	<i>P. falciparum</i>	<i>P. vivax</i>	Units	Source Location	Notes
p_G	Probability that an individual undergoing radical treatment dies from malaria (or treatment)	0.0066 (0.0045, 0.075)	0.000001 (0.0, 0.01)	unitless		Assumed. This is scenario specific with $p_{G,f} = 0.006605$ and $p_{G,v} = 0.0000105$ in scenarios with wider prescription of radical cure; this is to allow for a higher rate haemolytic events when radical cure is prescribed less conservatively. For baseline [6].
τ	Inverse of average time until individual with clinical malaria seeks treatment.	0.5 (0.1, 1.0)	0.5 (0.1, 1.0)	per day		Assumed. Time to treatment is 2 days, on average, with full coverage ($c = 1$) and 20 days with $c = 0.1$.

Let p_{haem} be the probability that an individual with G6PD< 30% will have haemolysis if treated with radical cure. The probability a patient has haemolysis after being prescribed radical cure (after screening for G6PD) is

$$prchaem = p_{haem} \frac{(1 - p_{inel})p_{g6pd}(1 - p_{sens})}{1 - p_{norc}}.$$

Let $p_{untreated}$ and p_{death} denote the probability of not being treated for haemolysis and the probability of death if untreated for haemolysis, respectively. The probability a patient that is prescribed radical cure dies is given by

$$prcdeath = prchaem p_{untreated} p_{death}.$$

For the parameters considered here p_{norc} , $prchaem$ and $prcdeath$ are 0.18 , 5×10^{-4} and 5×10^{-6} , respectively.

4 Full model time-series

This section gives figures of the total number of individuals in each compartment over time for *P. falciparum* and *P. vivax* for the scenarios presented in the main text (see Figures S2 and S3). Note that the total infections presented in Figure 2 is the sum of the *I* and the *A* compartments given in Figures S2 and S3.

5 Additional sensitivity analysis results

Here we present additional one-dimensional sensitivities to model parameters of various model outputs including: symptomatic (clinical) infections, deaths, relapses, individuals that received radical cure and individuals that received standard cure. We note that the parameters with the largest effect across all outcomes are broadly consistent with those associated with the total number of symptomatic infections. Small differences in relative sensitivity between measuring total infections versus those symptomatic are largely centred on the parameters having to do with proportions immune expected to develop clinical malaria upon reinfection (that is, p_R for *P. falciparum* and p_c for *P. vivax*).

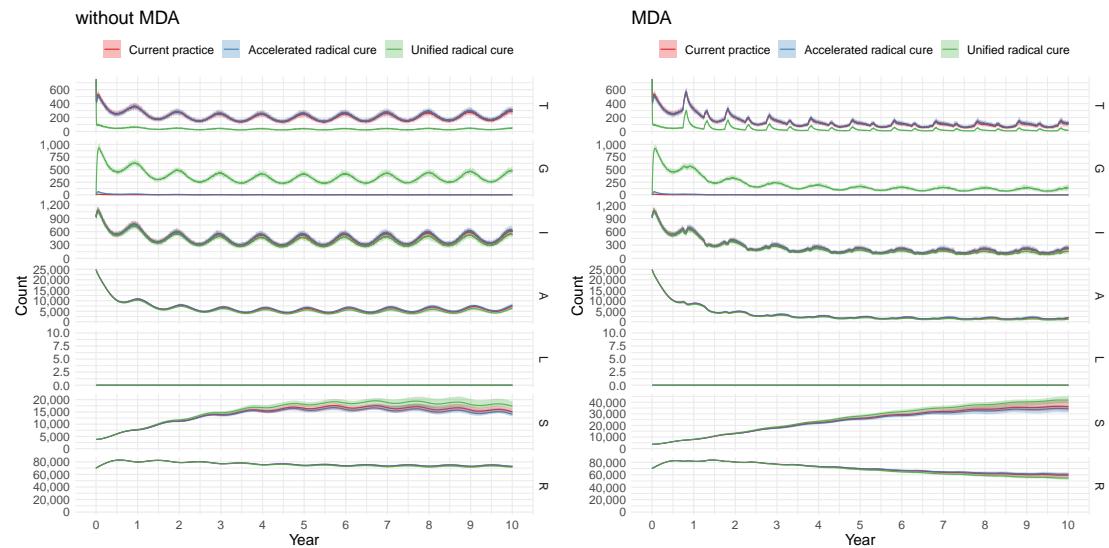


Figure S2: The state of humans in the multispecies model over time for *P. falciparum* under the regular treatment scenario (left) and the mass drug administration (MDA) scenario (right).

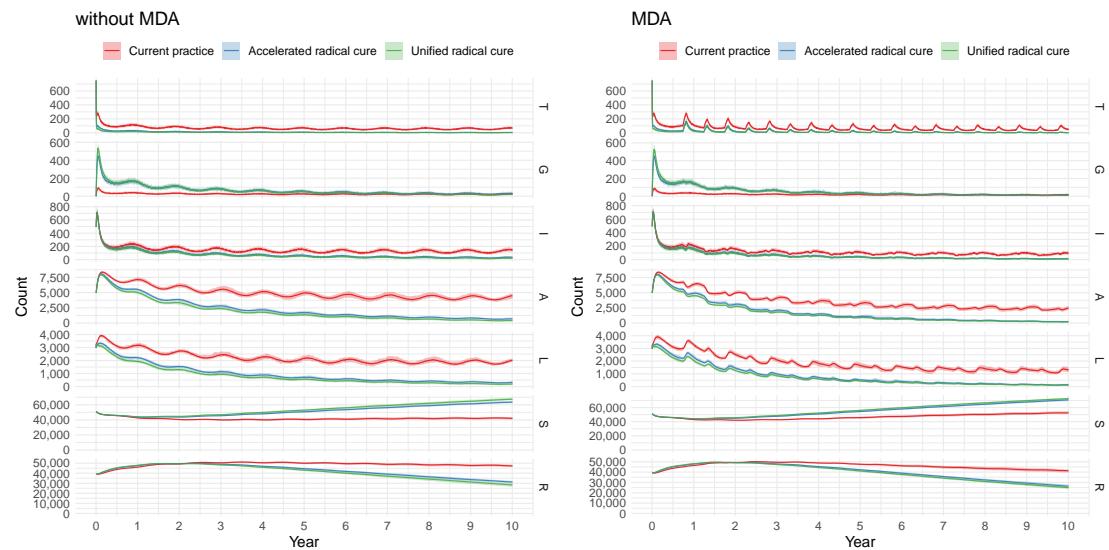
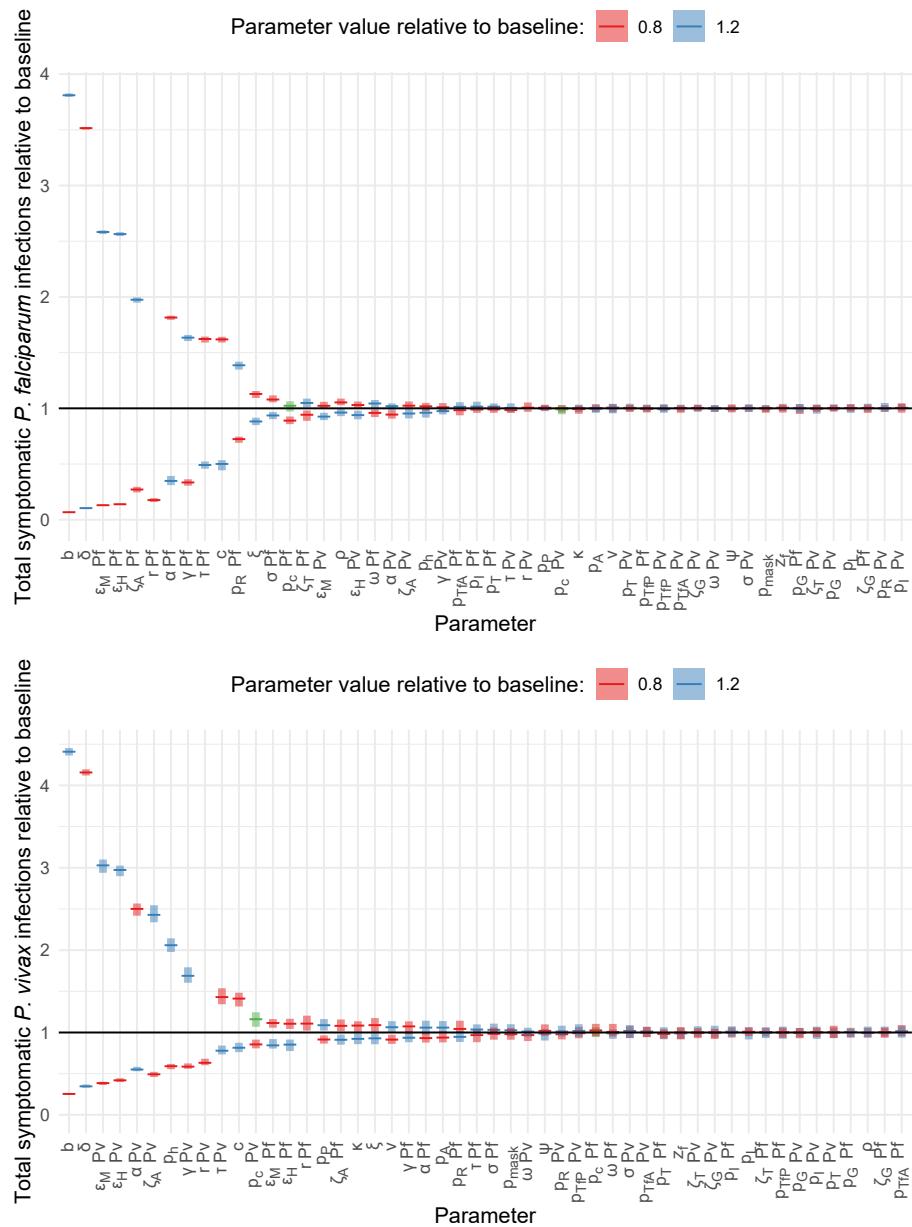
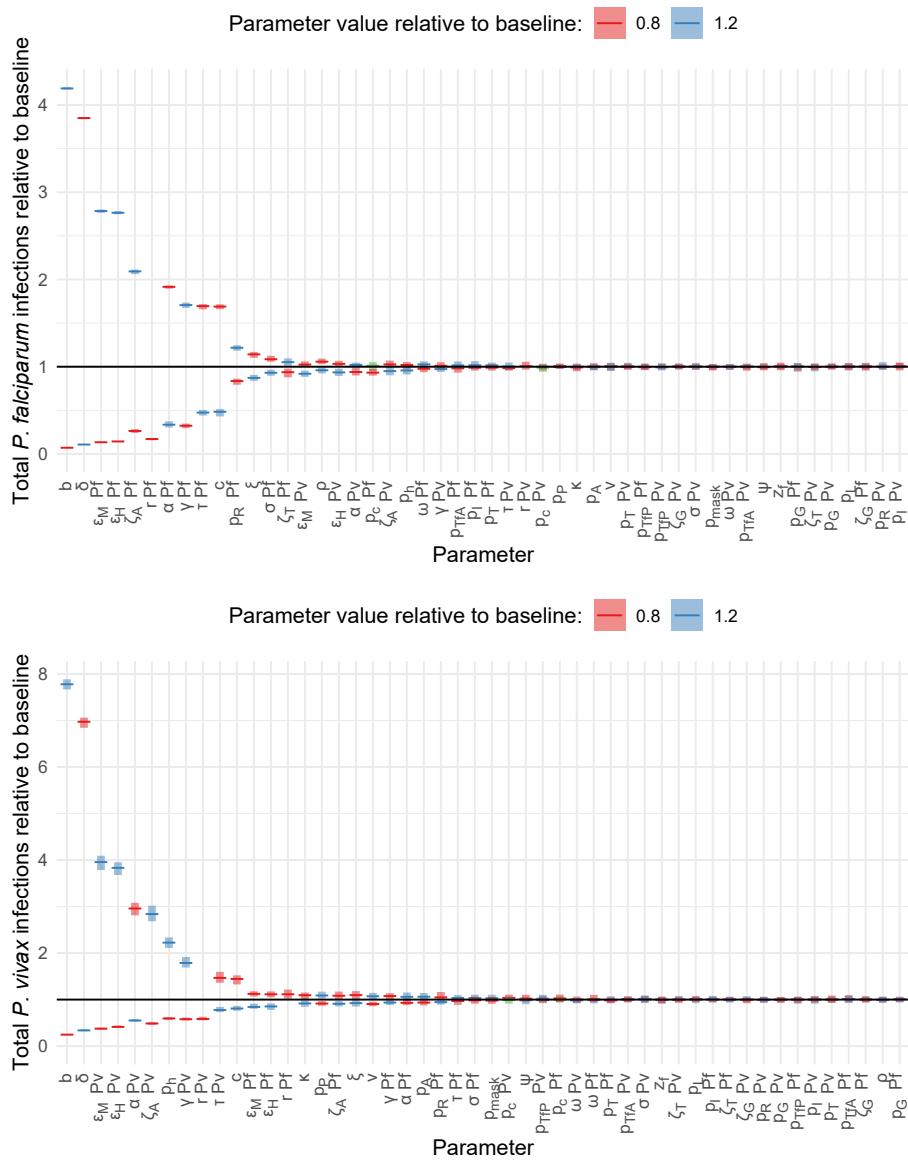
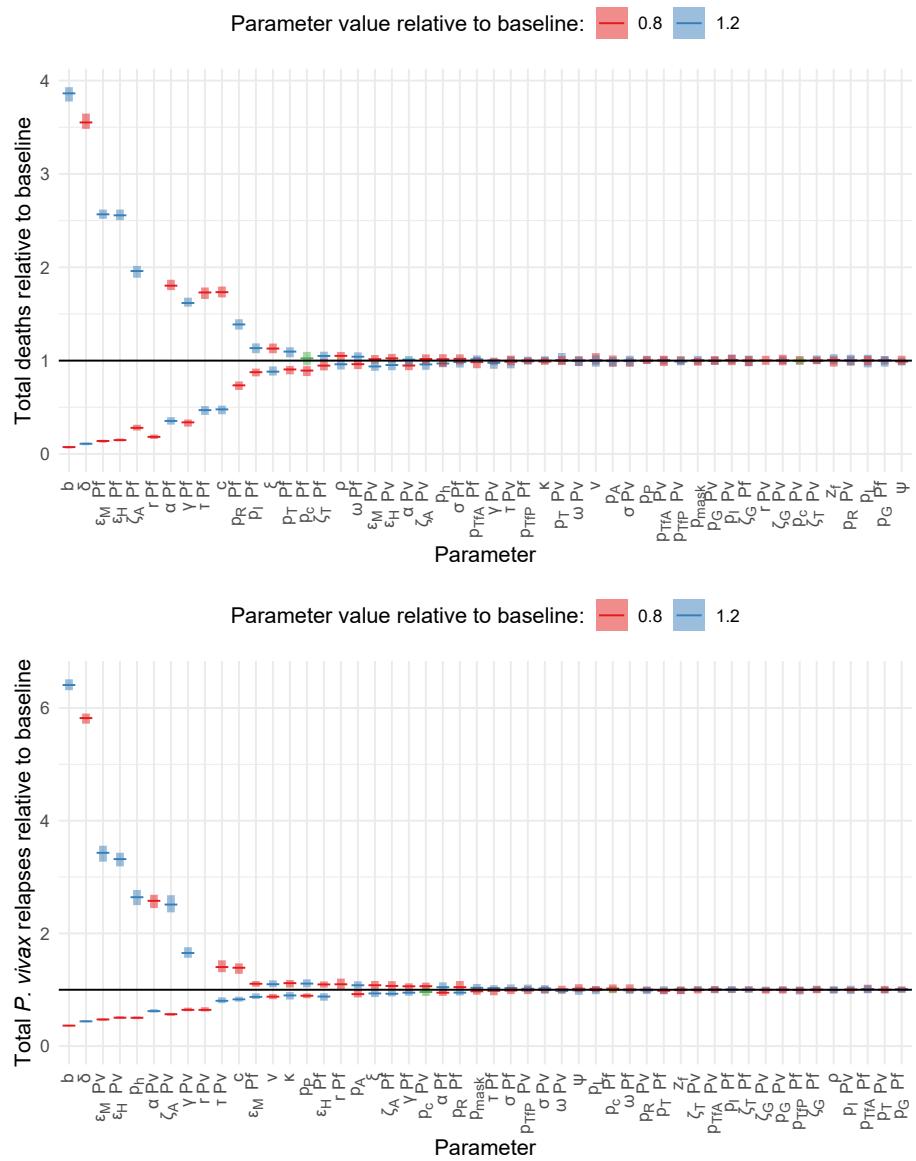


Figure S3: The state of humans in the multispecies model over time for *P. vivax* under the regular treatment scenario (left) and the MDA scenario (right).







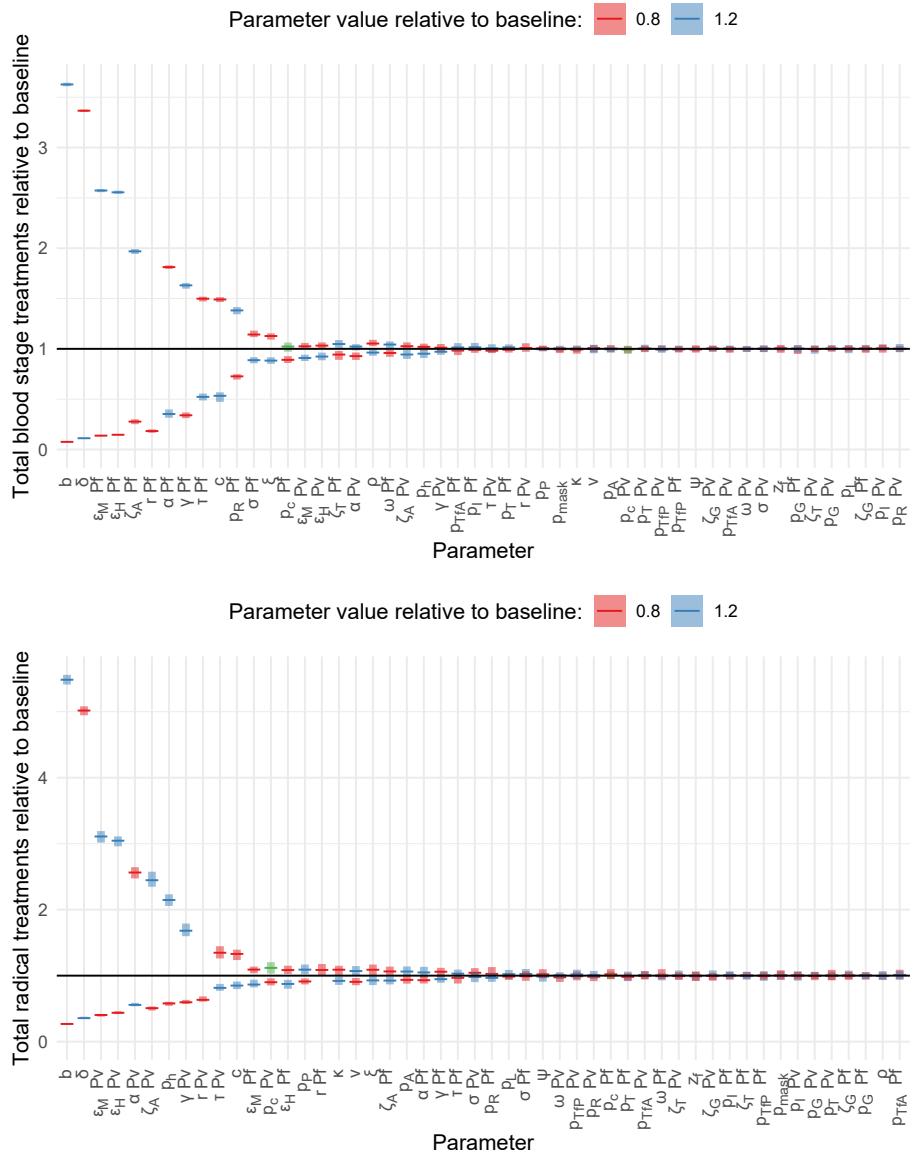


Figure S4: Sensitivities of cumulative symptomatic infections, infections, deaths, *P. vivax* relapses, individuals treated with standard cure and individuals treated with radical cure to changes in model parameters. These are presented in terms of the mean relative outcome, compared to baseline, when each parameter is scaled by 0.8 and 1.2. Red, blue and green horizontal lines represent the mean outcomes given a parameter scaling of 0.8, 1.2 and less than 1.2 (to keep probability terms less than 1), respectively. Error bars represent the minimum and maximum relative outcome, compared to baseline. Each minimum, mean and maximum calculated from 50 simulations.

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