Disclaimer: The conclusions based on the analysis in this report may be used in conjunction with other data sources to inform policy but the model is not reliably predictive and should not be used as a sole source of information upon which decisions are made

Abstract

Background

Thailand aims to achieve elimination status within the next 10 years as incidence is low. A large proportion of cases are imported from neighbouring high prevalence countries and as such interventions targeting these imported cases are effective but often not desirable. This report investigates the cost and effectiveness of various test and treat intervention packages including Glucose-6-phosphate dehydrogenase deficiency testing, Rapid Diagnostic Testing at the border, and primaquine and artemisinin combination therapy.

Methods

A multi-species compartmental model was adapted to reflect the key features of malaria transmission, control and elimination in Thailand. Intervention packages were compared and costed in order to investigate feasibility, cost and reduction in cases.

Results

The most effective and agreeable intervention package was found to be testing all individuals at the Thai border for malaria and treating those who test positive. This lead to a reduction in falciparum and vivax cases of 14,564 and 4,912 per year between 2010 and 2037 at a cost of $1,034,508.31 per year.

Conclusions

Although the number of yearly treatments and tests is lower in reality due to underreporting, this analysis showed that interventions targeting imported cases can be successful in working towards the goal of elimination within the desired timeframe.

Background

Malaria disease in Thailand is primarily caused by two species of anopheles mosquito: *plasmodium falciparum* and *plasmodium vivax*. Prevalence in recent years has been decreasing (World Health Organization 2021) and the national strategic plan for Thailand is elimination in the next decade (World Health Organization 2006). Universal healthcare is available to all nationals hence there is relatively little death and severe disease caused by malaria. Insecticide treated nets (ITNs) and long-lasting insecticide nets (LLINs) are widely used and have achieved high coverage in recent years, reducing transmission in endemic areas, while indoor room spray (IRS) is not widely accepted and contributes little to malaria control (Ministry of Public Health 2017). Artemisinin Combined Therapy (ACT) is the first line treatment for falciparum malaria and a 14-day dose of primaquine is recommended for treating vivax. Malaria caused by vivax can result in relapse due to the presence of hypnozoites, which are killed by primaquine treatment (Baird & Rieckmann 2003) but not ACT (Douglas et al. 2010). Individuals with glucose-6-phosphate dehydrogenase (G6PD) deficiency, however, may develop primaquine-induced haemolysis (Han et al. 2021, Watson et al. 2017). Roughly 12% of the Thai population is deficient

in G6PD (V S Tanphaichitr 1 et al. 1995) and G6PD deficiency testing is therefore recommended before primaquine treatment, and those deficient receive ACT.

Despite low transmission in Thailand, a high proportion of imported cases is reported from surrounding high prevalence countries such as Cambodia, Vietnam, Myanmar and Lao People's Democratic Republic (World Health Organization 2021). Reluctance to allocate resources to non-nationals makes these cases difficult to target, despite their significant contribution to Thailand's transmission. Rapid diagnostic tests (RDTs) are available that can detect the species as well as the presence of malaria (Agarwal et al. 2020). This report investigated the effect of using such tests at Thai borders. The treatments modelled in this report were based on those currently part of Thailand's national elimination strategy (World Health Organization 2006).

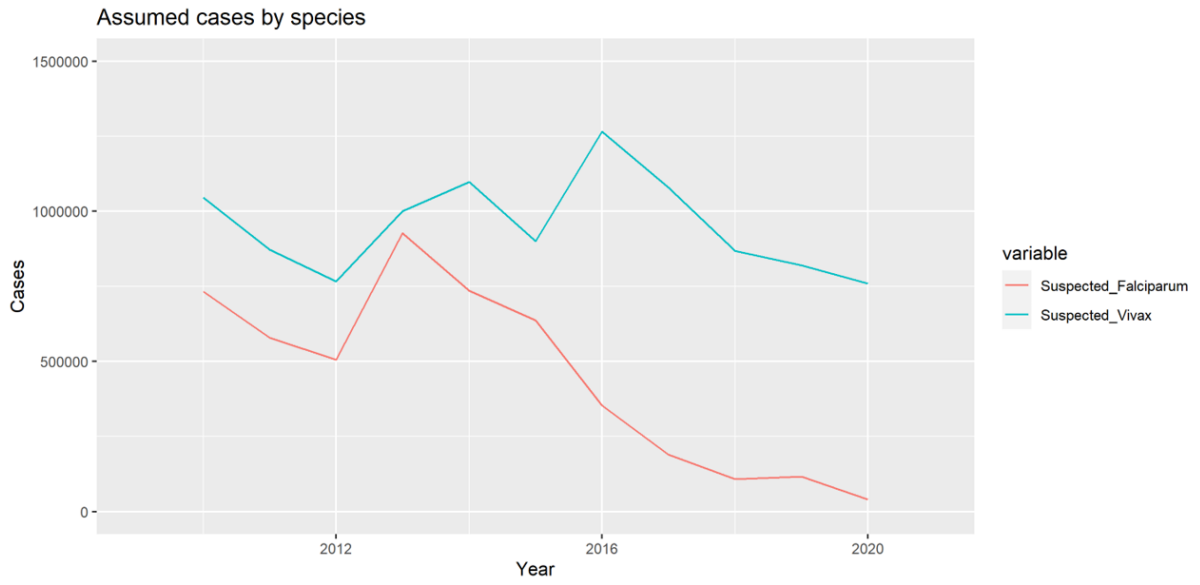


Figure 1: Assumed cases by species from 2010-2020

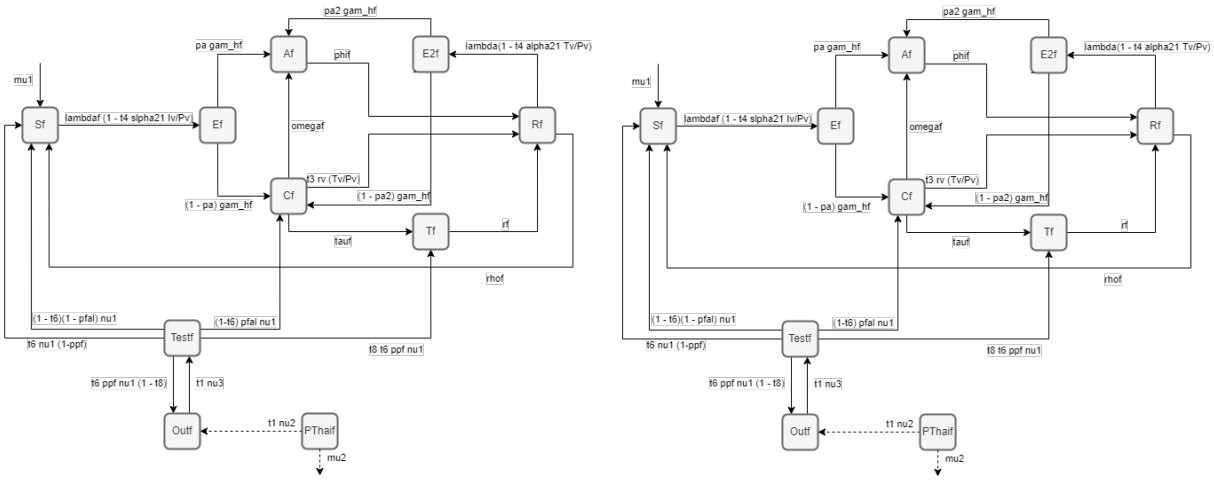
Methods

Data

The World Malaria Report 2021 was used to obtain data on total suspected cases in Thailand and surrounding countries between 2010 and 2020. Total cases reported by species were significantly less than total suspected cases so the ratio of the two species considered was extrapolated to all suspected cases and other species were treated as negligible. Figure 1 shows the suspected cases by species in Thailand between 2010 and 2020, assuming the same ratio as reported cases.

Transmission model

A compartmental model was used to describe two types of malaria transmission in Thailand: malaria disease caused by two species, each modelled by entangled transmission cycles. Figure 2 shows the compartmental model.



(a) Plasmodium falciparum malaria transmission model

(b) Plasmodium vivax malaria transmission model

Figure 2: Summary statistics for fitting of two models

Death caused by malaria was not included in the model; recent malaria death has been low in Thailand (Ministry of Public Health 2017) and was assumed negligible compared to natural deaths. Furthermore severe disease was assumed negligible and infected individuals were modelled as either asymptomatic or clinical. The model assumed only those exhibiting symptoms (clinical) required treatment, and that all individuals requiring treatment receive it from the same source. Although a treatment cascade could be considered, since Thailand provides universal healthcare to all citizens only one treatment source was modelled. ACT and primaquine for radical treatment were modelled as the two treatment types, depending on parasite species and intervention strategy.

Thailand exhibits seasonal incidence with a large peak in June and a smaller one in December (Mercado et al. 2019) and as such a seasonality function was incorporated in the force of infection, but the smaller peak was assumed negligible due to the time scale of 27 years and only a single peak per year was modelled. Although a common intervention in many malaria endemic settings, indoor room spray (IRS) was not included in the model as it is not widely accepted by the population and has achieved low coverage in the past (Ministry of Public Health 2017). Long-lasting insecticidal nets (LLINs) and insecticide treated nets (ITNs), however, are widely accepted in Thailand and as of the most recently published malaria report in 2017, 100% of the at-risk population are reported as being protected by ITNs(Ministry of Public Health 2017). An artificial decreasing function *nets* was incorporated into the model as a multiplier to the forces of infection in order to induce a reduction in cases over time in order to fit to the available data. The degree to which LLINs and ITNs reduce transmission is estimated by Yang et al. (2018) to be 56% and 41% respectively. The starting value (0.52) of the *nets* function was based on these figures and over time decreased to 0.1 assuming continued reduction in transmission due to widespread use of nets. Other parameters were modified to fit the data visually. Due to the time limitations of this assignment, no Bayesian or more complex fitting methods were used. The parameters modified to fit the data were m (mosquitoes per human) and $relv$ (relative transmission of vivax).

The primary output of the model was total and yearly incidence of cases by species, with daily results manipulated to be directly compared with the suspected yearly cases as reported in (World Health Organization 2021) (which was used to fit the model without

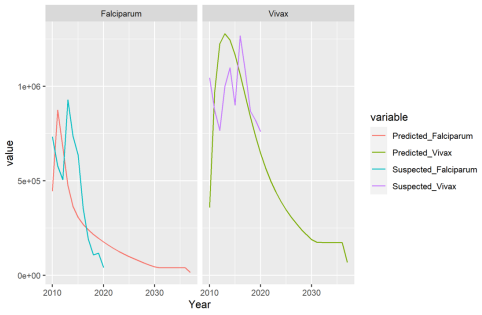
interventions applied). The case total was calculated by counting every individual that entered the exposed compartment for each species over the entire time period. The secondary output of the model was the yearly and total costs of treatment and screening tests. The total cost of each test and treatment was calculated by multiplying the unit cost by the number of people in the test or treat compartments. The average cost used in the scenario analysis was the cumulative cost divided by the number of years in the model (37). In order to compare multiple intervention scenarios, simple binary switches were incorporated into the model. In total there were seven: outer population, triggering relapse, dual treatment, cross immunity, G6PD deficiency testing, and border screening with and without treatment of imported cases. The migration switch was set to 1 for the duration of this analysis to model the high yearly influx of non-Thai nationals into the country, contributing to malaria incidence with imported cases. The resulting analysis showed the effect of the other switches on the outcomes of the model.

Appendix A gives a detailed description of each parameter and the associated assumptions. Appendix B gives a full list of the equations derived from the compartmental diagram in Figure 2. The full model with equation and parameter descriptions is available at `https://github.com/student1061175/malaria`.

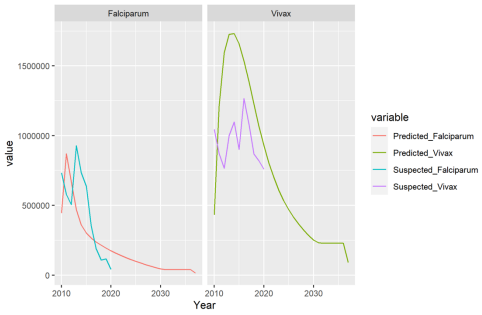
Results

The model was fitted to WHO data on suspected cases with no interventions employed as a baseline to which other intervention packages would be compared. Three neighbouring countries (Myanmar, Lao and Cambodia) were selected to contribute to migration as they have high malaria prevalence and contribute to Thailand's imported cases. Without the border testing intervention, disease-free individuals entering Thailand enter the susceptible compartment, whereas those with falciparum or vivax enter the clinical compartment for the relevant species' transmission cycle. For simplicity it was assumed that all imported cases are clinical, however a future model could consider the effect of asymptomatic cases entering undetected. With border screening in effect, individuals with a negative RDT result enter the susceptible compartment. Positive results entered the relevant treatment compartment or were turned away at the border. G6PD diagnostic testing, if active, was assumed to apply to all individuals in the clinical vivax compartment before they received relevant treatment. In the absence of G6PD screening, all clinical vivax cases are assumed to be treated with primaquine which is the first-line treatment in Thailand for vivax infection (Ministry of Public Health 2017). G6PD screening causes approximately 12% of the population to receive ACT treatment and hence along the transmission path where relapse is more likely, as ACT does not kill hypnozoites. As a result the number of vivax cases in scenario 2 increased compared to universal use of primaquine as treatment at baseline (+15,552 vivax cases per year). Scenario 2 incurred the lowest cost ($309,708.00 per year). Scenarios 3 and 4, turning imported cases away at the border with and without G6PD testing, reduced the number of cases to a similar degree compared to baseline (-14,886 falciparum cases per year, -41,126 and -41086 vivax cases per year respectively). Due to the high relative cost of RDTs ($2,86 per test) and the high migration rate in the model, the yearly costs incurred were significantly higher than scenario 2 ($1,027,966.00 and $1,028,284.33 per year). Scenarios 5 and 6 modelled the effect of treating imported cases in Thailand rather than refusing entry. Without G6PD testing, a lower number of vivax cases were prevented (-4,912 per year) but, due to the interventions targeting vivax rather than falciparum, the number of falciparum cases prevented was similar (-

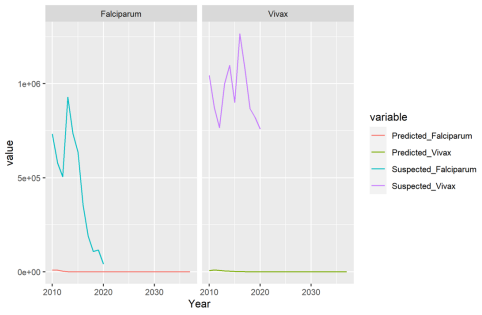
14,464 per year). The yearly cost was only slightly higher than scenarios 3 and 4 due to the cost of RDTs outweighing the increased treatment costs. Finally, border screening combined with treatment of imported cases and G6PD testing was the most expensive ($1,146,821.51 per year) and lead to the highest increase in vivax cases compared to baseline due to the higher number of relapses (+17,513 cases per year), with a similar number of falciparum cases prevented to other scenarios (-14,568 per year). Table **??** shows the full comparison of cases and cost for each scenario. Figure 3 shows the number of cases per year as predicted by the model overlaid with the number of suspected cases as reported by WHO (World Health Organization 2021). Further effects of binary switches and other parameters on daily cost and incidence can be explored with the R Shiny app which can be found at `https://github.com/student1061175/malaria`.



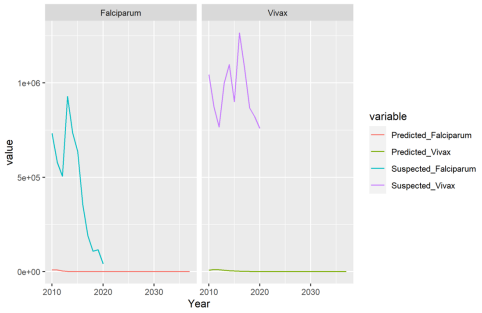
(a) Scenario 1: no interventions (baseline)



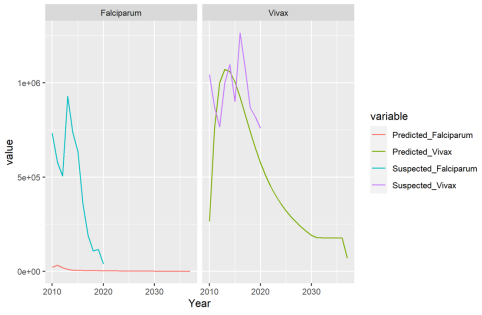
(b) Scenario 2: G6PD testing only



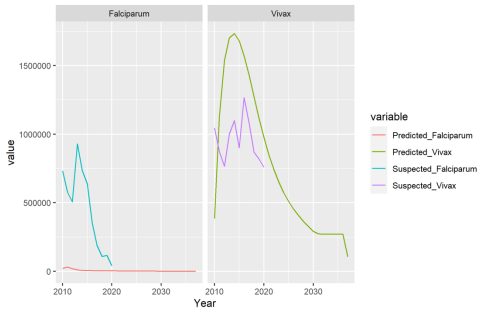
(c) Scenario 3: Border testing and turning away imported cases



(d) Scenario 4: Border testing and turning away imported cases with G6PD diagnostic testing



(e) Scenario 5: Border testing and treated imported cases without G6PD diagnostic testing



(f) Scenario 6: Border testing and treating imported cases with G6PD diagnostic testing

Figure 3: Cases predicted by model compared with WHO data on suspected cases by year and species

Discussion

The scenario analysis showed that the cheapest option was G6PD diagnostic testing alone, however the model suggested that this could lead to an increase in cases and inherently induce a higher cost and burden, which does not align with Thailand's national strategic plan for elimination and as such should not be considered a viable option. Border screening, although associated with much greater cost, lead to a considerable reduction in cases except when imported cases were treated in combination with G6PD testing. The scenario that lead to the greatest reduction in cases involved turning away individuals who test positive on an RDT. Although this protects Thai nationals from exposure to infection from imported malaria, refusal of entry is not feasible or acceptable as tourism and farming industries rely on open borders to flourish and contribute to national GDP. The relative cost of treating imported cases rather than turning them away was marginal and as such the most agreeable intervention package suggested by this model was to test individuals at the border and treat those who test positive for malaria. The health and economic burden of treating G6PD deficient individuals for primaquine-induced haemolysis was not considered so a conclusion as to whether G6PD testing is a viable option for Thailand cannot be made based on the results of this report. This work could also be built upon by incorporating seasonal tourism and farming into migration rates, as well as modelling the effect of testing 25, 50 and 75% of individuals at the border or for G6PD deficiency rather than 100%.

Conclusions

All scenarios require considerable investment in non-Thai residents which, although not necessarily desirable, may be necessary since the final stages of elimination may counter-intuitively incur a higher cost than earlier stages of malaria control. It should be noted that while the model suggested total cases of malaria, the actual number of individuals tested and treated in reality is far lower due to factors such as under-reporting and recovery without treatment. The number of reported cases of falciparum and vivax malaria in Thailand in 2020 was 155 and 2892 (World Health Organization 2021). Hence the total costs for tests and treatments in reality are much lower than given in this report. However, the relative cost of each intervention package suggests an intervention targeting and treating individuals passing through borders would be effective at reducing the number of malaria cases in Thailand.

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Report word count: 2000

Referencing: Harvard

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Supplementary information

Appendix A: Parameter table

Parameter Table				
Parameter	Value	Description	Assumptions	Source
t_1	0 or 1	Outer population switch	x	Under test
t_2	0 or 1	Triggering relapse switch	x	Under test
t_3	0 or 1	Dual treatment switch	x	Under test
t_4	0 or 1	Cross immunity switch	x	Under test
t_6	0 or 1	Border testing switch	Either all individuals are tested at the border or none	Under test
t_7	0 or 1	G6PD testing switch	Either all individuals in treatment compartment are screened for G6PD deficiency or none	x
t_8	0 or 1	Treat imported cases	Imported cases are treated rather than turned away	Under test
α_{12}	1	Cross immunity from falciparum to vivax	x	Expert opinion‡
α_{21}	0.5	Cross immunity from vivax to falciparum	x	Expert opinion‡
pa	0.1	Asymptomatic proportion for the falciparum immune	x	Shretta et al. (2019)
pa_2	0.9	Asymptomatic proportion for the falciparum non-immune	x	Shretta et al. (2019)
γ_{hf}	$\frac{1}{21}$	Latent rate in humans for falciparum (days^{-1})	x	Shretta et al. (2019)
γ_{hv}	$\frac{1}{17}$	Latent rate in humans for vivax (days^{-1})	x	Shretta et al. (2019)

Parameter Table				
Parameter	Value	Description	Assumptions	Source
τ_f	0.7	Rate of receiving ACT treatment for falciparum (days^{-1})	x	Expert opinion‡
τ_v	1	Rate of receiving ACT/primaquine treatment for vivax (days^{-1})	x	Expert opinion‡
ϕ_f	$\frac{1}{130}$	Natural recovery rate from falciparum infection (days^{-1})	x	Shretta et al. (2019)
ϕ_v	$\frac{1}{365.25}$	Natural recovery rate from vivax infection (days^{-1})	x	(Shretta et al. 2019)
ω_f	0.1	Rate of natural improvement from clinical to asymptomatic falciparum infection (days^{-1})	Old measurement: no ethical way to update data in a world with effective malaria treatment	Shretta et al. (2019)
ω_v	0.1	Rate of natural improvement from clinical to asymptomatic vivax infection (days^{-1})	Old measurement: no ethical way to update data in a world with effective malaria treatment	Shretta et al. (2019)
r_f	1	Rate of recovery after ACT treatment for falciparum (days^{-1})	24 hours to clear falciparum parasites with ACT in non-endemic setting: most of Thailand is a non-endemic zone	Pousibet-Puerto et al. (2016)
r_v	0.86	Rate of recovery after ACT treatment for vivax (days^{-1})	28 hours to clear vivax parasites with ACT	Douglas et al. (2010)
r_p	$\frac{1}{14}$	Rate of recovery after 14 day primaquine treatment (days^{-1})	14 days to clear parasites with primaquine treatment	Shretta et al. (2019)

Parameter Table				
Parameter	Value	Description	Assumptions	Source
ρ_f	$\frac{1}{365.25}$	Rate of loss of immunity from falciparum infection (days^{-1})	x	Shretta et al. (2019)
ρ_v	$\frac{1}{365.25}$	Rate of loss of immunity from vivax infection (days^{-1})	x	Shretta et al. (2019)
rel	0.01	Rate of relapse from vivax (days^{-1})	x	Shretta et al. (2019)
$prel$	0.68	Probability of relapse from vivax infection without primaquine treatment	x	Shretta et al. (2019)
$prelp$	0.13	Probability of relapse from vivax infection with primaquine treatment	x	Shretta et al. (2019)
$increl$	0.3	Increased rate of relapse from vivax infection due to triggering from falciparum infection	x	Shretta et al. (2019)
$dhyp$	$\frac{1}{400}$	Death rate of hypnozoites (days^{-1})	x	Shretta et al. (2019)
ψ	0.12	Proportion of population with G6PD deficiency	Proportion of population is constant across Thailand and all demographics	V S Tanphaichitr 1 et al. (1995), Devine Id et al. (2021)
amp	0.1	Amplitude of seasonality function	Large peak in December	Thimasarn et al. (n.d.), Mercado et al. (2019)
ϕ	0.5	Periodic shift of seasonality function	Large peak in December	Thimasarn et al. (n.d.), Mercado et al. (2019)
$peak$	1	Number of peaks within one season	Smaller June peak is negligible for the purposes of this model	Thimasarn et al. (n.d.), Mercado et al. (2019)

Parameter Table				
Parameter	Value	Description	Assumptions	Source
a	$\frac{1}{3}$	Human feeding rate: expected number of bites on humans per mosquito	x	Shretta et al. (2019)
b	0.5	Transmission efficiency of infectious mosquito on human	x	Shretta et al. (2019)
c	0.5	Transmission efficiency of infectious human on mosquito	Value equal for falciparum and vivax due to time limitations	Shretta et al. (2019)
m	0.8	Mosquitoes per human	Lower value due to low transmission in Thailand	Fit to data
μ_m	$\frac{1}{14}$	Death rate of mosquitoes (days^{-1})	1/ average life expectancy of mosquito in days	Shretta et al. (2019)
μ_2	$\frac{1}{77.15 \times 365.25}$	Death rate of humans (days^{-1})	Average life expectancy of human in days	World Bank
γ_{mf}	0.1	Rate of onset of infectiousness of falciparum infection in mosquito (days^{-1})	x	Shretta et al. (2019)
γ_{mv}	$\frac{1}{12}$	Rate of onset of infectiousness of vivax infection in mosquito (days^{-1})	x	Shretta et al. (2019)
$nets1$	decreasing function	Reducing transmission due to net useage	Decreasing value due to decreasing prevalence in Thailand	Fit to data
rel_v	0.29	Relative transmission of vivax compared to falciparum	x	Expert opinion‡, $fittodata$
g	1.00049	Population growth rate (days^{-1})	Constant population growth rate over time period modelled	World Bank
$fPrev_{Cam}$	0.00121 *	Prevalence of falciparum in Cambodia	Constant over time period modelled	World Health Organization (2021)
$vPrev_{Cam}$	0.0102∗	Prevalence of vivax in Cambodia	Constant over time period modelled	World Health Organization (2021)
P_{Cam}	11823489∗†	Population of Cambodia	Constant over time period modelled	World Health Organization (2021)

Parameter Table

Parameter	Value	Description	Assumptions	Source
$fPrev_{Lao}$	0.0694*	Prevalence of falciparum in Lao People's Democratic Republic	Constant over time period modelled	World Health Organization (2021)
$vPrev_{Lao}$	0.0830*	Prevalence of vivax in Lao People's Democratic Republic	Constant over time period modelled	World Health Organization (2021)
P_{Lao}	3785762*†	Population of Lao People's Democratic Republic	Constant over time period modelled	World Health Organization (2021)
$fPrev_{Mya}$	0.0294*	Prevalence of falciparum in Myanmar	Constant over time period modelled	World Health Organization (2021)
$vPrev_{Mya}$	0.0844*	Prevalence of vivax in Myanmar	Constant over time period modelled	World Health Organization (2021)
P_{Mya}	32383620*†	Population of Myanmar	Constant over time period modelled	World Health Organization (2021)
P_{Out}	47992871*†	Total population of modelled countries outside Thailand	Constant over time period modelled	World Health Organization (2021)

Parameter Table				
Parameter	Value	Description	Assumptions	Source
P_{Thai}	12750928†	Population of Thailand	Initial population taken from 2010	World Health Organization (2021)
ν_1	10^{11}	Border testing rate (days^{-1})	Extremely high rate of leaving: only passing through testing compartment, not spending any time at the border	Under test
ν_2	0.001	Emigration rate: individuals leaving Thailand (days^{-1})	x	Nations (n.d.)
ν_3	$\frac{1}{3500}$	Migration rate: individuals entering Thailand (days^{-1})	x	Nations (n.d.)
ζ_{af}	0.47	Relative infectiousness of asymptomatic falciparum infection compared to clinical	x	Shretta et al. (2019)
ζ_{av}	1	Relative infectiousness of asymptomatic vivax infection compared to clinical	x	Shretta et al. (2019)
ζ_{tf}	0.1	Relative infectiousness of treated falciparum infection compared to clinical	x	Expert opinion‡
ζ_{tv}	0.1	Relative infectiousness of treated vivax compared to clinical	x	Expert Opinion‡
$pfal$	0.10∗	Probability of migrating individual having falciparum malaria		World Health Organization (2021)
$pviv$	0.10∗	Probability of migrating individual having vivax malaria		World Health Organization (2021)

Parameter Table				
Parameter	Value	Description	Assumptions	Source
ppf	0.10∗	Probability of positive falciparum RDT result at border		World Health Organization (2021), Agarwal et al. (2020)
ppv	0.10∗	Probability of positive vivax RDT result at border		World Health Organization (2021), Agarwal et al. (2020)
c_{prim}	0.38	Cost per primaquine treatment (USD)	x	Devine Id et al. (2021)
c_{ACT}	0.28	Cost per ACT treatment (USD)	x	Devine Id et al. (2021)
c_{RDT}	2.86	Cost per RDT (USD)	x	Devine Id et al. (2021)
c_{G6PD}	3.03	Cost per G6PD test (USD)	x	Devine Id et al. (2021)

∗ Data taken from 2020 and values assumed constant over time period modelled: 2010-2037
† At-risk population, not total country population
‡ Expert opinion: taken from models used in class with Sheetal Silal

Appendix B: Equations

Total populations

$$PThai_f = Sf + Ef + Af + Cf + Tf + Rf + E2f$$

$$PThai_v = Sv + Ev + Av + Cv + TPv + TAv + Lv + Rv + E2v$$

Individuals treated for vivax

$$Tv = TP_v + TA_v$$

Populations considered outside of Thailand

$$P_{Out} = P_{Cam} + P_{Mya} + P_{Lao}$$

Birth rate greater than death rate

$$\mu_1 = g\ \mu_2$$

Infectious individuals

$$I_f = C_f + \zeta_{af}\ A_f + \zeta_{tf}\ T_f$$
$$I_v = C_v + \zeta_{av}\ A_v + \zeta_{tv}\ T_v$$

Seasonality

$$seas = 1 + amp\ \cos(2\pi(\frac{t}{365} - \phi))^{peak}$$

Force of infection

$$\lambda_f = seas\ nets\ \frac{a^2\ b\ c\ m\ \frac{I_f}{PThai_f}}{(a\ c\ \frac{I_f}{PThai_f} + \mu_m)\ (\frac{\gamma_{mf}}{\gamma_{mf}+\mu_m})}$$

$$\lambda_v = rel_v\ seas\ nets\ \frac{a^2\ b\ c\ m\ \frac{I_v}{PThai_v}}{(a\ c\ \frac{I_v}{PThai_v} + \mu_m)\ (\frac{\gamma_{mv}}{\gamma_{mv}+\mu_m})}$$

Probabilities an individual from outside of Thailand has malaria

$$p_{fal} = \frac{fPrev_{Cam}}{P_{Cam}} + \frac{fPrev_{Lao}}{P_{Lao}} + \frac{fPrev_{Mya}}{P_{Mya}}$$

$$p_{viv} = \frac{vPrev_{Cam}}{P_{Cam}} + \frac{vPrev_{Lao}}{P_{Lao}} + \frac{vPrev_{Mya}}{P_{Mya}}$$

Testing probabilities

$$pTPF = p_{fal}\ sens$$
$$pFPF = (1 - p_{fal})\ (1 - spec)$$
$$pTNF = (1 - p_{fal})\ spec$$
$$pFNF = p_{fal}\ (1 - sens)$$

$$pTPV = p_{viv}\ sens$$

$$pFPV = (1 - p_{viv})\ (1 - spec)$$
$$pTNV = (1 - p_{viv})\ spec$$
$$pFNV = p_{viv}\ (1 - sens)$$

Total positive results observed is sum of true and false positives

$$ppf = pTPF + pFPF$$
$$pnf = 1 - ppf$$
$$ppv = pTPV + pFPV$$
$$pnv = 1 - ppv$$

Falciparum system

$$\frac{dTestf}{dt} = t_1\ \nu_3\ Out_f - t_6\ \nu_1\ Testf - (1 - t_6)\ \nu_1\ Testf$$
$$\frac{dOutf}{dt} = t_1\ \nu_2\ PThai_f + (1 - t_8)\ t_6\ ppf\ \nu_1\ Test_f - t_1\ \nu_3\ Out_f$$

$$\frac{dS_f}{dt} = \mu_1\ PThai_f + t_6\ \nu_1\ (1 - ppf)Test_f + (1 - t_6)(1 - pfal)\nu_1\ Test_f - \lambda_f(1 - t_4\alpha_{21}\frac{I_v}{PThai_v})S_f + \rho_f\ R_f - t_1\ \nu_2\ S_f - \mu_2\ S_f$$

$$\frac{dE_f}{dt} = \lambda_f\ (1 - t_4\ \alpha_{21}\ \frac{I_f}{PThai_f}) - \gamma_{hf}\ E_f - t_1\ \nu_2\ E_f - \mu_2\ E_f$$
$$\frac{dA_f}{dt} = pa\ \gamma_{hf}\ E_f + pa_2\ \gamma_{hf}\ E2_f + \omega_f\ C_f - \phi_f\ A_f - t_1\ \nu_2\ A_f - \mu_2\ A_f$$

$$\frac{dC_f}{dt} = (1 - pa)\ \gamma_{hf}\ E_f + (1 - pa_2)\ \gamma_{hf}\ E2_f + (1 - t_6)\ pfal\ \nu_1\ Test_f - t_3\ rv\ \frac{T_v}{PThai_v}\ C_f - \omega_f\ C_f - \tau_f\ C_f - t_1\ \nu_2\ C_f - \mu 2_f\ C_f$$

$$\frac{dT_f}{dt} = \tau_f\ C_f + t_8\ t_6\ ppf\ \nu_1\ Test_f - rf\ T_f - t_1\nu_2\ T_f - \mu_2 T_f$$

$$\frac{dR_f}{dt} = rf\ T_f + \phi_f\ A_f + t_3\ rv\ \frac{T_v}{PThai_v}\ C_f - \lambda_f(1 - t_4\ \alpha_{21}\frac{T_v}{PThai_v})\ R_f - \rho_f\ R_f - t_1\ \nu_2\ R_f - \mu_2\ E2_f$$

$$\frac{dE2_f}{dt} = \lambda_f(1 - t_4\ \alpha_{21}\frac{T_v}{PThai_v})\ R_f - \gamma_{hf}\ E2_f - t_1\ \nu_2\ E2_f - \mu_2\ E2_f$$

Vivax system

$$\frac{dTest_v}{dt} = t_1\ \nu_3\ Out_v - (1 - t_6)\ \nu_1\ Test_v - t_6\ \nu_1\ (1 - ppv)\ Test_v - t_7\ \psi\ t_6\ \nu_1\ ppv\ Test_v - t_7(1 - \psi)\ t_6\ \nu_1\ ppv\ Test_v - (1 - t_7)\ t_6\ \nu_1\ ppv\ Test_v$$

$$\frac{dOut_v}{dt} = t_1\ \nu_2\ PThai_v + (1-t_8)\ t6\ \nu_1\ ppv\ Test_v - t_1\ \nu_3\ Out_v$$

$$\frac{dS_v}{dt} = \mu_1\ PThai_v - \lambda_v(1-t_4\alpha_{21}\frac{I_v}{PThai_v})\ S_v + (1-t_6)\ \nu_1\ (1-pviv)\ Test_v + t_6\ \nu_1\ (1-ppv)\ Test_v + \rho_v\ R_v + dhyp\ L_v - t_1\ \nu_2\ S_v - \mu_2\ S_v$$

$$\frac{dE_v}{dt} = \lambda_v\ (1-t_4\ \alpha_{21}\frac{I_v}{PThai_v})\ S_v - \gamma_{hv}\ E_v - t_1\ \nu_2\ E_v - \mu_2\ E_v$$

$$\frac{dA_v}{dt} = pa\ \gamma_{hv}\ E_v + pa_2\ \gamma_{hv}\ E2_v + \omega_v\ C_v - \phi_v\ A_v - t_1\ \nu_2\ A_v - \mu_2\ A_v$$

$$\frac{dC_v}{dt} = (1-pa)\ \gamma_{hv}\ E_v + (1-pa_2)\ \gamma_{hv}\ E2_v + (1-t6)\ \nu_1\ pviv\ Test_v - t_3\ r_f\ \frac{T_f}{PThai_f}\ C_v - \omega_v\ C_v - (1-t_7)\ \tau_v\ C_v - t_7\ \tau_v\ (1-\psi)\ C_v - t_7\tau_f\ psi\ C_v - t1\ \nu_2\ C_v - \mu_2\ C_v$$

$$\frac{dTP_v}{dt} = (1-t_7)\ \tau_v\ C_v + t_7\ \tau_v\ (1-\psi)\ C_v - r_p\ TPv + t_8\ (1-t_7)\ t_6\ \nu_1\ ppv\ Test_v + t_8\ t_7\ (1-\psi) * t_6\ \nu_1\ ppv\ Test_v - t_1\ \nu_2\ TPv - \mu_2\ TP_v$$

$$\frac{dTA_v}{dt} = t_7\ \tau_f\ \psi\ C_v - t_7\ r_v\ TA_v + t_8\ t_7\ \psi\ t_6\ \nu_1\ ppv\ Test_v - t_1\ \nu_2\ TAv - \mu_2\ TAv$$

$$\frac{dL_v}{dt} = prelp\ rp\ TP_v + t_7\ prel\ r_v\ TA_v + t_3\ (1-prel)\ r_f\ \frac{T_f}{PThai_f}\ C_v - rel\ L_v - t_2\ increl\ \frac{T_f}{PThai_f}\ Lv - dhyp\ L_v - t_1\ \nu_2\ L_v - \mu_2\ L_v$$

$$\frac{dR_v}{dt} = (1-prelp)\ r_p\ TP_v + t_7\ (1-prel)\ r_v\ TA_v + \phi_v\ A_v + t_3\ (1-prel)\ r_f\ \frac{T_f}{PThai_f}\ C_v - \rho_v\ R_v - \lambda\ (1-t_4\ \alpha_{12}\frac{I_f}{PThaif})\ R_v - t_1\ \nu_2\ R_v - \mu_2\ R_v$$

$$\frac{dE2_v}{dt} = \lambda_v\ (1-t_4\ \alpha_{12}\ \frac{I_f}{PThai_f})\ R_v + rel\ Lv + t_2\ increl\ \frac{T_f}{PThai_f}\ L_v - \gamma_{hv}\ E2_v - t_1\ \nu_2\ E2_v - \mu_2\ E2_v$$

Cumulative counters

$$\frac{dCInc_f}{dt} = \lambda_f(1-t_4\ \alpha_{21}\frac{I_v}{PThai_v})\ S_f + \lambda_f(1-t_4\ \alpha_{21}\frac{I_v}{PThai_v})\ R_f$$

$$\frac{dCInc_v}{dt} = \lambda_v(1 - t_4\ \alpha_{12}\ \frac{I_f}{PThai_f})\ S_v + \lambda_v(1 - t_4\ \alpha_{12}\ \frac{I_f}{PThai_f})\ R_v + rel\ L_v + t_2\ increl\ \frac{T_f}{PThai_f}\ Lv$$

$$\frac{dTrtf}{dt} = \tau_f\ C_f + t_3\ r_v\ \frac{TA_v + TP_v}{PThai_v}\ C_f + t_8\ t_6\ ppf\ \nu_1\ Test_f$$

Cumulative costs

$$\frac{dCPrim}{dt} = c_{prim}\ ((1 - t_7)\ \tau_v\ C_v + t_7\ \tau_v\ (1 - \psi)\ C_v + (1 - t_7)\ t_6\ \nu_1\ ppv\ t_8\ Testv + t_7\ (1 - \psi)\ t_6\ \nu_1\ ppv\ t_8\ Testv)$$

$$\frac{dCACT}{dt} = c_{ACT}\ (t_7\ \tau_f\ \psi\ C_v + \tau_f\ C_f + t_3\ r_f\ \frac{T_f}{PThai_f}\ C_v + t_7\ psi\ t_6\ \nu_1\ ppv\ t_8\ Testv)$$

$$\frac{dCCv}{dt} = t_7\ c_{G6PD}((1 - pa)\ \gamma_{hv}\ E_v + (1 - pa_2)\ \gamma_{hv}\ E2_v - (1 - t_6)\ \nu_1\ \ Testv)$$

$$\frac{dCTest}{dt} = t_6\ c_{RDT}\ (t_1\ \nu_3\ Out_f)$$

Appendix C: Code

Malaria in Thailand Model

```
# Load packages ####
library(pacman)
p_load(deSolve, tidyverse, doParallel, manipulate, readxl)

# Plot real case data ####

data <- as_tibble(as.data.frame(read_excel("populations_and_
   ↪ prevalence.xlsx", sheet="Case_data_Thailand", range="B20:D31
   ↪ ", col_names=TRUE)))
cases <- reshape2::melt(data, id.var='Year')

(ggplot(cases, aes(x=Year, y=value, col=variable)) %>%
    + geom_line() %>%
    + xlim(2009,2021)
  + ylim(0,1500000)
  + labs(title="Assumed␣cases␣by␣species", x ="Year", y = "Cases")
    ↪ )

# Times ####
times <- seq(0, 10000, 1) # approx 27 years

# Initial conditions ####
# Based on 2010 numbers from World Malaria Report 2021

inits <- read_excel("populations_and_prevalence.xlsx", sheet="
   ↪ Initial_values_Thailand", range="B7:C27", col_names=TRUE,
   ↪ col_types=c("text","numeric"))

Testf_0 <- as.numeric(inits[1,2])
Outf_0 <- as.numeric(inits[2,2])
Sf_0 <- as.numeric(inits[3,2])
Ef_0 <- as.numeric(inits[4,2])
Af_0 <- as.numeric(inits[5,2])
Cf_0 <- as.numeric(inits[6,2])
Tf_0 <- as.numeric(inits[7,2])
Rf_0 <- as.numeric(inits[8,2])
E2f_0 <- as.numeric(inits[9,2])

Testv_0 <- as.numeric(inits[10,2])
Outv_0 <- as.numeric(inits[11,2])
Sv_0 <- as.numeric(inits[12,2])
Ev_0 <- as.numeric(inits[13,2])
Av_0 <- as.numeric(inits[14,2])
Cv_0 <- as.numeric(inits[15,2])
TPv_0 <- as.numeric(inits[16,2])
TAv_0 <- as.numeric(inits[17,2])
Lv_0 <- as.numeric(inits[18,2])
```

```
Rv_0 <- as.numeric(inits[19,2])
E2v_0 <- as.numeric(inits[20,2])

CIncf_0 <- 0
CIncv_0 <- 0
CTrtf_0 <- 0
CPrim_0 <- 0
CACT_0 <- 0
CCv_0 <- 0
CTestf_0 <-0
CTestv_0 <- 0

istate <- c(Testf=Testf_0, Outf=Outf_0, Sf = Sf_0, Ef = Ef_0, Af =
   ↪  Af_0, Cf = Cf_0, Tf=Tf_0, Rf = Rf_0, E2f=E2f_0,
            Testv=Testv_0, Outv=Outv_0, Sv = Sv_0, Ev = Ev_0, Av =
               ↪  Av_0, Cv = Cv_0, TPv=TPv_0, TAv=TAv_0, Lv=Lv_0,
               ↪  Rv = Rv_0, E2v=E2v_0,
            CIncf=CIncf_0, CIncv=CIncv_0, CTrtf=CTrtf_0, CPrim=
               ↪ CPrim_0, CACT=CACT_0, CCv=CCv_0, CTestf=CTestf_
               ↪ 0, CTestv=CTestv_0 )

# Parameters ####

params <- as_tibble(as.data.frame(read_excel("parameters.xlsx",
   ↪ range="A1:B80", col_names=TRUE, col_types=c("text","numeric"
   ↪ )))) # Read excel file with all parameters

parameters <- rep(0,length(params$PARAMETER)) # create empty
   ↪ parameter vector

for (i in 1:length(params$PARAMETER)){ # populate parameter vector
   ↪  with parameter names and values
  parameters[i] <- params$VALUE[i]
  names(parameters) <- params$PARAMETER
}

#Read in reduction data
net_data <- read_excel("populations_and_prevalence.xlsx", sheet="
   ↪ Reduction_parameter", range="A1:D30", col_names=TRUE)


# Define model function ####

thailand_model<-function(t, state, parameters)
{
  with(as.list(c(state, parameters)),
       {

         # Populations

         PThaif <- (Sf + Ef + Af + Cf + Tf + Rf + E2f) # Total
```

```
   ↪ population of Thailand falciparum transmission
   ↪ system
PThaiv <- (Sv + Ev + Av + Cv + TPv + TAv + Lv + Rv + E2v)
   ↪  # Total population of Thailand vivax transmission
   ↪ system

Tv <- (TPv + TAv) # Total treated for vivax: ACT and
   ↪ primaquine

mu1 <- g * mu2 # Birth rate is higher than death rate

nets<-approx(net_data$Day, net_data$nets, t)$y # Reading
   ↪ artificial decreasing function from excel
#nets2<-approx(net_data$Day, net_data$nets2, t)$y #
   ↪ Reading artificial decreasing function from excel

# Infection variables

Infectiousf <- Cf + zeta_af * Af + zeta_tf * Tf #
   ↪ Relative infectiousness for asymptomatic and
   ↪ treated considered
Infectiousv <- Cv + zeta_av * Av + zeta_tv * Tv

seas <- 1 + amp * cos(2 * pi * (t / 365 - phi)) ^ peak #
   ↪ Seasonality

# Force of infection equations

lambdaf <- nets * seas*(a^2*b*c*m*Infectiousf/PThaif)/(a*
   ↪ c*Infectiousf/PThaif+mu_m)*(gam_mf/(gam_mf+mu_m))
lambdav <- relv * nets * seas*(a^2*b*c*m*Infectiousv/
   ↪ PThaiv)/(a*c*Infectiousv/PThaiv+mu_m)*(gam_mv/(gam_
   ↪ mv+mu_m))


# Falciparum

dTestf <- ( t1 * nu3 * Outf # Individuals being tested at
   ↪  the border
            - t6 * nu1 * Testf # Individuals entering
               ↪ Thailand transmission cycle with border
               ↪  testing on
            - (1 - t6) * nu1 * Testf ## Individuals
               ↪ entering Thailand transmission cycle
               ↪ with border testing off
)

dOutf <- (  t1 * nu2 * PThaif # Leaving Thailand and
   ↪ reentering 'outside
            + (1 - t8) * t6 * ppf * nu1 * Testf #
               ↪ Imported cases turned away at border
```

```
            - t1 * nu3 * Outf ) # Entering test
               ↪ compartment

dSf <- (  mu1 * PThaif # Birth
          + t6 * nu1 * (1 - ppf) * Testf # Negative
             ↪ border screening result entering
             ↪ susceptible
          + (1 - t6) * (1 - pfal) * nu1 * Testf # No
             ↪ screening, disease-free individuals enter
             ↪  susceptible
          - lambdaf * (1 - t4 * alpha21 * Infectiousv /
             ↪ PThaiv) * Sf # Individuals becoming
             ↪ exposed with cross immunity
          + rhof * Rf # Loss of immunity
          - t1 * nu2 * Sf # Leaving Thailand
          - mu2 * Sf ) # Natural death

dEf <- (  lambdaf * (1 - t4 * alpha21 * Infectiousv /
   ↪ PThaiv) * Sf # Individuals becoming infected with
   ↪ cross immunity
          - gam_hf * Ef # Infection developing into
             ↪ asymptomatic or clinical
          - t1 * nu2 * Ef # Leaving Thailand
          - mu2 * Ef ) # Natural death

dAf <- (  pa * gam_hf * Ef # Asymptomatic disease
          + pa2 * gam_hf * E2f # Asymptomatic disease
             ↪ from secondary infection
          + omegaf * Cf # Natural improvement from
             ↪ clinical to asymptomatic disease
          - phif * Af # Natural recovery from
             ↪ asymptomatic disease
          - t1 * nu2 * Af # Leaving Thailand
          - mu2 * Af ) # Natural death

dCf <- (  (1 - pa) * gam_hf * Ef # Exposed individuals
   ↪ developing clinical disease
          + (1 - pa2) * gam_hf * E2f # Exposed
             ↪ individuals developing clinical disease
             ↪ from secondary infection
          + (1 - t6) * pfal * nu1 * Testf # With no
             ↪ border screening, infected individuals
             ↪ from border are clinical
          - t3 * rv * (Tv / PThaiv) * Cf # Treatment for
             ↪ vivax treats falciparum
          - omegaf * Cf # Improvement from clinical to
             ↪ asymptomatic disease
          - tauf * Cf # Rate of receiving ACT treatment
          - t1 * nu2 * Cf # Leaving Thailand
          - mu2 * Cf ) # Natural death
```

```
dTf <- (  tauf * Cf # Receiving ACT treatment
          + t8 * t6 * ppf * nu1 * Testf # Individuals
             ↪ screened at the border with a positive
             ↪ result receive treatment
          - rf * Tf # Recovering after ACT treatment
          - t1 * nu2 * Tf # Leaving Thailand
          - mu2 * Tf ) # Natural death

dRf <- (  rf * Tf # Recovering after ACT treatment
          + phif * Af # Natural recovery from
             ↪ asymptomatic disease
          + t3 * rv * (Tv / PThaiv) * Cf # Treatment for
             ↪ vivax treats falciparum
          - lambdaf * (1 - t4 * alpha21 * Infectiousv /
             ↪ PThaiv) * Rf # Reinfection with cross
             ↪ immunity
          - rhof * Rf # Loss of immunity
          - t1 * nu2 * Rf # Leaving Thailand
          - mu2 * Rf ) # Natural death

dE2f <- (  lambdaf * (1 - t4 * alpha21 * Infectiousv /
   ↪ PThaiv) * Rf # Reinfection with cross immunity
           - gam_hf * E2f # Developing asymptomatic or
              ↪ clinical disease from secondary
              ↪ infection
           - t1 * nu2 * E2f # Leaving Thailand
           - mu2 * E2f ) # Natural death

# Vivax

dTestv <-( t1 * nu3 * Outv # Individuals from outside
   ↪ Thailand arriving at border screening
           - (1 - t6) * nu1 * Testv # Border screening
              ↪ off, individuals entering Sv or Ev
              ↪ depending on disease status
           - t6 * nu1 * (1 - ppv) * Testv # Border
              ↪ screening on, disease free individuals
              ↪ entering susceptible
           - t7 * psi * t6 * nu1 * ppv * Testv # Border
              ↪ screening and G6PD screening on,
              ↪ deficient vivax-positive individuals
              ↪ receiving ACT treatment
           - t7 * (1 - psi) * t6 * nu1 * ppv * Testv #
              ↪ Border screening and G6P screening on,
              ↪ non-deficient vivax-positive individuals
              ↪  receive primaquine
           - (1 - t7) * t6 * nu1 * ppv * Testv ) # Border
              ↪  screening, no G6PD. All vivax-positive
              ↪ individuals receive primaquine

dOutv <- (t1 * nu2 * PThaiv # Individuals leaving
```

```
   ↪ Thailand and reentering 'outside'
          + (1 - t8) * t6 * nu1 * ppv * Testv #
             ↪ Individuals testing positive at the
             ↪ border are turned away
          - t1 * nu3 * Outv) # Individuals entering
             ↪ border testing

dSv <- (  mu1 * PThaiv # Birth
          - lambdav * (1 - t4 * alpha12 * Infectiousf /
             ↪ PThaif) * Sv # Infection with cross
             ↪ immunity
          + (1 - t6) * nu1 * (1 - pviv) * Testv # No
             ↪ border screening, vivax-negative
             ↪ individuals enter susceptible population
          + t6 * nu1 * (1 - ppv) * Testv # Border
             ↪ screening on, individuals with negative-
             ↪ vivax result enter susceptible population
          + rhov * Rv # Loss of immunity
          + dhyp * Lv # Death of hypnozoites
          - t1 * nu2 * Sv # Leaving Thailand
          - mu2 * Sv ) # Natural death

dEv <- ( lambdav * (1 - t4 * alpha12 * Infectiousf /
   ↪ PThaif) * Sv # Infection with cross immunity
         - gam_hv * Ev # Developing asymptomatic or
            ↪ clinical disease
         - t1 * nu2 * Ev  # Leaving Thailand
         - mu2 * Ev ) # Natural death

dAv <- (  pa * gam_hv * Ev # Developing asymptomatic
   ↪ disease
          + pa2 * gam_hv * E2v # Developing asymptomatic
             ↪ disease from secondary infection
          + omegav * Cv # Natural improvement from
             ↪ clinical to asymptomatic
          - phiv * Av # Natural recovery from
             ↪ asymptomatic disease
          - t1 * nu2 * Av # Leaving Thailand
          - mu2 * Av ) # Natural death

dCv <- (  (1 - pa) * gam_hv * Ev # Developing clinical
   ↪ disease
          + (1 - pa2) * gam_hv * E2v # Developing
             ↪ clinical disease from secondary infection
          + (1 - t6) * nu1 * pviv * Testv # No border
             ↪ screening, individuals with vivax enter
             ↪ clinical compartment
          - t3 * rf * (Tf / PThaif) * Cv # Treatment for
             ↪ falciparum treats vivax
          - omegav * Cv # Natural improvement from
             ↪ clinical to asymptomatic
```

```
            - (1 - t7) * tauv * Cv # All vivax cases
               ↪ treated with primaquine if G6PD testing
               ↪ is switched off
            - t7 * tauv * (1 - psi) * Cv # Only non-
               ↪ deficient treated with primaquine if G6PD
               ↪  testing is switched on
            - t7 * tauf * psi * Cv # Deficient individuals
               ↪ treated with ACT when G6PD testing is
               ↪ switched on
            - t1 * nu2 * Cv # Leaving Thailand
            - mu2 * Cv ) # Natural death

dTPv <- ( (1 - t7) * tauv * Cv # All vivax cases treated
   ↪ with primaquine if G6PD testing is switched off
            + t7 * tauv * (1 - psi) * Cv # Only non-
               ↪ deficient treated with primaquine if G6PD
               ↪  testing is switched on
            - rp * TPv # Recovering with or without
               ↪ hypnozoites with primaquine
            + t8 * (1 - t7) * t6 * nu1 * ppv * Testv # No
               ↪ G6PD screening. Border-vivax-positive
               ↪ individuals all receive primaquine
            + t8 * t7 * (1 - psi) * t6 * nu1 * ppv * Testv
               ↪ # Non-deficient border-vivax-positive
               ↪ individuals receive primaquine
            - t1 * nu2 * TPv # Leaving Thailand
            - mu2 * TPv ) # Natural death

dTAv <- (  t7 * tauf * psi * Cv # Deficient individuals
   ↪ treated with ACT when G6PD testing is switched on)
             - t7 * rv * TAv # Recovering with or without
                ↪ hypnozoites after ACT treatment (no
                ↪ primaquine))
             + t8 * t7 * psi * t6 * nu1 * ppv * Testv #
                ↪ Border and G6PD screening on, vivax-
                ↪ positive  deficient individuals receive
                ↪ ACT
             - t1 * nu2 * TAv # Leaving Thailand
             - mu2 * TAv ) # Natural death

dLv <-  (  prelp * rp * TPv # Recovery with hypnozoites
   ↪ after primaquine treatment
             + t7 * prel * rv * TAv # Recovery with
                ↪ hypnozoites after ACT treatment
             + t3 * prel * rf * (Tf / PThaif) * Cv # Dual
                ↪ treatment: treatment for falciparum
                ↪ treats vivax
             - rel * Lv # Relapse to secondary infection
             - t2 * increl * (Tf / PThaif) * Lv #
                ↪ Falciparum infection triggering vivax
                ↪ relapse
```

```
            - dhyp * Lv # Death of hypnozoites
            - t1 * nu2 * Lv # Leaving Thailand
            - mu2 * Lv ) # Natural death

dRv <- (    (1 - prelp) * rp * TPv # Recovery without
   ↪ hypnozoites after primaquine treatment
            + t7 * (1 - prel) * rv * TAv # Recovery
               ↪ without hypnozoites after ACT treatment
            + phiv * Av # Recovery without hypnozoites
               ↪ from asymptomatic infection
            + t3 * (1 - prel) * rf * (Tf / PThaif) * Cv #
               ↪ Dual treatment: treatment for falciparum
               ↪  treats vivax
            - rhov * Rv # Loss of immunity
            - lambdav * (1 - t4 * alpha12 * Infectiousf /
               ↪ PThaif) * Rv # Secondary infection with
               ↪ cross-immunity
            - t1 * nu2 * Rv # Leaving Thailand
            - mu2 * Rv ) # Natural death

dE2v <- (  lambdav * (1 - t4 * alpha12 * Infectiousf /
   ↪ PThaif) * Rv # Reinfection with cross immunity
            + rel * Lv # Relapse due to hypnozoites
            + t2 * increl * (Tf / PThaif) * Lv #
               ↪ Falciparum infection triggering vivax
               ↪ relapse
            - gam_hv * E2v # Developing asymptomatic or
               ↪ clinical disease from secondary
               ↪ infection
            - t1 * nu2 * E2v # Leaving Thailand
            - mu2 * E2v ) # Natural death


# Counters
dCIncf <- (  lambdaf * (1 - t4 * alpha21 * Infectiousv /
   ↪ PThaiv) * Sf
             + lambdaf * (1 - t4 * alpha21 * Infectiousv
                ↪ / PThaiv) * Rf )

dCIncv <- (  lambdav * (1 - t4 * alpha12 * Infectiousf /
   ↪ PThaif) * Sv
             + lambdav * (1 - t4 * alpha12 * Infectiousf
                ↪ / PThaif) * Rv
             + rel * Lv
             + t2 * increl * Tf / PThaif * Lv )

dCTrtf <- (  tauf * Cf
             + t3 * rv * ((TAv+TPv) / PThaiv) * Cf
             + t8 * t6 * ppf * nu1 * Testf)

# Cumulative cost of primaquine treatments
```

```
        dCPrim <- ( c_prim * ((1 - t7) * tauv * Cv # All vivax
           ↪ cases treated with primaquine if G6PD testing is
           ↪ switched off
                              + t7 * tauv * (1 - psi) * Cv # Only
                                 ↪  non-deficient individuals
                                 ↪ treated with primaquine if
                                 ↪ G6PD testing is switched on
                              + (1 - t7) * t6 * nu1 * ppv * t8 *
                                 ↪ Testv
                              + t7 * (1 - psi) * t6 * nu1 * ppv *
                                 ↪  t8 * Testv) )

        # Cumulative cost of ACT treatments

        dCACT <- ( c_ACT * ( t7 * tauf * psi * Cv # G6PD
           ↪ deficient individuals treated with ACT for vivax (
           ↪ if G6PD screening is on)
                             + tauf * Cf # All individuals
                                ↪ treated with ACT for
                                ↪ falciparum
                             + t3 * rf * (Tf / PThaif) * Cv #
                                ↪ Dual treatment
                             + t7 * psi * t6 * nu1 * ppv * t8 *
                                ↪ Testv)  )

        # Cumulative cost of G6PD testing
        dCCv <- ( t7 * c_G6PD * (  (1 - pa) * gam_hv * Ev #
           ↪ Cumulative clinical cases
                                  + (1 - pa2) * gam_hv * E2v
                                  + (1 - t6) * nu1 * pviv *
                                     ↪ Testv) )

        # Cumulative cost of RDTs. Code function check: the two
           ↪ below should be the same

        dCTestf <- t6 * c_RDT * (t1 * nu3 * Outf) # Cumulative
           ↪ tests

        dCTestv <- t6 * c_RDT * (t1 * nu3 * Outv) # Cumulative
           ↪ tests

        # return the rate of change
        list(c(dTestf, dOutf, dSf, dEf, dAf, dCf, dTf, dRf, dE2f,
               dTestv, dOutv, dSv, dEv, dAv, dCv, dTPv, dTAv, dLv
                  ↪ , dRv, dE2v,
               dCIncf, dCIncv, dCTrtf, dCPrim, dCACT, dCCv,
                  ↪ dCTestf, dCTestv ))
    }
)
```

```
}
# Run the model ####
output <- ode(times = times, y = istate, func = thailand_model,
   ↪ parms = parameters)

# Manipulate data ####

df1<-as_tibble(as.data.frame(output)) %>%
  mutate(PThaif = (Sf+Ef+Af+Cf+Tf+Rf+E2f),
         PThaiv = (Sv+Ev+Av+Cv+TPv+TAv+Lv+Rv+E2v),
         Pf=(Outf+Testf+PThaif),
         Pv=(Outv+Testv+PThaiv),
         If = (Ef+Af+Cf+Tf),
         Iv = (Ev+Av+Cv+TPv+TAv),
         P = PThaif+PThaiv,
         CTrtv=CACT+CPrim,
         Incf = c(0, diff(CIncf)),
         Incv = c(0, diff(CIncv)),
         Trtf = c(0, diff(CTrtf)),
         Trtv = c(0, diff(CTrtv)),
         CostPrim = c(0, diff(CPrim)),
         CostACT = c(0,diff(CACT)),
         CostG6PD = c(0, diff(CCv)),
         CostRDTf = c(0, diff(CTestf)),
         CostRDTv = c(0, diff(CTestv))) %>%
  pivot_longer(names_to = "variable", cols = !1) %>%
  mutate(SP = ifelse(str_ends(variable, "f"), "Pf", "Pv")
  )

# Yearly incidence from model to compare with data

predicted_cases <- as.data.frame(seq(from=2010,to=2037,by=1))
names(predicted_cases)[names(predicted_cases) == colnames(
   ↪ predicted_cases)[1]] <- "Year"

df_falc <- as.data.frame(df1 %>%  filter(variable %in% c("Incf")))
   ↪ $value
falc_by_year <- unname(tapply(df_falc, (seq_along(df_falc)-1) %/%
   ↪ 365, sum))
names(falc_by_year)[names(falc_by_year) == colnames(falc_by_year)
   ↪ [1]] <- "Predicted_Falciparum"

df_viv <- as.data.frame(df1 %>%  filter(variable %in% c("Incv")))$
   ↪ value
viv_by_year <- unname(tapply(df_viv, (seq_along(df_viv)-1) %/%
   ↪ 365, sum))
names(viv_by_year)[names(viv_by_year) == colnames(viv_by_year)[1]]
   ↪  <- "Predicted_Vivax"

predicted_cases$Predicted_Falciparum <- as.numeric(falc_by_year)
predicted_cases$Predicted_Vivax <- as.numeric(viv_by_year)
```

```
data_compare <- as.data.frame(read_excel("populations_and_
   ↪ prevalence.xlsx", sheet="Case_data_Thailand", range="B20:D48
   ↪ ", col_names=TRUE))

cases_compare <- merge(data_compare,predicted_cases,by="Year")

all_cases1<-cases_compare %>%
  pivot_longer(names_to = "variable", cols = !1) %>%
  mutate(species = ifelse(str_ends(variable, "um"), "Falciparum",
     ↪ "Vivax")
  )


# Prediction vs data ####

ggplot(all_cases1, aes(x=Year, y=value, group=variable)) +
  geom_line(aes(color=variable)) +
  facet_wrap(~species)

# Population checks ####
# Population of Thailand only
df1 %>%
  filter(variable %in% c("PThaif", "PThaiv")) %>%
  ggplot()+
  geom_line(aes(x = time, y=value))+
  theme_minimal() +
  labs(title = "Populations", y =("population")) +
  facet_wrap(~SP)
# Population of total system
df1 %>%
  filter(variable %in% c("Pf", "Pv")) %>%
  ggplot()+
  geom_line(aes(x = time, y=value))+
  theme_minimal() +
  labs(title = "Populations", y =("population")) +
  facet_wrap(~SP)

tail(output)


# Primaquine costing ####
yearly_cost_prim <- as.data.frame(seq(from=2010,to=2037,by=1))
names(yearly_cost_prim)[names(yearly_cost_prim) == colnames(yearly
   ↪ _cost_prim)[1]] <- "Year"

df_cprim <- as.data.frame(df1 %>%  filter(variable %in% c("
   ↪ CostPrim")))$value
yearly_prim_cost <- unname(tapply(df_cprim, (seq_along(df_cprim)
   ↪ -1) %/% 365, sum))
names(yearly_prim_cost)[names(yearly_prim_cost) == colnames(yearly
```

```
   ↪ _prim_cost)[1]] <- "Primaquine_Cost"

yearly_cost_prim$Primaquine_Cost <- as.numeric(yearly_prim_cost)

ggplot(data=yearly_cost_prim, aes(x=Year, y=Primaquine_Cost, group
   ↪ =1)) +
  geom_line(colour="darkorchid") +
  labs(title = "Yearly␣primaquine␣cost", y =("USD"))

# ACT costing ####

yearly_cost_ACT <- as.data.frame(seq(from=2010,to=2037,by=1))
names(yearly_cost_ACT)[names(yearly_cost_ACT) == colnames(yearly_
   ↪ cost_ACT)[1]] <- "Year"

df_cACT <- as.data.frame(df1 %>%  filter(variable %in% c("CostACT"
   ↪ )))$value
yearly_ACT_cost <- unname(tapply(df_cACT, (seq_along(df_cACT)-1) %
   ↪ /% 365, sum))
names(yearly_ACT_cost)[names(yearly_ACT_cost) == colnames(yearly_
   ↪ ACT_cost)[1]] <- "ACT_Cost"

yearly_cost_ACT$ACT_Cost <- as.numeric(yearly_ACT_cost)

ggplot(data=yearly_cost_ACT, aes(x=Year, y=ACT_Cost, group=1)) +
  geom_line(colour="deeppink") +
  labs(title = "Yearly␣ACT␣cost", y =("USD"))

# G6PD costing ####

yearly_cost_G6PD <- as.data.frame(seq(from=2010,to=2037,by=1))
names(yearly_cost_G6PD)[names(yearly_cost_G6PD) == colnames(yearly
   ↪ _cost_G6PD)[1]] <- "Year"

df_cG6PD <- as.data.frame(df1 %>%  filter(variable %in% c("
   ↪ CostG6PD")))$value
yearly_G6PD_cost <- unname(tapply(df_cG6PD, (seq_along(df_cG6PD)
   ↪ -1) %/% 365, sum))
names(yearly_G6PD_cost)[names(yearly_G6PD_cost) == colnames(yearly
   ↪ _G6PD_cost)[1]] <- "G6PD_Cost"

yearly_cost_G6PD$G6PD_Cost <- as.numeric(yearly_G6PD_cost)

ggplot(data=yearly_cost_G6PD, aes(x=Year, y=G6PD_Cost, group=1)) +
  geom_line(colour="orange") +
  labs(title = "Yearly␣G6PD␣cost", y =("USD"))

# RDT costing ####

yearly_cost_RDT <- as.data.frame(seq(from=2010,to=2037,by=1))
names(yearly_cost_RDT)[names(yearly_cost_RDT) == colnames(yearly_
```

```
   ↪ cost_RDT)[1]] <- "Year"

df_cRDT <- as.data.frame(df1 %>%  filter(variable %in% c("CostRDTf
   ↪ "))$value
yearly_RDT_cost <- unname(tapply(df_cRDT, (seq_along(df_cRDT)-1) %
   ↪ /% 365, sum))
names(yearly_RDT_cost)[names(yearly_RDT_cost) == colnames(yearly_
   ↪ RDT_cost)[1]] <- "RDT_Cost"

yearly_cost_RDT$RDT_Cost <- as.numeric(yearly_RDT_cost)

ggplot(data=yearly_cost_RDT, aes(x=Year, y=RDT_Cost, group=1)) +
  geom_line(colour="red") +
  labs(title = "Yearly␣RDT␣cost", y =("USD"))
```

```
# Human Compartments ####
`%nin%` = Negate(`%in%`)

df1 %>%
  filter(variable %nin% c("PThaif", "PThaiv","P", "CIncf", "CIncv"
     ↪ , "Incf", "Incv", "Trtv", "Trtf", "CTrtf", "CTrtv")) %>%
  group_by(variable) %>%
  ggplot()+
  geom_line(aes(x = time, y=value, colour = as_factor(variable)))+
  theme_minimal() +
  labs(title = "Human␣Compartments", y =("population"), colour="
     ↪ Compartment")+
  facet_wrap(~SP)
# Daily incidence ####

df1 %>%
  filter(variable %in% c("Incf", "Incv")) %>%
  group_by(variable) %>%
  ggplot()+
  geom_line(aes(x = time, y=value, colour = as_factor(variable)))+
  theme_minimal() +
  labs(title = "Incidence", y =("population"), colour="Compartment
     ↪ ")+
  facet_wrap(~SP)

# Treatment ####
df1 %>%
  filter(variable %in% c("Trtf", "Trtv")) %>%
  group_by(variable) %>%
```

```
  ggplot()+
  geom_line(aes(x = time, y=value, colour = as_factor(variable)))+
  theme_minimal() +
  labs(title = "Treated cases", y =("population"), colour="
     ↪ Compartment")+
  facet_wrap(~SP)

# Cases ####
# Plot real case data

data <- as_tibble(as.data.frame(read_excel("populations_and_
   ↪ prevalence.xlsx", sheet="Case_data_Thailand", range="C20:E31
   ↪ ", col_names=TRUE)))
comparison <- merge(data, df1, by="time")
comparison <- reshape2::melt(data, id.var='Days')

(ggplot(cases, aes(x=Year, y=value, col=variable)) %>%
    + geom_line() %>%
    + xlim(2009,2021)
  + ylim(0,1500000)
  + labs(title="Assumed cases by species", x ="Year", y = "Cases")
     ↪ )



df1 %>%
  filter(variable %in% c("If", "Iv")) %>%
  group_by(variable) %>%
  ggplot()+
  geom_line(aes(x = time, y=value, colour = as_factor(variable)))+
  theme_minimal() +
  labs(title = "Cases", y =("population"), colour="Compartment")+
  facet_wrap(~SP)

tail(output)
```

Malaria in Thailand R Shiny App

```
source("R/packages.R")
source("R/model.R")

# Define UI for application
ui <- fluidPage(

  # Title
  titlePanel("Malaria in Thailand"),

  # Sidebar with slider inputs
  sidebarLayout(
    sidebarPanel(
      actionButton("go", "Go"),
      sliderInput(inputId="t1", label = "Migration", value = 1,
```

```
      ↪ min=0, max=1,step=1),
    sliderInput(inputId="t6", label = "Border testing", value =
      ↪ 0, min=0, max=1,step=1),
    sliderInput(inputId="t7", label = "G6PD testing", value = 0,
      ↪  min=0, max=1,step=1),
    sliderInput(inputId="t8", label = "Treat imported cases",
      ↪ value = 0, min=0, max=1,step=1),

    bsCollapse(
      # Mosquito parameters
      bsCollapsePanel("Transmission parameters",
                      sliderInput(inputId="a", label = "human
                        ↪ feeding rate per mosquito", value =
                        ↪ 0.3, min=0, max=10,step=0.01),
                      sliderInput(inputId="b", label = "
                        ↪ transmission efficiency mosquito to
                        ↪ human", value = 0.5, min=0, max=1,
                        ↪ step=0.01),
                      sliderInput(inputId="c", label = "
                        ↪ transmission efficiency human to
                        ↪ mosquito", value = 0.5, min=0, max
                        ↪ =1,step=0.01),
                      sliderInput(inputId="m", label = "
                        ↪ Mosquitoes per human", value = 0.8,
                        ↪ min=0.1, max=3,step=0.1),
                      sliderInput(inputId="relv", label = "
                        ↪ Relative infectiousness of vivax
                        ↪ compared to falciparum", value =
                        ↪ 0.29, min=0.1, max=1,step=0.01),
                      sliderInput(inputId="nu2", label = "
                        ↪ Migration rate: leaving Thailand",
                        ↪ value = 0.001, min=0, max=0.002,step
                        ↪ =0.0005),
                      sliderInput(inputId="nu3", label = "
                        ↪ Emigration rate: entering Thailand",
                        ↪  value = 0.000285, min=0.0001, max
                        ↪ =0.0004,step=0.0001)

    )
  )
),

# Tabs for incidence and costs
mainPanel(
  tabsetPanel(type = "tabs",
              tabPanel("Cases", plotOutput("modelPlot") %>%
                ↪ withSpinner()),
              tabPanel("Incidence", plotOutput("incPlot") %>%
                ↪ withSpinner()),
              tabPanel("RDT Cost", plotOutput("rdtPlot") %>%
                ↪ withSpinner()),
```

```
                    tabPanel("G6PD␣Screening␣Cost", plotOutput("
                       ↪ g6pdPlot") %>% withSpinner()),
                    tabPanel("ACT␣Cost", plotOutput("actPlot") %>%
                       ↪ withSpinner()),
                    tabPanel("Primaquine␣cost", plotOutput("primPlot
                       ↪ ") %>% withSpinner())
      )
    )
  )
)

# Server
server <- function(input, output) {
  modelOut <- eventReactive(input$go, {
    # Overwrite the parms with inputs
    parameters["t1"] <- input$t1
    parameters["t6"] <- input$t6
    parameters["t7"] <- input$t7
    parameters["t8"] <- input$t8
    parameters["a"] <- input$a
    parameters["b"] <- input$b
    parameters["c"] <- input$c
    parameters["m"] <- input$m
    parameters["relv"] <- input$relv
    parameters["nu2"] <- input$nu2
    parameters["nu3"] <- input$nu3
    #parms["gamma_m"] <- input$gamma_m
    #parms["mu_m"] <- input$mu_m

    # Run the model
    result <- ode(times=times, y=istate, func=thailand_model,
       ↪ parms=parameters) %>%
    as.data.frame() %>%
    as_tibble() %>%
    mutate(PThaif = (Sf+Ef+Af+Cf+Tf+Rf+E2f),
           PThaiv = (Sv+Ev+Av+Cv+TPv+TAv+Lv+Rv+E2v),
           Pf=(Outf+Testf+PThaif),
           Pv=(Outv+Testv+PThaiv),
           If = (Ef+Af+Cf+Tf),
           Iv = (Ev+Av+Cv+TPv+TAv),
           P = PThaif+PThaiv,
           CTrtv=CACT+CPrim,
           Incf = c(0, diff(CIncf)),
           Incv = c(0, diff(CIncv)),
           Trtf = c(0, diff(CTrtf)),
           Trtv = c(0, diff(CTrtv)),
           CostPrim = c(0, diff(CPrim)),
           CostACT = c(0,diff(CACT)),
           CostG6PD = c(0, diff(CCv)),
           CostRDTf = c(0, diff(CTestf)),
           CostRDTv = c(0, diff(CTestv))) %>%
```

```
    pivot_longer(names_to = "variable", cols = !1) %>%
    mutate(SP = ifelse(str_ends(variable, "f"), "Pf", "Pv")
    )
})

#Define Plots

predicted_cases <- as.data.frame(seq(from=2010,to=2037,by=1))

output$modelPlot <- renderPlot({
  modelOut() %>%
    filter(variable %in% c("If", "Iv")) %>%
    group_by(variable) %>%
    ggplot()+
    geom_line(aes(x = time, y=value, colour = as_factor(variable
       ↪ )))+
    theme_minimal() +
    labs(title = "Cases", y =("population"), colour="Compartment
       ↪ ")+
    facet_wrap(~SP)
})

output$incPlot <- renderPlot({
  modelOut() %>%
    filter(variable %in% c("Incf", "Incv")) %>%
    group_by(variable) %>%
    ggplot()+
    geom_line(aes(x = time, y=value, colour = as_factor(variable
       ↪ )))+
    theme_minimal() +
    labs(title = "Incidence", y =("population"), colour="
       ↪ Compartment")+
    facet_wrap(~SP)
})

output$primPlot <- renderPlot({
  modelOut() %>%
    filter(variable %in% c("CostPrim"), time>100) %>%
    group_by(variable) %>%
    ggplot()+
    geom_line(aes(x = time, y=value, colour = as_factor(variable
       ↪ )))+
    theme_minimal() +
    labs(title = "Daily␣Primaquine␣Cose", y =("USD"), colour="
       ↪ Compartment")+
    facet_wrap(~SP)
})

output$actPlot <- renderPlot({
  modelOut() %>%
    filter(variable %in% c("CostACT"), time>100) %>%
```

```
      group_by(variable) %>%
      ggplot()+
      geom_line(aes(x = time, y=value, colour = as_factor(variable
         ↪ )))+
      theme_minimal() +
      labs(title = "Daily␣ACT␣Cost", y =("USD"), colour="
         ↪ Compartment")+
      facet_wrap(~SP)
  })

  output$rdtPlot <- renderPlot({
    modelOut() %>%
      filter(variable %in% c("CostRDTf"), time>100) %>%
      group_by(variable) %>%
      ggplot()+
      geom_line(aes(x = time, y=value, colour = as_factor(variable
         ↪ )))+
      theme_minimal() +
      labs(title = "Daily␣RDT␣Cost", y =("USD"), colour="
         ↪ Compartment")+
      facet_wrap(~SP)
  })

  output$g6pdPlot <- renderPlot({
    modelOut() %>%
      filter(variable %in% c("CostG6PD"), time>100) %>%
      group_by(variable) %>%
      ggplot()+
      geom_line(aes(x = time, y=value, colour = as_factor(variable
         ↪ )))+
      theme_minimal() +
      labs(title = "Daily␣G6PD␣Screening␣Cost", y =("USD"), colour
         ↪ ="Compartment")+
      facet_wrap(~SP)
  })

}

# Run the application
shinyApp(ui = ui, server = server)
```