Modelling Falciparum Malaria in Three High-Transmission Provinces in Indonesia: The Impact of Health Economic Evaluation on Policy and Disease Dynamics

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Introduction

Malaria is a mosquito-borne disease caused by Plasmodium spp. In falciparum malaria, clinical cases range from asymptomatic infection, uncomplicated malaria, and complicated malaria (e.g. cerebral malaria) (1). Although the incidence of malaria is mainly concentrated in tropical regions, particularly in Sub-Saharan Africa, where about 95% of all cases and 96% of deaths worldwide are found (2), the South-East Asia Region is the Region with the second highest estimated malaria burden globally (3). It is estimated that there are 248 million malaria cases worldwide of which 90% occur in the African region. The annual spending globally on the malaria programme costs more than 2.6 billion USD (4). The average mortality rate is as low as 0.1%, but children aged 6 months to 5 years are those with the highest risks, and where 76% of the total malaria deaths occurred in this population (5).

Malaria is largely neglected in the South-East Asia Region (SEAR), although it has the highest number of people susceptible to the disease (6). Following the 9th East Asia Summit in 2014, the SEAR is targeting to achieve malaria elimination by 2030 (World Health Organization, 2022c). Several measures from vector control (e.g. ITN, RIS) to vaccination (e.g. RTS vaccination for children) have been done for malaria control and elimination programs (7). In Indonesia, the malaria burden has reduced considerably in the last few decades. However, the trend in the past few years is increasing. Even though the high endemic status was held only by 39 Indonesian regencies and cities, which represented 2% of the Indonesian population, as many as 28% of the Indonesian population remains at risk of malaria (5).

Spatial geographical analysis in 2017 showed that malaria was still highly endemic in some regions, mainly in Papua. It becomes the province with the highest burden with the API of 64, consisting 91% of the national cases. While Papua, West Papua, and Maluku regions altogether share 95% of the total malaria cases (8). A lack of infrastructure, difficult natural landscapes, and poor people's behaviour are among the factors impeding its progress. Meanwhile, there is increasing competition for resources from other critical health problems. The problem in policymaking is how to best allocate these finite resources. For this reason, this essay aims to evaluate several scenarios under a resource constraint for subnational malaria control strategy for these three regions.

Methodology

Scenarios and model fitting

All scenarios consider treating patients who come to a health centre (95% of outpatients and 100% of hospitalised patients were treated). All patients are assumed to be treated in a public primary health centre as there is a health facility centre in each village. The baseline scenario used the current bed-nets allocation (100% nets and 0% MDA coverage), while the other scenarios evaluate the impact of behaviour change, number of nets, and MDA coverage on net health benefit (NHB) and disease dynamics. NHB of each scenario was compared to the baseline scenario as described in equations (46) through (48), while disease dynamics was predicted using a mathematical model described by equations (9) through (37).

Since malaria transmission in Indonesia is concentrated only in certain areas, considering the whole population of (273.7 million) (9) for the intervention would not be appropriate. Also, Papua, Western Papua, and Maluku share 95% of total malaria cases. Therefore, the model was fitted using the reported incidence from Indonesia in World Malaria Report document's Annex 4–I. A daily incidence was extrapolated assuming that daily incidence follows seasonality given by a cosine function as the following:

$$seasonality_{daily} = \left(1 + 0.5cos\left(2\pi \times \frac{day}{365}\right) + X\right) \quad (1)$$

To consider stochasticity, X is added to the equation, whereby X is a randomly drawn value from a normal distribution given by probability density of $f(x)$ with standard deviation, σ = 0.1, and mean, μ = 0.1.

$$f(x) = \frac{1}{sqrt(2\pi)\times\sigma} e^{-\frac{(x-\mu)^2}{2\sigma^2}} \quad (2)$$

To make sure that the resulting seasonality factor for each day for a year (365 days) sums to one, it is divided by the total one-year seasonality.

$$Incidence_{daily} = \frac{seasonality_{daily}}{Total_{daily\ seasonality\ for\ a\ year}} \times Incidence_{yearly} \quad (3)$$

The model was then fitted with the daily incidence using a function optim in R version 4.2.2 to estimate the initial number of susceptible (Sf_0) and person per net (ppn) parameter. To ensure that the fitting result was at the global minimum, a grid search from 0% to 100% number of nets and 0% to 90% MDA coverage was also performed.

Parameters	Description	Value	Unit	References
a	Human feeding rate per mosquito	0.3	-	(10)
b	Transmission efficiency M to H	0.093	-	(11)
c	Transmission efficiency H to M	0.5	-	(10)

m	Ratio of female mosquitoes to humans	3	-	
(10,12)γ_m	Rate of onset of infectiousness in mosquitoes	1/10	Day^{-1}	(13)
μ_m	Natural death rate in mosquitoes	1/10	Day^{-1}	(10)
μ_h	Natural death rate in humans	1/(69*365)	Day^{-1}	(14)
ζ_a	relative infectiousness of asymptomatic infections	12.6/27	-	(15)
ζ_t	relative infectiousness of treated infections	1/100	-	(16)
ppn	The average number of persons under a bednet	3.14	-	Model fitting
P_{af}	Asymptomatic proportion for non-immune	0.1	-	(12)
γ_{hf}	Incubation rate of plasmodium falciparum in human	1/21	Day^{-1}	(12,17)
δ_f	Natural recovery rate of *Plasmodium falciparum*	1/130	Day^{-1}	(18)
ω_f	Rate of loss of symptoms in untreated clinical infection	1/10	Day^{-1}	(12)
r_v	rate of treatment recovery (1/pct) ACT	1/3	Day^{-1}	(19)
τ_f	Treatment seeking rate (for uncomplicated malaria)	1/2	Day^{-1}	(20)
ν_f	rate of progress to severe infection	1/7	Day^{-1}	(21)

ε_f	rate of loss of severe symptoms in untreated severe infections	1/10	Day^{-1}	(12)
μ_{sev}	rate of death in severe illness	1	%	(5,22)
τ_{sev}	treatment seeking rate of severe infection to hospital	3/4	-	(23)
μ_{hosp}	In-hospital death rate of severe illness	0.02	%	(22)
r_{hosp}	rate of recovery in a hospitalised patient	1/7	Day^{-1}	(24)
r_f	rate of recovery in patients received Pf treatment (3d ACT + 1d Primaquine)	1/3	Day^{-1}	(19)
ρ_f	Loss of immunity rate after Plasmodium falciparum infection	1/365	Day^{-1}	(12)
P_{a2f}	Asymptomatic proportion for the immune	0.9	-	(12)
p_{seek}	Proportion of seeking treatment in uncomplicated cases	0.6	-	(20)
p_{test_slide}	Proportion of being tested by slide	0.3	-	(5)
p_{test_RDT}	Proportion of being tested by RDT	0.7	-	(5)
p_{sens_slide}	Sensitivity of the microscopy test	59	%	(25–28)
p_{sens_RDT}	Sensitivity of the RDT	53.7	%	(28)

p_{treat}	Proportion of being treated when coming to the health centre	95	%	(8)

Table 1. This table provides the description and value for each parameter used for the falciparum malaria model. The reference for each parameter was also reported.

The parameters used in the model were described in table 1. These parameters were derived either from literature or the world malaria report documents. Some parameters were used to derive the other parameters described in table 2.

Parameters	Description	Function of time
$\lambda_f(t)$	The force of infection	Time-dependent
$Infectious_f(t)$	The number of infectious individuals	Time-dependent
π_t	The effectiveness of treatment	Time-independent
$\pi_{net}(t)$	The effectiveness of nets	Time-dependent
$\Phi(t)$	The rate of allocated nets	Time-dependent
$\theta(t)$	The nets coverage	Time-dependent

Table 2. This table describes the derived parameters. Time-dependent means that this is a function of time, while time-independent means that this is not a function of time.

Equation

Force of infection:

$$\lambda_f(t) = seas \times \frac{a^2 bcm \times Infectious_{f(t)}}{P_{f(t)}} \times \frac{\frac{\mu_m}{\mu_m+\mu_m}}{\frac{ac \times Infectious_f}{P_f}+\mu_m} \quad (4)$$

$$Infectious_f(t) = Cf + Ctf + Sev + \zeta_a A_f + \zeta_t(T_f + H) \quad (5)$$

Intervention:

$$\pi_t = p_{seek} \times p_{treat}(p_{test_{slide}} \times p_{sensitivity_{slide}} + p_{test_{RDT}} \times p_{sensitivity_{RDT}}) \quad (6)$$

$$\pi_{net}(t) = \theta(t) \times p_{coverage} \times p_{use} \times p_{effectiveness} \quad (7)$$

$$\frac{d\theta}{dt} = \Phi(t) - (\mu_{net} + \eta)\theta \quad (8)$$

Model:

$$\frac{dS_f}{dt} = \mu_h P_f + \rho_f R_f + snap.S_{fh} - \left(m_{rate} + \lambda_f + \mu_h\right)S_f \quad (9)$$

$$\frac{dE_f}{dt} = \lambda_f S_f + snap.E_{fh} - (m_{rate} - \gamma_{hf} + \mu_h)E_f \quad (10)$$

$$\frac{dA_f}{dt} = p_{af}\gamma_{hf}E_f + \omega_f C_f + snap.A_{fh} - \left(m_{rate} + \delta_f + \mu_h\right)A_f \quad (11)$$

$$\frac{dC_f}{dt} = (1 - p_{af})(1 - \pi_t)\gamma_{hf}E_f + \varepsilon_f Sev + snap.C_{fh} - \left(m_{rate} + \omega_f + \upsilon_f + \mu_h\right)C_f \quad (12)$$

$$\frac{dCt_f}{dt} = (1 - p_{af})\pi_t\gamma_{hf}E_f + snap.Ct_{fh} - \left(m_{rate} + \tau_f + \mu_h\right)Ct_f \quad (13)$$

$$\frac{dT_f}{dt} = \tau_f Ct_f - (r_f + \mu_h)T_f \quad (14)$$

$$\frac{dSev}{dt} = \upsilon_f C_f + snap.Sev_h - \left(m_{rate} + \varepsilon_f + \tau_{sev} + \mu_{sef}\right)Sev \quad (15)$$

$$\frac{dH}{dt} = \tau_{sev}Sev - \left(r_{hosp} + \mu_{hosp}\right)H \quad (16)$$

$$\frac{dR_f}{dt} = \delta_f A_f + r_{hosp}H + r_f T_f + snap.R_{fh} + \kappa Rf_f - \left(m_{rate} + \rho_f + \lambda_f + \mu_h\right)R_f \quad (17)$$

$$\frac{dRp_f}{dt} = r_f T_f + r_{hosp}H - (m_{rate} + \kappa + \mu_h)R_f \quad (18)$$

$$\frac{dS_{fm}}{dt} = m_{rate}S_f - \left(m_{protect} + \mu_h\right)S_{fm} \quad (19)$$

$$\frac{dT_{fm}}{dt} = m_{rate}\left(E_f + A_f + C_f + Ct_f\right) + \tau_f Ct_{fh} - \left(r_f + \mu_h\right)T_{fm} \quad (20)$$

$$\frac{dR_{fm}}{dt} = m_{rate}\left(Rp_f + R_f\right) + r_f Tf_m + r_{hosp}H_m - (m_{protect} + \mu_h)R_{fm} \quad (21)$$

$$\frac{dH_m}{dt} = m_{rate}Sev + \tau_{sev}Sev_h - (r_{hosp} + \mu_{hosp} + \mu_h)H_m \quad (22)$$

$$\frac{dS_{fh}}{dt} = m_{protect}S_{fm} - (\lambda_f + snap + \mu_h)S_h \quad (23)$$

$$\frac{dR_{fh}}{dt} = m_{protect}R_{fm} + \delta_f A_{fh} - (snap + \mu_h)R_{fh} \quad (24)$$

$$\frac{dE_{fh}}{dt} = \lambda_f S_{fh} - (\gamma_{hf} + snap + \mu_h)E_{fh} \quad (25)$$

$$\frac{dA_{fh}}{dt} = p_{af}\gamma_{hf}E_{fh} + \omega_f C_{fh} - (\delta_f + snap + \mu_h)A_{fh} \quad (26)$$

$$\frac{dC_{fh}}{dt} = \left(1 - p_{af}\right)(1 - \pi_t)\gamma_{hf}E_{fh} - (\omega_f + \nu_f + snap + \mu_h)C_{fh} \quad (27)$$

$$\frac{dCt_{fh}}{dt} = \left(1 - p_{af}\right)\pi_t\gamma_{hf}E_{fh} - (\tau_f + snap + \mu_h)Ct_{fh} \quad (28)$$

$$\frac{dSev_h}{dt} = \nu_f C_{fh} - (\varepsilon_f + \tau_{sev} + \mu_{sev} + snap + \mu_h)Sev_h \quad (29)$$

$$\frac{dCinc}{dt} = \lambda_f(S_f + S_{fh}) \quad (30)$$

$$\frac{dCtrt}{dt} = \tau_f(Ct_f + Ct_{fh}) \quad (31)$$

$$\frac{dChosp}{dt} = \tau_{sev}(Sev + Sev_h) \quad (32)$$

$$\frac{dCtrt.total}{dt} = \frac{dCtrt}{dt} + \frac{dChosp}{dt} \quad (33)$$

$$\frac{dCMDA}{dt} = m_{rate}(S_f + E_f + A_f + C_f + Rp_f + R_f + Ct_f + Sev) \quad (34)$$

$$\frac{dCsnap}{dt} = snap(S_{fh} + R_{fh} + E_{fh} + A_{fh} + C_{fh} + Ct_{fh} + Sev_h) \quad (35)$$

$$\frac{dCtest}{dt} = \frac{1}{p_{test_{RDT}} RDT_{pos} + p_{test_{slide}} slide_{pos}} \left(\frac{dCtrt}{dt} \times \frac{1}{p_{treat}} + \frac{dChosp}{dt} \times 1\right) \quad (36)$$

$$\frac{dD}{dt} = \mu_{sev}(Sev + Sev_h) + \mu_{hosp}(H + H_m) \quad (37)$$

Death serves as an absorbing compartment from Sev, Sev_h, H and H_m compartments.

Economic model equation

Item	**Cost (USD)**
Commodities	
LLIN	5
RDT (pack of 25)	30
Slide for microscopy (1 unit)	1.2
Primaquine (diphosphate) 7.5 mg tabs, blister 10 x 10	3.8
Artemether 20 mg + Lumefantrine 120 mg tabs, blister 4x6, box of 30	18
Malaria programme services	
LLIN distribution (per net)	2
Outpatient visit	5.5
Inpatient admission (3-day length of stay + treatment)	33.5
Healthcare system unit cost per person per year (e.g. surveillance, monitoring and evaluation, programme management)	4.5
The average cost for the behaviour change intervention (BCI) per village per year (e.g. health education at village hall or health	500

centre, community health workers training, leaflet printing cost)	

Table 3. A list of intervention programme costs. This is a reference cost in 2022. A discounting rate of 3% per year was considered for total investment needed in 2017.

Cost calculation

The cost variables were healthcare system cost, treatment cost, diagnostic cost, and programme costs, which consist of bed-nets cost, MDA cost, and BCI cost. All economic calculations were in USD. The calculation reference for cost calculation is summarised in **table 3** with the discount rate assumed to be 3% per year.

$$Treatment\ cost = Hospitalised \times 33.5 + Outpatient \times (5.5 + 0.293)\ \text{USD} \quad (38)$$

$$Diagnostic\ cost = Number\ of\ test\ \times 1.2\ \text{USD} \quad (39)$$

$$Bednet\ cost = \ Number\ of\ allocated\ net \times (5 + 2)\ \text{USD} \quad (40)$$

$$MDA\ cost = MDA\ delivered \times (5.5 + 0.293)\ \text{USD} \quad (41)$$

$$Behaviour\ change\ intervention\ cost = 500 \times 5 \times Number\ of\ village\ \text{USD} \quad (42)$$

The total number of villages in three different provinces were 8795 (5560 in Papua, 1987 in West Papua, and 1268 in Maluku) (8).

DALY calculation

$$DALY\ = YLL\ +\ YLD \quad (43)$$

$$YLL = 50 \times Death \quad (44)$$

$$YLD = 0.211 \times cases_{uncomplicated} + 0.436 \times cases_{complicated} \quad (45)$$

YLL should be a function of age, but for this model, it is assumed that the average years of life lost due to premature death in malaria be constant at 50 as most cases occurred in children (5) and the life expectancy in Indonesia is 71 years in 2021 (14). Additionally, it is estimated that YLD for non-severe cases and severe cases are 0.211 and 0.436, respectively (29).

Measuring NHB

In the economic model, the measure of NHB of each scenario was compared to the baseline to rank the cost-effective scenarios. The following is the equation for measuring NHB from each scenario:

$$NHB = DALY\ gained - \frac{Difference\ in\ cost}{Threshold} \quad (46)$$

$$DALY\ gained = DALY_{scenario} - DALY_{baseline} \quad (47)$$

$$Difference\ in\ cost = Total\ cost_{scenario} - Total\ cost_{baseline} \quad (48)$$

The threshold used follows WHO recommendation that a cost-effective intervention is not more than 3 x GDP per capita per health outcome gained, in this case, is DALY. The Indonesian GDP per capita was 3820 USD (30). A negative NHB means that a particular scenario is not more cost-effective than the baseline.

In this scenario, budget constraint is defined as the amount of spending from the current (baseline) program. Thus, under a budget constraint, all scenarios with NHB less than the baseline and total cost more than the baseline were discarded. The remaining scenarios are less costly but have better health benefits compared to the baseline.

Results

Model fitting for Sf_0 and ppn parameter

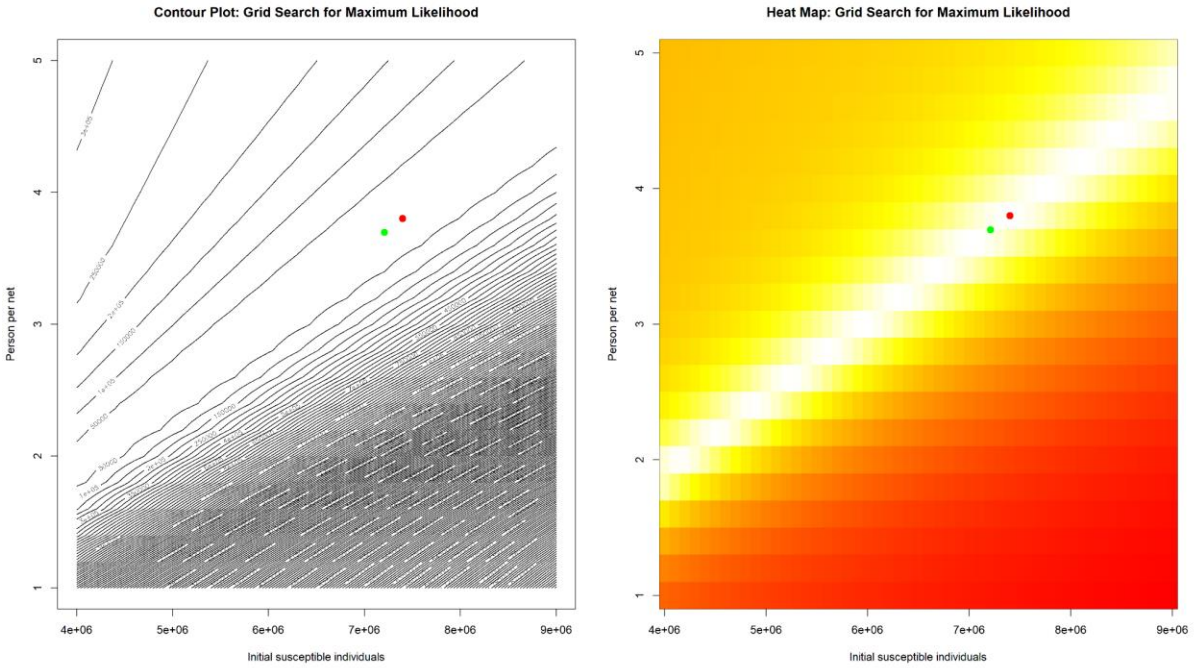

Figure 1. The red dot (Sf_0 =7,209,746 and ppn = 3.69) and the green dot (Sf_0 =7,400,000 and ppn = 3.8) were the combination with the highest likelihood searched using optim function and a grid search in R, respectively. A further grid search combination was performed as a confirming result to ensure that the result search from the optim function is the global minimum.

From the optim function, Sf_0=7,209,746and ppn=3.69 was a combination with the highest likelihood. To check the robustness of these results, a grid search was performed, and the result was similar (Sf_0=7,200,000 and ppn=3.8), confirming that it is the global minimum.

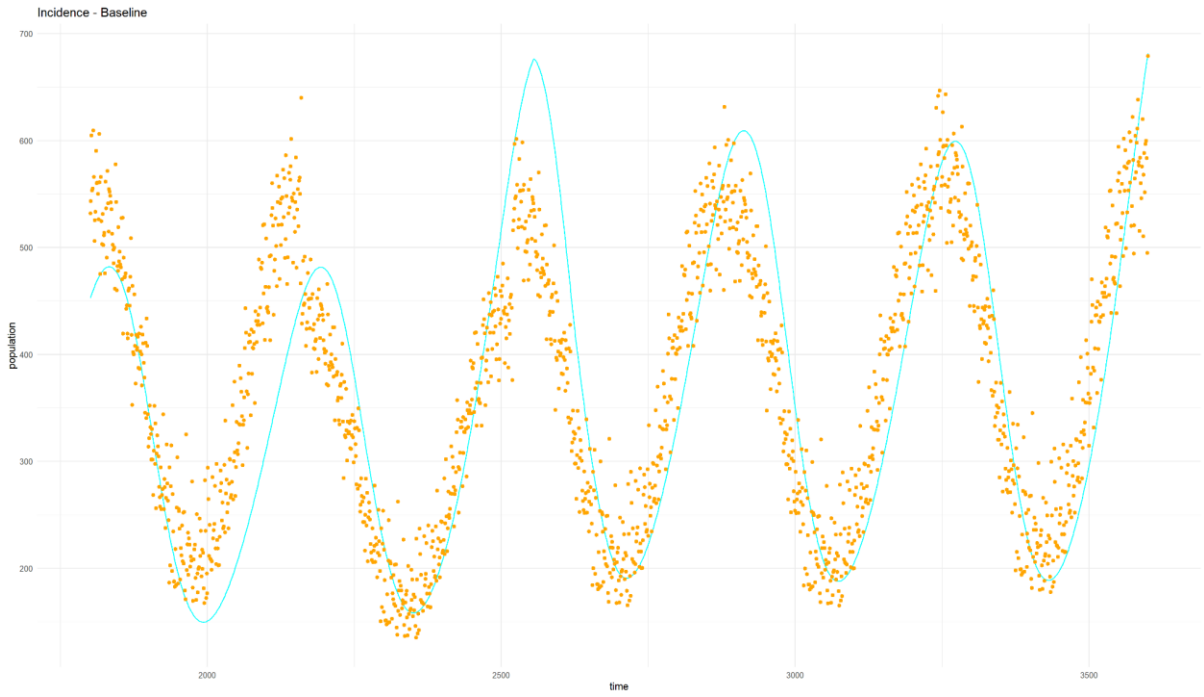

Figure 2. It shows the daily incidence plot (blue line) and daily cases (orange dots) from 2017 to 2021.

The model was run using the fitted Sf_0 and ppn. The plot of the daily incidence with the daily cases was depicted in **figure 2**. Visually inspected, the model has a good fit to the data.

Scenario Analysis

In the scenario analysis, the NHB and total cost was searched starting from 0% to 100% nets coverage and 0% to 90% MDA coverage with and without BCI. In total, there were 198 scenarios analysed (99 for each of with or without BCI). For NHB and total cost of scenarios without BCI are summarised in **table 4** and **5**, respectively, while for scenarios with BCI in **table 6** and **7**.

Table 4. This table summarises the NHB per 1000 DALY from each scenario without BCI from January 2017 to December 2021. The scenario of 100% net coverage and 0% MDA coverage is the baseline.

NHB of scenarios without BCI		MDA Coverage									
		0%	10%	20%	30%	40%	50%	60%	70%	80%	90%
Bed-nets coverage	0	-563.6	-330.2	-143	-9	77	126.9	153.9	167.9	175.3	179.6
	10%	-414.9	-218.7	-69.5	33.3	98	136	157.2	168.8	175.4	179.5

	20%	-290.2	-130.9	-14.6	63.7	112.9	142.4	159.5	169.4	175.4	179.4
	30%	-190.4	-64.2	25.5	85.4	123.5	146.9	161.1	169.9	175.4	179.3
	40%	-113.4	-14.8	54.4	100.8	131	150.1	162.3	170.2	175.4	179.2
	50%	-63.9	16.1	72.3	110.3	135.6	152.1	163	170.3	175.4	179.1
	60%	-39	31.4	81	114.9	137.8	153.1	163.4	170.4	175.3	178.9
	70%	-22.5	41.4	86.6	117.9	139.2	153.7	163.5	170.4	175.2	178.8
	80%	-11.7	48	90.4	119.9	140.2	154.1	163.6	170.3	175.1	178.7
	90%	-4.8	52.2	92.8	121.2	140.8	154.3	163.7	170.3	175	178.6
	100%	0	55.2	94.5	122.1	141.3	154.5	163.7	170.2	174.9	178.5

Table 5. This table summarises the total investment per million USD from each scenario without BCI from January 2017 to December 2021. The scenario of 100% net coverage and 0% MDA coverage is the baseline. This value is based on the year 2017.

Total Cost of scenarios without BCI		MDA Coverage									
		0%	10%	20%	30%	40%	50%	60%	70%	80%	90%
Bed-nets coverage	0	56.6	58.2	60.6	63.8	67.8	72.4	77.3	82.5	87.8	93.2
	10%	55.4	57.7	60.7	64.4	68.8	73.6	78.6	83.9	89.2	94.6
	20%	54.7	57.5	61.1	65.2	69.9	74.8	80	85.2	90.5	95.9
	30%	54.3	57.7	61.7	66.2	71	76.1	81.3	86.5	91.9	97.3
	40%	54.3	58.2	62.6	67.3	72.3	77.4	82.6	87.9	93.2	98.7
	50%	54.8	59.1	63.6	68.5	73.6	78.7	84	89.2	94.6	100
	60%	55.8	60.2	64.9	69.8	74.9	80.1	85.3	90.6	95.9	101.4
	70%	56.8	61.3	66.1	71.1	76.2	81.4	86.7	92	97.3	102.7
	80%	58	62.6	67.4	72.4	77.5	82.7	88	93.3	98.7	104.1
	90%	59.2	63.9	68.7	73.7	78.9	84.1	89.4	94.7	100	105.4
	100%	60.5	65.2	70	75.1	80.2	85.5	90.7	96	101.4	106.8

The baseline scenario costs 60.5 million USD. As there is no MDA or BCI, this includes only the cost of treatment, diagnosis, and bed-nets. Removing all bed-nets would result in NHB=-563,600 despite saving 3.9 million USD. Allocating the same budget as baseline for 60% nets and 10% MDA coverage would result in NHB=31.400. If there was no budget constraint, the maximum NHB would be obtained from the 90% MDA and 0% bed-net scenario at NHB=179,600. This scenario would cost 93.2 million USD over 5 years, 32.7 million USD higher than that of the baseline.

Table 6. This table summarises the NHB per 1000 DALY from each scenario with BCI from January 2017 to December 2021. The scenario of 100% net coverage and 0% MDA coverage is the baseline.

NHB of scenarios with BCI		MDA Coverage									
		0%	10%	20%	30%	40%	50%	60%	70%	80%	90%
Bed-nets coverage	0%	-126.6	-21.3	53	102.1	133.2	152.2	163.8	171	175.8	179.2
	10%	-66.3	17.2	75.4	114	138.9	154.6	164.6	171.2	175.8	179.1
	20%	-20	45.9	91.8	122.6	143	156.4	165.3	171.3	175.7	179
	30%	14.7	67.1	103.8	129	146	157.7	165.7	171.4	175.6	178.9
	40%	40.6	82.7	112.6	133.6	148.3	158.6	166	171.4	175.6	178.8
	50%	57	92.5	118.1	136.5	149.7	159.2	166.2	171.4	175.5	178.7
	60%	65.1	97.3	120.9	138	150.4	159.5	166.3	171.4	175.4	178.6
	70%	70.5	100.6	122.7	138.9	150.8	159.6	166.3	171.3	175.3	178.5
	80%	74.1	102.7	123.9	139.5	151.1	159.7	166.2	171.2	175.2	178.3
	90%	76.6	104.2	124.7	140	151.3	159.8	166.2	171.2	175.1	178.2
	100%	78.3	105.3	125.3	140.3	151.4	159.8	166.2	171.1	174.9	178.1

Table 7. This table summarises the total investment per million USD from each scenario with BCI from January 2017 to December 2021. The scenario of 100% net coverage and 0% MDA coverage is the baseline. This value is based on the year 2017.

Total Cost of scenarios with BCI		MDA Coverage									
		0%	10%	20%	30%	40%	50%	60%	70%	80%	90%
Bed-nets coverage	0	55.7	59.2	63.4	67.9	72.8	77.9	83.1	88.4	93.7	99.2
	10%	55.9	59.9	64.3	69	74.1	79.2	84.4	89.7	95.1	100.5
	20%	56.3	60.7	65.3	70.2	75.3	80.5	85.8	91.1	96.4	101.9
	30%	57	61.6	66.4	71.5	76.6	81.9	87.1	92.4	97.8	103.2
	40%	57.9	62.6	67.6	72.7	77.9	83.2	88.5	93.8	99.2	104.6
	50%	58.9	63.8	68.9	74	79.3	84.5	89.8	95.2	100.5	105.9
	60%	60.1	65.1	70.2	75.4	80.6	85.9	91.2	96.5	101.9	107.3
	70%	61.3	66.4	71.5	76.7	81.9	87.2	92.5	97.9	103.2	108.7
	80%	62.6	67.7	72.8	78	83.3	88.6	93.9	99.2	104.6	110
	90%	63.9	69	74.2	79.4	84.6	89.9	95.2	100.6	105.9	111.4
	100%	65.3	70.3	75.5	80.7	86	91.3	96.6	101.9	107.3	112.7

With behaviour change, removing all bed-nets would result in NHB=-126,600. Allocating the same budget as baseline for 60% nets and 10% MDA coverage would result in NHB=97.3, higher than that without BCI. If there was no budget constraint, the maximum NHB would be obtained from the 90% MDA and 0% bed-net scenario at NHB=179,200, similar to that without BCI. This scenario would cost 99.2 million USD over 5 years, 38.7 million USD higher than that of the baseline.

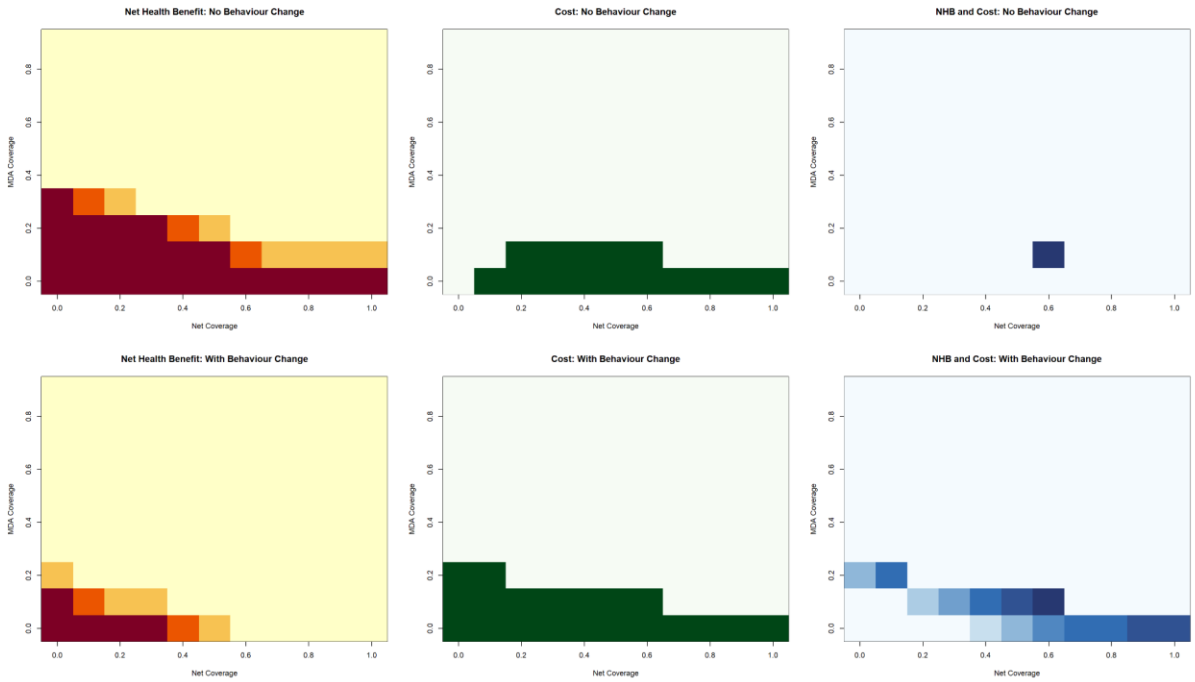

Figure 3. Panels (A) and (B) provide visualisation for NHB from table 4 and total cost from table 5. While panels (D) and (E) provide the visualisation for NHB from table 6 and total cost from table 7. All scenarios that do not meet the budget constraint condition, i.e., if it is more costly than that of baseline scenario regardless of its NHB value, was discarded. Panel C and F summarises which remaining scenario is cost-effective under a budget constraint.

The disease dynamics from 2016 to 2021

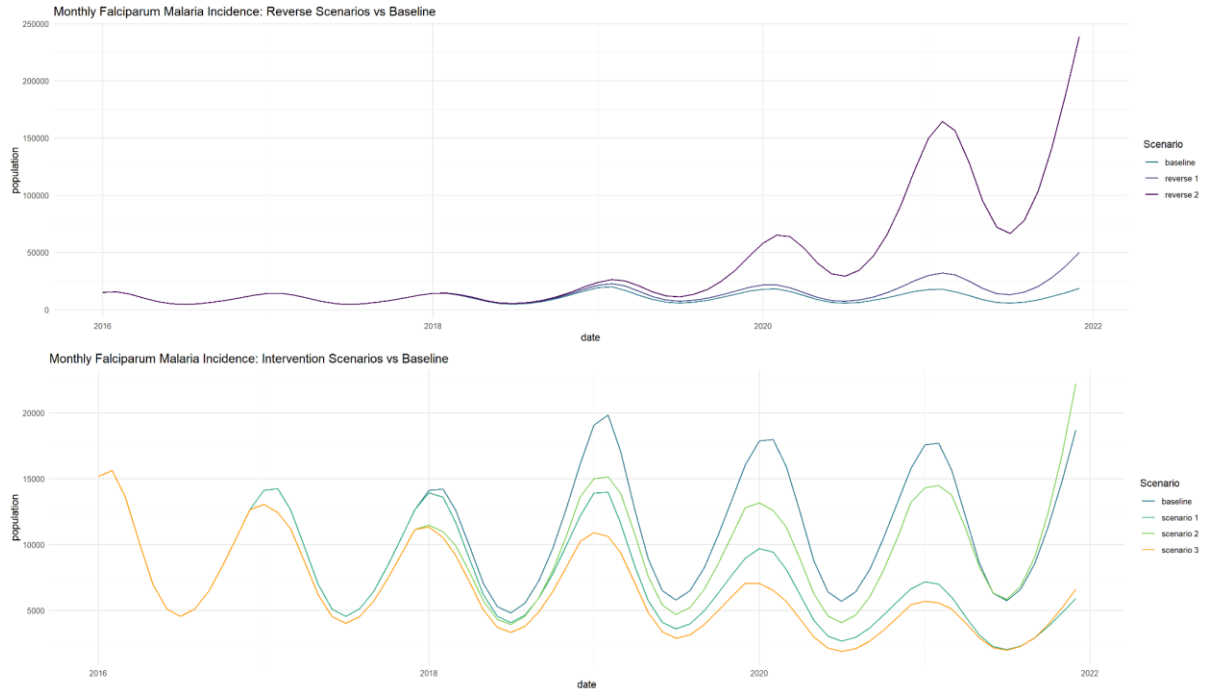

Figure 5. This figure summarises monthly incidence for each scenario from January 2016 to December 2021. from January 2016 to December 2016, the incidence is the same for all scenarios because the intervention starts in January 2017. For behaviour change, there is a lag time of 1 year before it starts to take effect. Thus, the effect from BCI starts in January 2018.

In addition to baseline, reverse 1 (50% nets) and reverse 2 (0% nets) scenarios, three scenarios were proceeded to further analysis, namely scenario 1 (100% nets with BCI), scenario 2 (60% nets and 10% MDA coverage), and scenario 3 (100% nets and 10% MDA coverage with BCI). Removing nets will yield an increased malaria transmission. While the other scenarios demonstrate reduction in malaria transmission.

Discussion

Of all explored scenarios, the result showed that reducing the number of nets to 60% and adding MDA by 10% coverage would yield the maximum benefit under a budget constraint. Interestingly, after mid-2021, the monthly incidence of scenario 2 becomes higher than the baseline scenario. It shows that low MDA coverage may be effective if malaria transmission is high but at a reduced transmission rate, it is not superior to ITN. However, with the same ITN and MDA coverage, applying behaviour change can considerably reduce the incidence to approximately one-third in 2022 but then after mid-2021, scenario 3 becomes inferior in reducing malaria incidence compared to scenario 1. These results demonstrate that a seemingly effective intervention in a short term is not necessarily applicable in a long term. Thus, a regular policy review should be recommended to decide whether a policy change is needed.

Ten percent MDA coverage seems reasonable to be achieved since distribution can be a challenge in Papua, West Papua, and Maluku due to the difficult natural landscape. Thus, areas with the highest malaria burden should be prioritised. Meanwhile, Indonesia has 17 million people at risk, but only 3.3 million nets are distributed every 3 years. In fact, adequate coverage is needed to achieve good malaria control, but the low number of distributed nets can be compensated with the number of people who live under the nets, although consistent net use is necessary to prevent mosquito biting.

The effectiveness of BCI was recognised in several settings (20,31,32). However, its application in Papua, West Papua, and Maluku may be limited as the number of health professionals in these regions is lacking. Thus, an intensive training of nonphysician health-care workers and community health workers (CHWs) may be required. Moreover, a regular exposure to health literacy is required to maintain a good health behaviour (33).

Today, there is no universal plan for eradicating malaria, as each region or country has its unique set of challenges that require case-by-case solutions (34). Continuous malaria-related expenses are still needed although elimination is achieved until global eradication is achieved (4,34).

Limitation

This essay has several limitations. First, it only analysed retrospective data for falciparum malaria without an attempt to forecast. Thus, it does not give an information the likely period of malaria elimination. Secondly, it focuses only on falciparum malaria because of some complexity of vivax-falciparum interaction that is not well understood yet. In fact, vivax malaria in Indonesia is still prevalent. Thirdly, it does not include an age-structured model although malaria mortality is highly age-dependent. Hence, future research and analysis addressing these limitations are recommended.

Conclusion

It is advisable that the BCI is included in an intervention package to get a better health impact within a 5-year timeframe. However, a regular policy review is recommended. Further analysis by incorporating Vivax malaria as well as future disease projections to better inform the policy of malaria elimination in 2030 is needed. Also, future research addressing how vivax-falciparum malaria interacts is recommended so it can be well understood, and a more accurate model can be developed.

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Annex I – Supplementary figures

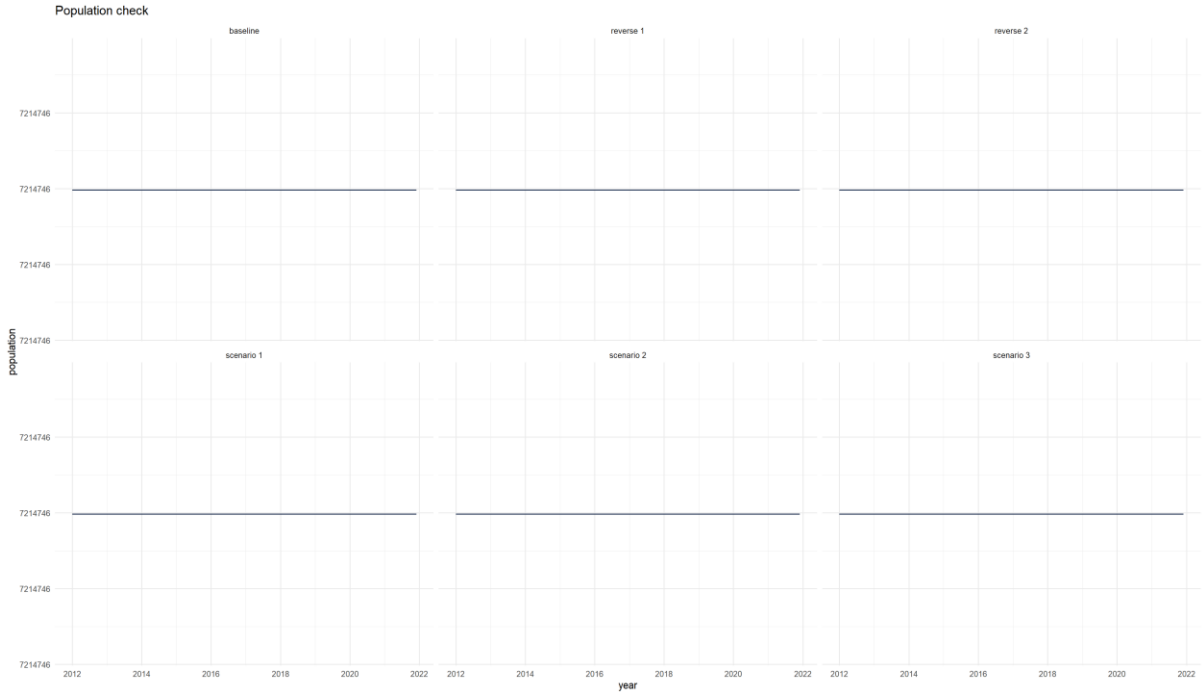

Figure S1. Population checks from All Scenarios.

Figure S2. Asymptomatic, Uncomplicated, and Complicated Malaria Cases from All Scenarios.

Figure S3. Uncomplicated and Complicated Malaria Cases from All Scenarios.

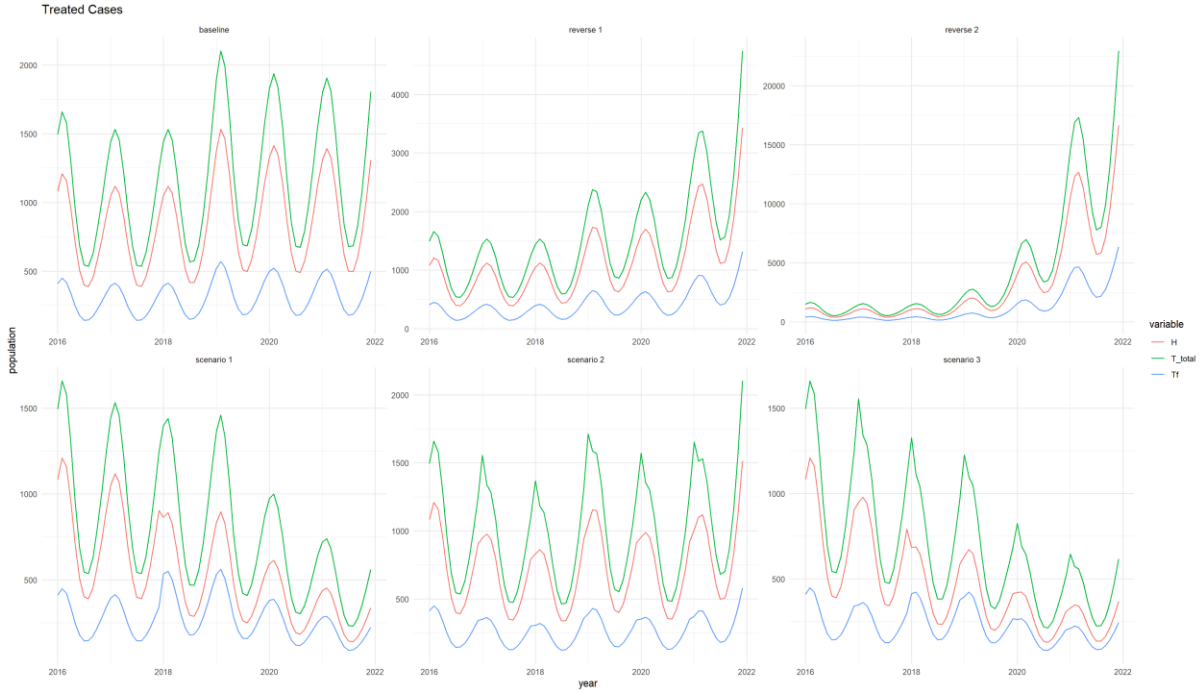

Figure S4. Treated Malaria Cases from All Scenarios.

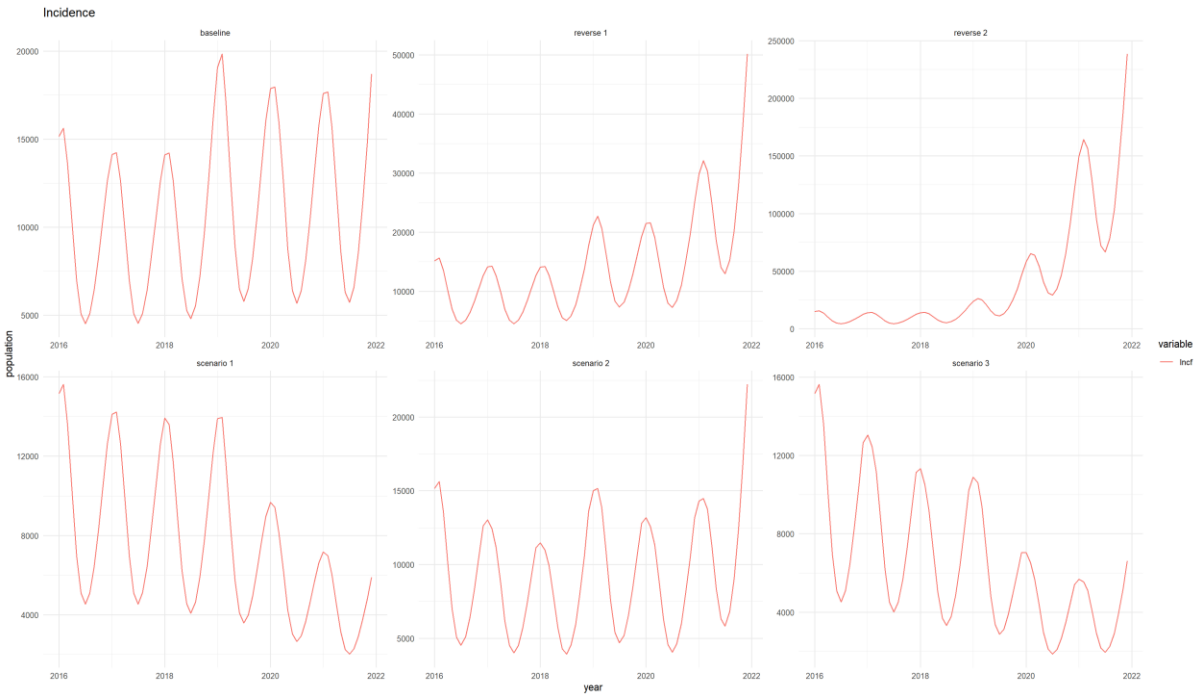

Figure S5. Monthly Malaria Deaths from All Scenarios.

Annex II – The Code in One Run

```
rm(list = ls())
# the whole code may take approximately 1.5 hours to run

start.time <- Sys.time()
#########################################################################
######
# CHAPTER 1: DATA GENERATION FOR DAILY INCIDENCE
###############################
#########################################################################
######

# 1. load data of yearly incidence from world malaria report Annex ####
library(pacman)
p_load(deSolve, tidyverse, gridExtra, readxl, ggplot2)

malaria.incidence <- read_excel("incidence_yearly.xlsx")
malaria.incidence <- as.data.frame(malaria.incidence)

# 2. taking the last 5 years data from the report ####
#pfpv.incidence <- malaria.incidence[1, c('2017', '2018', '2019', '2020',
'2021')]
pf.incidence <- malaria.incidence[2, c('2017', '2018', '2019', '2020',
'2021')]*0.95
#pv.incidence <- malaria.incidence[3, c('2017', '2018', '2019', '2020',
'2021')]

# 3. preparing for turning yearly to daily incidence ####
# creating a multiplication factor for each day
# assuming the daily incidence has seasonality resembling cosine function
# for simplicity, the phase angle is set to be 0 so that the peak occurs
at the beginning of the year
set.seed(123)
a <- c()
for(i in 1:360){
  a <- c(a,1+0.5*cos(2*pi*i/360) + rnorm(1, 0.1, 0.1))
}

# 4. make sure that the vector sum adds up to 1 ####
```

```
b <- a/sum(a)


# 5. multiplying the yearly incidence by daily multiplication factor ####

# pfpv.cases <- c(b*pfpv.incidence$'2017',b*pfpv.incidence$'2018',
b*pfpv.incidence$'2019', b*pfpv.incidence$'2020', b*pfpv.incidence$'2021')

# setNames(pfpv.cases, 1:1800)


pf.cases <- c(b*pf.incidence$'2017',b*pf.incidence$'2018',
b*pf.incidence$'2019', b*pf.incidence$'2020', b*pf.incidence$'2021')

setNames(pf.cases, 1:1800)


# pv.cases <- c(b*pv.incidence$'2017',b*pv.incidence$'2018',
b*pv.incidence$'2019', b*pv.incidence$'2020', b*pv.incidence$'2021')

# setNames(pv.cases, 1:1800)


# 6. visual assessment of the daily incidence of the past 5 years ####

par(mfrow=c(1,1))

# plot(pfpv.cases, type="l", ylab = "population", xlab = "days", main =
"P. falciparum and P. vivax")

plot(pf.cases, type="l", ylab = "population", xlab = "days", main = "P.
falciparum")

# plot(pv.cases, type="l", ylab = "population", xlab = "days", main = "P.
vivax")


# note that this data generation will be used for model fitting of
susceptible compartment

# taking the whole population as the denominator would not make any sense
as majority of indonesian area are not malaria-free

# however, the cases are clustered and concentration in certain areas,
about 80% of cases in Papua region

# moreover, Indonesia consists of thousands of island so that cross-island
transmission is less likely to be significant although not impossible

# For this reason, this model does not account for spatial analysis and
imported cases

# Based on this generated data, a model fitting to estimate the number of
susceptible population will be made


# CHAPTER 2: MODEL FITTING
####################################################

#####################################################################
######

### 1. Model Fitting using maximum likelihood method to find the best fit
for S0 and ppn ####
```

```
# S0 = initial susceptible

# ppn = person per net


time <- 0                                # set initial time


t_start<- 0

n <- 10

t_end <- n*360

step <- 1


times <- seq(t_start, t_end, step)


## 1.1. Parameters ####

falciparum <- read_excel("Parameters and initial condition - falciparum.xlsx", sheet = "default") # loading excel data

parameters_value.vector <- c(falciparum$value)  # taking the value of parameters from data frame into a vector

parameters_name.vector <- c(falciparum$name)    # taking the name of parameters from data frame into a vector


names(parameters_value.vector) <- parameters_name.vector  # giving the parameters value with name


parms <- parameters_value.vector


## 1.2. ITN data ####

itndata <- read_excel("itndata.xlsx")


## 1.3. Initial conditions ####

initSf <- 5000000  # initial susceptible population

initEf <- 1000  # initial number of exposed compartment

initAf <- 0     # initial number of asymptomatic malaria

initCf <- 1000  # initial number of malaria cases with clinical symptoms

initCtf <- 0    # initial number of symptomatic malaria who are destined to be treated

initTf <- 0     # initial number of treated cases

initRf <- 3000  # initial number of recovered individuals

initSev <- 0    # initial number of severe malria cases

initH <- 0      # initial number of hospitalised patients
```

```
initCinc <- 0   # initial value for incidence counter
initCtr <- 0    # initial value for treatment counter
initCtrt_total <- 0 # initial value for total treatment counter
(outpatients + hospitalised)
initCtest <- 0  # initial value for test counter


initITN <- 0     # assigning the initial number of ITN


start <- c(Sf = initSf,
           Ef = initEf,
           Af = initAf,
           Cf = initCf,
           Ctf = initCtf,
           Tf = initTf,
           Sev = initSev,
           H = initH,
           Rf = initRf,
           Rpf = 0,
           Cinc = initCinc,
           Ctrt = initCtr,
           Chosp = 0,
           Ctrt_total = initCtrt_total,
           Ctest = initCtest,
           ITN = initITN,
           Death = 0,
           Sfm = 0,
           Tfm = 0,
           Rfm = 0,
           Hm = 0,
           Sfh = 0,
           Rfh = 0,
           Efh = 0,
           Afh = 0,
           Cfh = 0,
           Ctfh = 0,
           Sevh = 0,
           CMDA = 0,
           CSnap = 0)
```

```
### 2. Define dynamic Pf Human-static Vector Plasmodium falciparum (pf) model ####

## 2.1. the model with behaviour change ####

behaviour_change.model <- function(t, x, parms)  {

  with(as.list(c(parms, x)), {


    # defining total population

    Pf = Sf+Ef+Af+Cf+Ctf+Tf+Sev+H+Rf+Rpf+Sfm+Tfm+Rfm+Hm+Sfh+Rfh+Efh+Afh+Cfh+Ctfh+Sevh          # the population does not account for death


    ## A. INTERVENTION PART ####

    ## A.1. Bednets: Baseline ####

    # ITN effectiveness

    factor = 1

    if (t>360*5) {factor = net.coverage}


    itn_cov = itndata$nets/360*ppn/Pf*factor

    itn_t = itndata$time

    itn_dist<-approx(itn_t, itn_cov, t, method="constant")$y

    eta <- -log(1-(1-0.6))/(3*360) #loss due to attrition rate


    # plot(1:10000, approx(itn_t, itn_cov, 1:10000,method="constant")$y , ty="l")

    # points(itn_t, itn_cov, col="red")


    itn = min(ITN,1)*p_use*p_effectiveness    # gives the cap limit to one as coverage cannot be more than 100%


    ## A.2. Seasonal Mass Drug Administration (MDA) #### not necessary for model fitting

    # Several rounds: MDA takes place in January (for 30 days) for 5 360s


    # rounds = 5            # 5 rounds of MDA campaign (1 round: 30 days in a year)

    # mdur = 30             # 30 days

    # pulse = c(rep(0, 360*5),

    #           rep(c(rep(1, mdur), rep(0, (360-mdur))),rounds),

    #           rep(0, (360*5+rounds*360)))
```

```
    # par(mfrow = c(1,1))
    # plot(pulse, ty="l")


    mrate <- snap <-0


    #browser()


    # the first 5 years data are discarded, 5 years starts from year-5 to
year-10
    # if(t> (360*5) & t <= (360*10)) {
    #  mrate = approx(1:length(pulse), (-log(1-mcov)/mdur)*pulse, t,
method="constant", rule=2)$y
    #  snap = approx(1:length(pulse), (snapr*lag(pulse, default=0,
n=mdur)), t, method="constant", rule=2)$y
    #}


    ## A.3. Behaviour change #### not necessary for model fitting
    # behaviour change intervention: it takes 2 phases
    # the 1st phase:
    # int.start<- 360*5         # since the first 5 years data are
discarded, so the behaviour change intervention begins at the beginning of
the 360
    # int.lag <- 360*1          # there is a lag time before an
intervention takes an effect (e.g. due to preparation of the program)
    # int.target_time <- 360*2  # it is assumed that the target will be
reached within 2 years from the point when the effect starts


    # the target for bednets usage, 80% of people use bed nets and 80% of
people seek for treatment
    # int.target_net
    # int.target_seek


    # if(t > (int.start + int.lag)){
    #  p_use = log(t-int.target_time)/log(int.target_time)*(int.target_net
- 0.54) + 0.54  # it follows log function, with the cap limit is 0.8
    #  pseek = log(t-
int.target_time)/log(int.target_time)*(int.target_seek - 0.60) + 0.60 # it
follows log function, with the cap limit is 0.8
    #}
```

```
    # plot((log(1:730))/log(730)*(0.8-0.54)+0.54, type = "l")   # this
plot is to check the dynamics of behaviour change for nets usage

    # plot((log(1:730))/log(730)*(0.8-0.6)+0.6, type = "l")     # this
plot is to check the dynamics of behaviour change for treatment seeking



    # the 2nd phase:

    # else if (t > (int.start + int.lag + int.target_time)){  # the
intervention continuous at the second year

    # p_use = int.target_net   # the proportion of net use increases to
80%

    # pseek = int.target_seek   # the proportion of patients who seek for
treatment increases to 80%

    #}



    # B. MODEL PART ####

    # treatment cascade

    pi_t = pseek*(ptest_slide*psens_slide + ptest_RDT*psens_RDT)*ptreat

    ptrt = pi_t



    # force of infection

    Infectious = Cf+Ctf+Sev+zeta_a*Af+zeta_t*(Tf+H) # Infectious
contribution to the population

    seas <- 1+amp*cos(2*pi*(t/360 - phi))^peak           # seasonality,
assuming there is no phase angle meaning the peak occurs at the beginning
of each cycle cycle

    lambdaf = (1-
itn)*seas*(a^2*b*c*m*Infectious/Pf)/(a*c*Infectious/Pf+mu_m)*(gamma_m/(gam
ma_m+mu_m))



    # compartment model

    dSf = mu_h*Pf - lambdaf*Sf + rho_f*Rf - mu_h*Sf - mrate*Sf + snap*Sfh

    dEf = lambdaf*Sf - (gamma_hf + mu_h)*Ef - mrate*Ef + snap*Efh

    dAf = pa_f*gamma_hf*Ef + omega_f*Cf - (delta_f + mu_h)*Af - mrate*Af +
snap*Afh

    dCf = (1-pa_f)*(1-ptrt)*gamma_hf*Ef +  epsilon_f*Sev - (omega_f + nu_f
+ mu_h)*Cf - mrate*Cf + snap*Cfh

    dCtf = (1-pa_f)*ptrt*gamma_hf*Ef - (tau_f+ mu_h)*Ctf - mrate*Ctf +
snap*Ctfh

    dSev = nu_f*Cf - (epsilon_f + tau_sev + mu_sev + mu_h)*Sev - mrate*Sev
+ snap*Sevh

    dTf = tau_f*Ctf - (r_f + mu_h)*Tf

    dH = tau_sev*Sev - (r_hosp+ mu_hosp + mu_h)*H
```

```
    dRf = delta_f*Af  - (rho_f + mu_h)*Rf - mrate*Rf + snap*Rfh +
kappa*Rpf


    # for this MDA model, instead of Tf and H that go to Rf, they go to
Rpf first then to Rf, with the rate of change from Rpf to Rf = kappa.
    dRpf = r_f*Tf + r_hosp*H - (kappa + mrate + mu_h)*Rpf


    dSfm = mrate*Sf - (mprotect + mu_h)*Sfm
    dTfm = mrate*(Ef+Af+Cf+Ctf) + tau_f*Ctfh - (r_f + mu_h)*Tfm
    dRfm = mrate*(Rpf+Rf) + r_f*Tfm +r_hosp*Hm - (mprotect + mu_h)*Rfm
    dHm = mrate*Sev + tau_sev*Sevh - (r_hosp + mu_hosp + mu_h)*Hm   #


    dSfh = mprotect*Sfm - (lambdaf + snap + mu_h)*Sfh # state of
susceptibility for those on MDA but not protected
    dRfh = mprotect*Rfm + delta_f*Afh - (snap + mu_h)*Rfh # state of
Recovered for those on MDA but not protected
    dEfh = lambdaf*Sfh - (gamma_hf + snap + mu_h)*Efh
    dAfh = pa_f*gamma_hf*Efh + omega_f*Cfh - (delta_f + snap + mu_h)*Afh
    dCfh = (1-pa_f)*(1-ptrt)*gamma_hf*Efh + epsilon_f*Sevh - (omega_f +
nu_f + snap + mu_h)*Cfh
    dCtfh = (1-pa_f)*ptrt*gamma_hf*Efh - (tau_f + snap + mu_h)*Ctfh
    dSevh = nu_f*Cfh - (epsilon_f + tau_sev + snap + mu_sev + mu_h)*Sevh


    # Counters
    dD = mu_sev*(Sev+Sevh) + mu_hosp*(H+Hm)   # death counter, as now
death also comes from those in the MDA compartments (Sevh and Hm)


    dCinc = lambdaf*(Sf+Sfh)             # cumulative incidence
    dCtrt = tau_f*(Ctf+Ctfh)             # cumulative treated patients
with uncomplicated malaria
    dChosp = tau_sev*(Sev+Sevh)          # cumulative hospitalised
patients
    dCtrt_total = tau_f*(Ctf+Ctfh) + tau_sev*(Sev+Sevh)   # cumulative
treated patients by all means


    dCMDA = mrate*(Sf+Ef+Af+Cf+Rpf+Rf+Ctf+Sev)
    dCsnap = snap*(Sfh+Rfh+Efh+Afh+Cfh+Ctfh+Sevh)


    dCtest = tau_f*(Ctf + Ctfh)/ptreat/(ptest_RDT*RDT_pos +
ptest_slide*slide_pos) + # cumulative number of tests
      tau_sev*(Sev + Sevh)/1/(ptest_RDT*RDT_pos + ptest_slide*slide_pos) #
all severe cases are assumed to be treated
```

```
    # ITN
    dITN = itn_dist - (eta + mu_net)*ITN # coverage of the population with
potential to be protected by nets CURRENTLY IN CIRCULATION


    # returning the rate of change
    output <- c(dSf, dEf, dAf, dCf, dCtf, dTf, dSev, dH, dRf, dRpf, dCinc,
dCtrt, dChosp, dCtrt_total, dCtest, dITN, dD,
                dSfm, dTfm, dRfm, dHm, dSfh, dRfh, dEfh, dAfh, dCfh,
dCtfh, dSevh, dCMDA, dCsnap)
    list(output)
  })
}


## 2.2. the model without behaviour change ####
no_behaviour_change.model <- function(t,x,parms){
  parms['int.target_net'] <- parms['p_use']
  parms['int.target_seek'] <- parms['pseek']
  behaviour_change.model(t,x,parms)
}


## 2.3. Run models ####
ncov1 <- parms['net.coverage'] <- 1
mcov1 <- parms['mcov'] <- 0


hm.0 <- ode(times=times, y=start,
func=no_behaviour_change.model,parms=parms)


### 3. data generated ####
pf.cases <- c(b*pf.incidence$'2017', b*pf.incidence$'2018',
b*pf.incidence$'2019', b*pf.incidence$'2020', b*pf.incidence$'2021')


N1 <- pf.cases


### 4. creating a function to calculate negative likelihood (NLL) ####
calcNLL <- function(params){
  # returns NLL assuming binomial observations with N trials and d
successes
  # with initial 'Sf' and 'ppn' specified as the first 2 elements of the
params vector
```

```
  # constructing the model
  start['Sf'] <- exp(params[1])
  parms['ppn'] <- params[2]    # this value is also going to be fitted


  model_output.df <- data.frame(lsoda(
    y = start,               # Initial conditions for population
    times = times,             # Timepoints for evaluation
    func = no_behaviour_change.model,                   # Function to
evaluate
    parms = parms                 # Vector of parameters
  ))


  ## construct the new infection: lambda
  # extracting the number of row for the model output
  num.timepoints <- dim(model_output.df)[1]


  # taking the difference of the cumulative incidence returns to the
incidence
  new.infections<-round(c(model_output.df$Cinc[1],
                          model_output.df$Cinc[2:num.timepoints] -
model_output.df$Cinc[1:(num.timepoints-1)] ))
  lambda <- new.infections


  ## returning the output NLL value given the inputs
  # the output that are fitted are those in equilibrium. It is assumed
that the dynamics of the model becomes stable after 5 years, so the first
5 years are discarded
  # then, the the following 5 years are fitted with the past 5 years of
incidence report
  NLL <- -sum(dpois(round(N1),  lambda[(360*5+1):(360*10)], log = TRUE))
  return(NLL)
}


# 5. Fitting the model using optim ####
# running the optim function from certain starting values of params[1] and
params[2]
set.seed(123)
fit1<-optim(c(log(5e6), 2),
            calcNLL,
```

```
            control=list(reltol=1e-12),
            hessian = T)
fit1

# backtransforming the parameters
S0.fit <- exp(fit1$par[1])
ppn.fit <- fit1$par[2]



# calculating 95%CI
sds.for.parameters <- sqrt(diag(solve(fit1$hessian)))

S0.fit_lower.95CI <- S0.fit - 1.96*exp(sds.for.parameters[1])
S0.fit_upper.95CI <- S0.fit + 1.96*exp(sds.for.parameters[1])

ppn_lower.95CI <- ppn.fit - 1.96*sds.for.parameters[2]
ppn_upper.95CI <- ppn.fit + 1.96*sds.for.parameters[2]

# initial Sf value
S0.fit
S0.fit_lower.95CI
S0.fit_upper.95CI

# person per net
ppn.fit
ppn_lower.95CI
ppn_upper.95CI

# initial Sf value
S0.fit

# person per net
ppn.fit

## 5. contour plot ####

S0.grid <- seq(4000000, 9000000, 100000)
```

```
ppn.grid <- seq(1, 5, 0.2)
dim1 <- length(S0.grid)
dim2 <- length(ppn.grid)
NLL.grid <- matrix(NA, nrow = dim1, ncol = dim2)

for(i in 1:dim1){
  for(j in 1:dim2){
    NLL.grid[i,j] <- calcNLL(c(log(S0.grid[i]), ppn.grid[j]))
    print(i)
    print(j)
    print(S0.grid[i])
    print(ppn.grid[j])
    print(NLL.grid[i,j])
  }
}

#NLL.df <- as.data.frame(NLL.grid)
#colnames(NLL.grid) <- ppn.grid
#rownames(NLL.grid) <- S0.grid

S0.position <- c()
ppn.position <- c()
for(i in 1:dim1){
  for(j in 1:dim2){
    if(NLL.grid[i,j] == min(NLL.grid)) {
      best.fit.S0 <- S0.grid[i]
      best.fit.ppn <- ppn.grid[j]
      S0.position <- i
      ppn.position <- j
    }
  }
}

par(mfrow = c(1,2))
contour(NLL.grid, nlevels = 250,x = S0.grid, y = ppn.grid,
        xlab = "Initial susceptible individuals", ylab = "Person per net",
main = "Contour Plot: Grid Search for Maximum Likelihood")
points(x = best.fit.S0, y = best.fit.ppn, pch= 20, col = "red", cex = 2)
```

```
points(x = S0.fit, y = ppn.fit, pch= 20, col = "green", cex = 2)



image(S0.grid, ppn.grid, -log(NLL.grid), col = heat.colors(10000),
      xlab="Initial susceptible individuals",ylab="Person per net", main =
"Heat Map: Grid Search for Maximum Likelihood")
points(x = best.fit.S0, y = best.fit.ppn, pch= 20, col = "red", cex = 2)
points(x = S0.fit, y = ppn.fit, pch= 20, col = "green", cex = 2)



best.fit.S0
best.fit.ppn


S0.fit
ppn.fit


# 6. Model check  ####
ncov1 <- parms['net.coverage'] <- 1
mcov1 <- parms['mcov'] <- 0
start['Sf'] <- S0.fit
parms['ppn'] <- ppn.fit


hm.fit <- ode(times=times, y=start,
func=no_behaviour_change.model,parms=parms)


df.fit <- as_tibble(as.data.frame(hm.fit)) %>%
  mutate(P =
Sf+Ef+Af+Cf+Ctf+Sev+Tf+H+Rf+Rpf+Sfm+Tfm+Rfm+Hm+Sfh+Rfh+Efh+Afh+Cfh+Ctfh+Se
vh,
         P_total = P + Death,
         C_total = Cf + Ctf + Sev,
         T_total = Tf + H,
         Deathf = c(0, diff(Death)),
         Incf = c(0, diff(Cinc)),
         Trtf = c(0, diff(Ctrt))) %>%
  pivot_longer(names_to = "variable", cols = !1)


# Population check
df.fit  %>%
```

```
  filter(variable %in% c("P_total")) %>%
  ggplot()+
  geom_line(aes(x = time, y=value))+
  theme_minimal() +
  labs(title = "Populations", y =("population"))


# Incidence and nets ####
plot_incidence.fit <- df.fit %>%
  filter(variable %in% c("Incf")) %>%
  filter(time > 360*5) %>%
  ggplot()+
  geom_line(aes(x = time, y=value), colour = "cyan")+
  geom_point(aes(x = time, y = pf.cases), colour = "orange") +
  theme_minimal() +
  labs(title = "Incidence - Baseline", y =("population"))


plot_incidence.fit


# CHAPTER 3: SCENARIO ANALYSIS
################################################

#########################################################################
######
### 1. Load packages ####
library(pacman)
p_load(deSolve, tidyverse, gridExtra, readxl, ggplot2)


### 2. Input definitions ####
# 2.1. define the number of days to run the model ####
t_start<- 0
n <- 10
t_end <- n*360
step <- 30


times <- seq(t_start, t_end, step)


# 2.2. Parameters ####
falciparum <- read_excel("Parameters and initial condition -
falciparum.xlsx", sheet = "default") # loading excel data
```

```
parameters_value.vector <- c(falciparum$value)  # taking the value of
parameters from data frame into a vector

parameters_name.vector <- c(falciparum$name)    # taking the name of
parameters from data frame into a vector


names(parameters_value.vector) <- parameters_name.vector  # giving the
parameters value with name


parms <- parameters_value.vector


# 2.3. ITN data ####

itndata <- read_excel("itndata.xlsx")


# 2.4. Initial conditions ####

initSf <- S0.fit  # initial susceptible population

initEf <- 1000  # initial number of exposed compartment

initAf <- 0     # initial number of asymptomatic malaria

initCf <- 1000  # initial number of malaria cases with clinical symptoms

initCtf <- 0    # initial number of symptomatic malaria who are destined
to be treated

initTf <- 0     # initial number of treated cases

initRf <- 3000  # initial number of recovered individuals

initSev <- 0    # initial number of severe malria cases

initH <- 0      # initial number of hospitalised patients

initCinc <- 0   # initial value for incidence counter

initCtr <- 0    # initial value for treatment counter

initCtrt_total <- 0 # initial value for total treatment counter
(outpatients + hospitalised)

initCtest <- 0  # initial value for test counter


start <- c(Sf = S0.fit,          # initial susceptible cases

           Ef = 1000,            # initial exposed cases

           Af = 0,               # initial asymptomatic cases

           Cf = 1000,            # initial uncomplicated cases who are not
going to be treated

           Ctf = 0,              # initial uncomplicated cases who are
destined to be treated

           Tf = 0,               # initial treated patients

           Sev = 0,              # initial severe patients

           H = 0,                # initial hospitalised patients
```

```
            Rf = 3000,            # initial recovered inidividuals

            Rpf = 0,              # initial

            Cinc = 0,             # initial cumulative incidence

            Ctrt = 0,             # initial number of uncomplicated malaria
patients who receive treatment (outpatient)

            Chosp = 0,            # initial number of complicated malaria
pastients who receive treatment (hospitalised)

            Ctrt_total = 0,       # initial number of those receiving
treatment by all means

            Ctest = 0,            # initial number of tests

            ITN = 0,              # assigning the initial number of ITN

            Death = 0,            # initial death

            Sfm = 0,              #

            Tfm = 0,              #

            Rfm = 0,              #

            Hm = 0,               #

            Sfh = 0,              # initial number of those in state of
susceptibility for those on MDA but not protected

            Rfh = 0,              # initial state of recovery for those on
MDA but not protected

            Efh = 0,              #

            Afh = 0,              #

            Cfh = 0,              #

            Ctfh = 0,             #

            Sevh = 0,             # initial number of severe cases after

            CMDA = 0,             # MDA administered at time 0

            CSnap = 0)            # those who are snap back to the original
compartment


### 3. Define dynamic Pf Human-static Vector Plasmodium falciparum (pf)
model ####

## 3.1. the model with behaviour change ####

behaviour_change.model <- function(t, x, parms)  {

  with(as.list(c(parms, x)), {


    # defining total population

    Pf =
Sf+Ef+Af+Cf+Ctf+Tf+Sev+H+Rf+Rpf+Sfm+Tfm+Rfm+Hm+Sfh+Rfh+Efh+Afh+Cfh+Ctfh+Se
vh          # the population does not account for death


    ## A. INTERVENTION PART ####
```

```
    ## A.1. Bednets: Baseline ####
    # ITN effectiveness
    factor = 1
    if (t>360*5) {factor = net.coverage}

    itn_cov = itndata$nets/360*ppn.fit/Pf*factor
    itn_t = itndata$time
    itn_dist<-approx(itn_t, itn_cov, t, method="constant")$y
    eta <- -log(1-(1-0.6))/(3*360) #loss due to attrition rate

    # plot(1:10000, approx(itn_t, itn_cov, 1:10000,method="constant")$y ,
ty="l")
    # points(itn_t, itn_cov, col="red")

    itn = min(ITN,1)*p_use*p_effectiveness    # gives the cap limit to one
as coverage cannot be more than 100%

    ## A.2. Seasonal Mass Drug Administration (MDA) ####
    # Several rounds: MDA takes place in January (for 30 days) for 5 360s

    rounds = 5            # 5 rounds of MDA campaign (1 round: 30 days in
a year)
    mdur = 30             # 30 days
    pulse = c(rep(0, 360*5),
              rep(c(rep(1, mdur), rep(0, (360-mdur))),rounds),
              rep(0, (360*5+rounds*360)))

    # par(mfrow = c(1,1))
    # plot(pulse, ty="l")

    mrate <- snap <-0

    #browser()

    # the first 5 years data are discarded, 5 years starts from year-5 to
year-10
    if(t> (360*5) & t <= (360*10)) {
      mrate = approx(1:length(pulse), (-log(1-mcov)/mdur)*pulse, t,
method="constant", rule=2)$y
```

```
      snap = approx(1:length(pulse), (snapr*lag(pulse, default=0,
n=mdur)), t, method="constant", rule=2)$y

    }


    ## A.3. Behaviour change ####

    # behaviour change intervention: it takes 2 phases

    # the 1st phase:

    int.start<- 360*5         # since the first 5 years data are
discarded, so the behaviour change intervention begins at the beginning of
the 360

    int.lag <- 360*1          # there is a lag time before an intervention
takes an effect (e.g. due to preparation of the program)

    int.target_time <- 360*2  # it is assumed that the target will be
reached within 2 years from the point when the effect starts



    # the target for bednets usage, 80% of people use bed nets and 80% of
people seek for treatment

    # int.target_net

    # int.target_seek


    if(t > (int.start + int.lag)){

      p_use = log(t-int.target_time)/log(int.target_time)*(int.target_net
- 0.54) + 0.54  # it follows log function, with the cap limit is 0.8

      pseek = log(t-int.target_time)/log(int.target_time)*(int.target_seek
- 0.60) + 0.60 # it follows log function, with the cap limit is 0.8

    }



    # plot((log(1:730))/log(730)*(0.8-0.54)+0.54, type = "l")   # this
plot is to check the dynamics of behaviour change for nets usage

    # plot((log(1:730))/log(730)*(0.8-0.6)+0.6, type = "l")     # this
plot is to check the dynamics of behaviour change for treatment seeking



    # the 2nd phase:

    else if (t > (int.start + int.lag + int.target_time)){  # the
intervention continuous at the second year

      p_use = int.target_net   # the proportion of net use increases to
80%

      pseek = int.target_seek   # the proportion of patients who seek for
treatment increases to 80%

    }



    # B. MODEL PART ####

    # treatment cascade
```

```
    pi_t = pseek*(ptest_slide*psens_slide + ptest_RDT*psens_RDT)*ptreat

    ptrt = pi_t


    # force of infection

    Infectious = Cf+Ctf+Sev+zeta_a*Af+zeta_t*(Tf+H) # Infectious
contribution to the population

    seas <- 1+amp*cos(2*pi*(t/360 - phi))^peak           # seasonality,
assuming there is no phase angle meaning the peak occurs at the beginning
of each cycle cycle

    lambdaf = (1-
itn)*seas*(a^2*b*c*m*Infectious/Pf)/(a*c*Infectious/Pf+mu_m)*(gamma_m/(gam
ma_m+mu_m))


    # compartment model

    dSf = mu_h*Pf - lambdaf*Sf + rho_f*Rf - mu_h*Sf - mrate*Sf + snap*Sfh

    dEf = lambdaf*Sf - (gamma_hf + mu_h)*Ef - mrate*Ef + snap*Efh

    dAf = pa_f*gamma_hf*Ef + omega_f*Cf - (delta_f + mu_h)*Af - mrate*Af +
snap*Afh

    dCf = (1-pa_f)*(1-ptrt)*gamma_hf*Ef +  epsilon_f*Sev - (omega_f + nu_f
+ mu_h)*Cf - mrate*Cf + snap*Cfh

    dCtf = (1-pa_f)*ptrt*gamma_hf*Ef - (tau_f+ mu_h)*Ctf - mrate*Ctf +
snap*Ctfh

    dSev = nu_f*Cf - (epsilon_f + tau_sev + mu_sev + mu_h)*Sev - mrate*Sev
+ snap*Sevh

    dTf = tau_f*Ctf - (r_f + mu_h)*Tf

    dH = tau_sev*Sev - (r_hosp+ mu_hosp + mu_h)*H

    dRf = delta_f*Af  - (rho_f + mu_h)*Rf - mrate*Rf + snap*Rfh +
kappa*Rpf


    # for this MDA model, instead of Tf and H that go to Rf, they go to
Rpf first then to Rf, with the rate of change from Rpf to Rf = kappa.

    dRpf = r_f*Tf + r_hosp*H - (kappa + mrate + mu_h)*Rpf


    dSfm = mrate*Sf - (mprotect + mu_h)*Sfm

    dTfm = mrate*(Ef+Af+Cf+Ctf) + tau_f*Ctfh - (r_f + mu_h)*Tfm

    dRfm = mrate*(Rpf+Rf) + r_f*Tfm +r_hosp*Hm - (mprotect + mu_h)*Rfm

    dHm = mrate*Sev + tau_sev*Sevh - (r_hosp + mu_hosp + mu_h)*Hm   #


    dSfh = mprotect*Sfm - (lambdaf + snap + mu_h)*Sfh # state of
susceptibility for those on MDA but not protected

    dRfh = mprotect*Rfm + delta_f*Afh - (snap + mu_h)*Rfh # state of
Recovered for those on MDA but not protected

    dEfh = lambdaf*Sfh - (gamma_hf + snap + mu_h)*Efh
```

```
    dAfh = pa_f*gamma_hf*Efh + omega_f*Cfh - (delta_f + snap + mu_h)*Afh

    dCfh = (1-pa_f)*(1-ptrt)*gamma_hf*Efh + epsilon_f*Sevh - (omega_f +
nu_f + snap + mu_h)*Cfh

    dCtfh = (1-pa_f)*ptrt*gamma_hf*Efh - (tau_f + snap + mu_h)*Ctfh

    dSevh = nu_f*Cfh - (epsilon_f + tau_sev + snap + mu_sev + mu_h)*Sevh


    # Counters

    dD = mu_sev*(Sev+Sevh) + mu_hosp*(H+Hm)   # death counter, as now
death also comes from those in the MDA compartments (Sevh and Hm)


    dCinc = lambdaf*(Sf+Sfh)             # cumulative incidence

    dCtrt = tau_f*(Ctf+Ctfh)             # cumulative treated patients
with uncomplicated malaria

    dChosp = tau_sev*(Sev+Sevh)          # cumulative hospitalised
patients

    dCtrt_total = tau_f*(Ctf+Ctfh) + tau_sev*(Sev+Sevh)   # cumulative
treated patients by all means


    dCMDA = mrate*(Sf+Ef+Af+Cf+Rpf+Rf+Ctf+Sev)

    dCsnap = snap*(Sfh+Rfh+Efh+Afh+Cfh+Ctfh+Sevh)


    dCtest = tau_f*(Ctf + Ctfh)/ptreat/(ptest_RDT*RDT_pos +
ptest_slide*slide_pos) + # cumulative number of tests

      tau_sev*(Sev + Sevh)/1/(ptest_RDT*RDT_pos + ptest_slide*slide_pos) #
all severe cases are assumed to be treated


    # ITN

    dITN = itn_dist - (eta + mu_net)*ITN # coverage of the population with
potential to be protected by nets CURRENTLY IN CIRCULATION


    # returning the rate of change

    output <- c(dSf, dEf, dAf, dCf, dCtf, dTf, dSev, dH, dRf, dRpf, dCinc,
dCtrt, dChosp, dCtrt_total, dCtest, dITN, dD,

                dSfm, dTfm, dRfm, dHm, dSfh, dRfh, dEfh, dAfh, dCfh,
dCtfh, dSevh, dCMDA, dCsnap)

    list(output)

  })

}


## 3.2. the model without behaviour change ####

no_behaviour_change.model <- function(t,x,parms){
```

```
  parms['int.target_net'] <- parms['p_use']
  parms['int.target_seek'] <- parms['pseek']
  behaviour_change.model(t,x,parms)
}


## 3.3. Run models ####
ncov1 <- parms['net.coverage'] <- 1
mcov1 <- parms['mcov'] <- 0


hm.0 <- ode(times=times, y=start,
func=no_behaviour_change.model,parms=parms)


# 3.4. check the basic model ####
# mutate
df.0 <- as_tibble(as.data.frame(hm.0)) %>%
  mutate(P =
Sf+Ef+Af+Cf+Ctf+Sev+Tf+H+Rf+Rpf+Sfm+Tfm+Rfm+Hm+Sfh+Rfh+Efh+Afh+Cfh+Ctfh+Se
vh,
         P_total = P + Death,
         C_total = Cf + Ctf + Cfh + Ctfh+ Sev,
         T_total = Tf + Tfm + H+ Hm,
         Deathf = c(0, diff(Death)),
         Incf = c(0, diff(Cinc)),
         Trtf = c(0, diff(Ctrt))) %>%
  pivot_longer(names_to = "variable", cols = !1)


# Population check
df.0  %>%
  filter(variable %in% c("P_total")) %>%
  ggplot()+
  geom_line(aes(x = time, y=value))+
  theme_minimal() +
  labs(title = "Populations", y =("population"))


# run the models again
hm.behaviour_change <- ode(times=times, y=start,
func=behaviour_change.model,parms=parms)
hm.no_behaviour_change <- ode(times=times, y=start,
func=no_behaviour_change.model,parms=parms)
```

```
### 4. health benefit analysis (HBA) ####

## 4.1. HBA in scenarios with behaviour change ####

# preparing for an array to contain the outputs

netcoverage.grid <- seq(0, 1, 0.1)

mdacoverage.grid <- seq(0, 0.9, 0.1)  # as in the function, 100% coverage
would result in inf, so here the max coverage is set to be 0.9

out.name <- c("nhb", "nmb", "cost", "daly", "diff.cost", "daly.gained")


dim.net <- length(netcoverage.grid)

dim.mda <- length(mdacoverage.grid)

dim.out <- length(out.name)


nhb.grid <- array(NA,
                  dim=c(dim.net, dim.mda, dim.out),
                  dimnames = list(netcoverage.grid, mdacoverage.grid,
out.name))


hba.bc <- function(x) {

  # preparing for an array to contain the outputs ####

  netcoverage.grid <- seq(0, 1, 0.1)

  mdacoverage.grid <- seq(0, 0.9, 0.1)  # as in the function, 100%
coverage would result in inf, so here the max coverage is set to be 0.9

  out.name <- c("nhb", "nmb", "cost", "daly", "diff.cost", "daly.gained")


  dim.net <- length(netcoverage.grid)

  dim.mda <- length(mdacoverage.grid)

  dim.out <- length(out.name)


  nhb.grid <- array(NA,
                    dim=c(dim.net, dim.mda, dim.out),
                    dimnames = list(netcoverage.grid, mdacoverage.grid,
out.name))


  # setting up for threshold for health benefit measurement

  indonesian.gdp.per.capita <- 3820 #
https://data.worldbank.org/indicator/NY.GDP.PCAP.KD?locations=ID

  threshold <- 3*indonesian.gdp.per.capita
```

```
  # defining variable and parameters for baseline ####
  ncov <- parms['net.coverage'] <- 1
  parms['mcov'] <- 0


  hm <-ode(times=times, y=start,
func=no_behaviour_change.model,parms=parms)


  # sum uncomplicated cases
  uncomplicated <- sum(hm[x, ('Cf')] + hm[x,'Ctf'] + hm[x,'Cfh'] +
hm[x,'Ctfh'])


  # sum severe cases
  complicated <- sum(hm[x, ('Sev')] + hm[x,'Sevh'])


  # sum deaths
  death <- sum(diff(hm[x, 'Death']))


  # sum hospitalised
  hospitalised <- sum(diff(hm[x, 'Chosp']))


  # sum outpatients
  outpatient <- sum(diff(hm[x, 'Ctrt']))


  # sum tests
  test <- sum(diff(hm[x, 'Ctest']))


  # sum nets
  net <- sum(itndata$nets[5:9])


  # sum mda
  mda <- sum(diff(hm[x, 'CMDA']))


  # Health Cost ####
  # treatment cost: hospitalised*(33.5) + outpatient*(5.5 + 0.293)
  treatment.cost <- hospitalised*(33.5) + outpatient*(5.5 + 0.293)


  # test cost: test*(1.2)
  test.cost <- test*(1.2)
```

```
  # bed-net cost: nets*(5+2)
  net.cost <- net*(5+2)

  # mda cost: mda*(5.5 + 0.293)
  mda.cost <- mda*(5.5 + 0.293)

  # health system cost: total_population*no_of_year*(4.5)
  health.system.cost <- sum(start)*5*(4.5)

  # total cost: accounting 3% discount rate for 5 years as this is the
total investment in 2017
  total.cost.baseline <- (treatment.cost + test.cost + net.cost*ncov+
mda.cost + health.system.cost)/((1+0.3)^5)

  # DALY ####
  # DALY: uncomplicated*(0.211) + complicated*(0.436) + death*(50)
[https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3991722/#!po=36.1111]
  daly.baseline <- uncomplicated*(0.211) + complicated*(0.436) +
death*(50)

  # sensitivity analysis ####
  for(i in 1:dim.net){
    for(j in 1:dim.mda){
      # defining variable and parameters ####
      ncov <- parms['net.coverage'] <- netcoverage.grid[i]
      parms['mcov'] <- mdacoverage.grid[j]

      hm <-ode(times=times, y=start,
func=behaviour_change.model,parms=parms)

      # sum uncomplicated cases
      uncomplicated <- sum(hm[x, ('Cf')] + hm[x,'Ctf'] + hm[x,'Cfh'] +
hm[x,'Ctfh'])

      # sum severe cases
      complicated <- sum(hm[x, ('Sev')] + hm[x,'Sevh'])

      # sum deaths
      death <- sum(diff(hm[x, 'Death']))
```

```
      # sum hospitalised
      hospitalised <- sum(diff(hm[x, 'Chosp']))

      # sum outpatients
      outpatient <- sum(diff(hm[x, 'Ctrt']))

      # sum tests
      test <- sum(diff(hm[x, 'Ctest']))

      # sum nets
      net <- sum(itndata$nets[5:9])

      # sum mda
      mda <- sum(diff(hm[x, 'CMDA']))

      # Health Cost ####
      # treatment cost: hospitalised*(33.5) + outpatient*(5.5 + 0.293)
      treatment.cost <- hospitalised*(33.5) + outpatient*(5.5 + 0.293)

      # test cost: test*(1.2)
      test.cost <- test*(1.2)

      # bed-net cost: nets*(5+2)
      net.cost <- net*(5+2)

      # mda cost: mda*(5.5 + 0.293)
      mda.cost <- mda*(5.5 + 0.293)

      # behaviour change cost: no of village * cost per village per year *
year = 8747*500*5
      bc.cost <- parms['bc']

      # health system cost: total_population*no_of_year*(4.5)
      health.system.cost <- sum(start)*5*(4.5)

      # total cost: accounting 3% discount rate for 5 years as this is the
total investment in 2017
```

```
      total.cost <- (treatment.cost + test.cost + net.cost*ncov + mda.cost
+ bc.cost + health.system.cost)/((1+0.3)^5)


      # cost difference

      diff.cost <- total.cost - total.cost.baseline


      # DALY ####

      # DALY: uncomplicated*(0.211) + complicated*(0.436) + death*(50)
[https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3991722/#!po=36.1111]

      daly <- uncomplicated*(0.211) + complicated*(0.436) + death*(50)


      # daly gained

      daly.gained <- daly.baseline - daly


      # HEALTH BENEFIT MEASUREMENT ####

      # Net health benefit (NHB): daly gained - total cost/threshold

      nhb <- daly.gained - (diff.cost)/threshold

      nmb <- nhb*threshold


      nhb.grid[i,j,1] <- nhb

      nhb.grid[i,j,2] <- nmb

      nhb.grid[i,j,3] <- total.cost

      nhb.grid[i,j,4] <- daly

      nhb.grid[i,j,5] <- diff.cost

      nhb.grid[i,j,6] <- daly.gained


      print(c("total cost baseline" = total.cost.baseline))

      print(c("nhb" = nhb))

      print(c('net' = parms['net.coverage'], 'mda' = parms['mcov'], 'cost'
= total.cost, 'diff.cost' = diff.cost, 'daly.gained' = daly.gained))

    }

  }

  return(nhb.grid)

}


## 4.2. HBA in scenarios without behaviour change ####

hba.nbc <- function(x) {

  # preparing for an array to contain the outputs ####
```

```
  netcoverage.grid <- seq(0, 1, 0.1)

  mdacoverage.grid <- seq(0, 0.9, 0.1)  # as in the function, 100%
coverage would result in inf, so here the max coverage is set to be 0.9

  out.name <- c("nhb", "nmb", "cost", "daly", "diff.cost", "daly.gained")


  dim.net <- length(netcoverage.grid)

  dim.mda <- length(mdacoverage.grid)

  dim.out <- length(out.name)


  nhb.grid <- array(NA,
                    dim=c(dim.net, dim.mda, dim.out),
                    dimnames = list(netcoverage.grid, mdacoverage.grid,
out.name))


  # setting up for threshold for health benefit measurement

  indonesian.gdp.per.capita.2017 <- 3820

  threshold <- 3*indonesian.gdp.per.capita.2017 # WHO threshold for a
cost-effective intervention (no more than 3 gdp)


  # defining variable and parameters for baseline ####

  ncov <- parms['net.coverage'] <- 1

  parms['mcov'] <- 0


  hm <-ode(times=times, y=start,
func=no_behaviour_change.model,parms=parms)


  # sum uncomplicated cases

  uncomplicated <- sum(hm[x, ('Cf')] + hm[x,'Ctf'] + hm[x,'Cfh'] +
hm[x,'Ctfh'])


  # sum severe cases

  complicated <- sum(hm[x, ('Sev')] + hm[x,'Sevh'])


  # sum deaths

  death <- sum(diff(hm[x, 'Death']))


  # sum hospitalised

  hospitalised <- sum(diff(hm[x, 'Chosp']))
```

```
  # sum outpatients
  outpatient <- sum(diff(hm[x, 'Ctrt']))

  # sum tests
  test <- sum(diff(hm[x, 'Ctest']))

  # sum nets
  net <- sum(itndata$nets[5:9])

  # sum mda
  mda <- sum(diff(hm[x, 'CMDA']))

  # Health Cost ####
  # treatment cost: hospitalised*(33.5) + outpatient*(5.5 + 0.293)
  treatment.cost <- hospitalised*(33.5) + outpatient*(5.5 + 0.293)

  # test cost: test*(1.2)
  test.cost <- test*(1.2)

  # bed-net cost: nets*(5+2)
  net.cost <- net*(5+2)

  # mda cost: mda*(5.5 + 0.293)
  mda.cost <- mda*(5.5 + 0.293)

  # health system cost: total_population*no_of_year*(4.5)
  health.system.cost <- sum(start)*5*(4.5)

  # total cost: accounting 3% discount rate for 5 years as this is the
total investment in 2017
  total.cost.baseline <- (treatment.cost + test.cost + net.cost*ncov +
mda.cost + health.system.cost)/((1+0.3)^5)

  # DALY ####
  # DALY: uncomplicated*(0.211) + complicated*(0.436) + death*(50)
[https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3991722/#!po=36.1111]
  daly.baseline <- uncomplicated*(0.211) + complicated*(0.436) +
death*(50)
```

```
  # sensitivity analysis ####
  for(i in 1:dim.net){
    for(j in 1:dim.mda){
      # defining variable and parameters ####
      ncov <- parms['net.coverage'] <- netcoverage.grid[i]
      parms['mcov'] <- mdacoverage.grid[j]


      hm <-ode(times=times, y=start,
func=no_behaviour_change.model,parms=parms)


      # sum uncomplicated cases
      uncomplicated <- sum(hm[x, ('Cf')] + hm[x,'Ctf'] + hm[x,'Cfh'] +
hm[x,'Ctfh'])


      # sum severe cases
      complicated <- sum(hm[x, ('Sev')] + hm[x,'Sevh'])


      # sum deaths
      death <- sum(diff(hm[x, 'Death']))


      # sum hospitalised
      hospitalised <- sum(diff(hm[x, 'Chosp']))


      # sum outpatients
      outpatient <- sum(diff(hm[x, 'Ctrt']))


      # sum tests
      test <- sum(diff(hm[x, 'Ctest']))


      # sum nets
      net <- sum(itndata$nets[5:9])


      # sum mda
      mda <- sum(diff(hm[x, 'CMDA']))


      # Health Cost ####
      # treatment cost: hospitalised*(33.5) + outpatient*(5.5 + 0.293)
      treatment.cost <- hospitalised*(33.5) + outpatient*(5.5 + 0.293)
```

```
      # test cost: test*(1.2)
      test.cost <- test*(1.2)

      # bed-net cost: nets*(5+2)
      net.cost <- net*(5+2)

      # mda cost: mda*(5.5 + 0.293)
      mda.cost <- mda*(5.5 + 0.293)

      # behaviour change cost: no of village * cost per village per year *
year = 8795*500*5
      bc.cost <- 0

      # health system cost: total_population*no_of_year*(4.5)
      health.system.cost <- sum(start)*5*(4.5)

      # total cost: accounting 3% discount rate for 5 years as this is the
total investment in 2017
      total.cost <- (treatment.cost + test.cost + net.cost*ncov + mda.cost
+ bc.cost + health.system.cost)/((1+0.3)^5)

      # cost difference
      diff.cost <- total.cost - total.cost.baseline

      # DALY ####
      # DALY: uncomplicated*(0.211) + complicated*(0.436) + death*(50)
[https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3991722/#!po=36.1111]
      daly <- uncomplicated*(0.211) + complicated*(0.436) + death*(50)

      # daly gained
      daly.gained <- daly.baseline - daly

      # HEALTH BENEFIT MEASUREMENT ####
      # Net health benefit (NHB): daly gained - total cost/threshold
      nhb <- daly.gained - (diff.cost)/threshold
      nmb <- nhb*threshold

      nhb.grid[i,j,1] <- nhb
```

```
      nhb.grid[i,j,2] <- nmb
      nhb.grid[i,j,3] <- total.cost
      nhb.grid[i,j,4] <- daly
      nhb.grid[i,j,5] <- diff.cost
      nhb.grid[i,j,6] <- daly.gained


      print(c("total cost baseline" = total.cost.baseline))
      print(c("nhb" = nhb))
      print(c('net' = parms['net.coverage'], 'mda' = parms['mcov'], 'cost'
= total.cost, 'diff.cost' = diff.cost, 'daly.gained' = daly.gained))
    }
  }
  return(nhb.grid)
}


## 4.3. Running the HBA ####
interval = 61:121   # running from the start of 2017 to the end of 2021


# running the function
nhb.grid.bc <- hba.bc(interval)
nhb.grid.nbc <- hba.nbc(interval)


# time needed for running the code
finish.time <- Sys.time()
finish.time - start.time


# check the output for net health benefit
nhb.grid.bc[,,'nhb']
nhb.grid.nbc[,,'nhb']


## 4.4. Analysing which one has the highest net health benefit (NHB):
without behaviour change ####
# 4.4.1. net health benefit analysis for behaviour change intervention
####
nbc.nhb <- matrix(0, nrow = dim.net, ncol = dim.mda)
rownames(nbc.nhb) <- as.character(netcoverage.grid)
colnames(nbc.nhb) <-as.character(mdacoverage.grid)
for(i in 1:dim.net){
```

```
  for(j in 1:dim.mda){
    if (nhb.grid.nbc[i,j,'nhb'] <= 0) {nbc.nhb[i,j] <- 0}
    else if (0 < nhb.grid.nbc[i,j,'nhb'] && nhb.grid.nbc[i,j,'nhb'] <=
50000) {nbc.nhb[i,j] <- 1}
    else if (50000 < nhb.grid.nbc[i,j,'nhb'] && nhb.grid.nbc[i,j,'nhb'] <=
100000) {nbc.nhb[i,j] <- 2}
    else {nbc.nhb[i,j] <- 3}
  }
}

# 4.4.2. total cost analysis for behaviour change intervention ####
nbc.cost <- matrix(0, nrow = dim.net, ncol = dim.mda)
rownames(nbc.cost) <- netcoverage.grid
colnames(nbc.cost) <-mdacoverage.grid
for(i in 1:dim.net){
  for(j in 1:dim.mda){
    if (nhb.grid.nbc[i,j,'cost'] <= (nhb.grid.nbc[11,1,'cost']))
{nbc.cost[i,j] <- 1}
    else {nbc.cost[i,j] <- 0}
  }
}
nbc.cost

# 4.4.3. nhb under budget constraints analysis for behaviour change
intervention ####
nbc.nhb.cost.accepted <- matrix(0, nrow = dim.net, ncol = dim.mda)
rownames(nbc.nhb.cost.accepted) <- netcoverage.grid
colnames(nbc.nhb.cost.accepted) <-mdacoverage.grid
for(i in 1:dim.net){
  for(j in 1:dim.mda){
    if (nbc.cost[i,j] == 1 & nbc.nhb[i,j] > 0) {nbc.nhb.cost.accepted[i,j]
<- nhb.grid.nbc[i,j,'nhb']}
    else {nbc.nhb.cost.accepted[i,j] <- 0}
  }
}
nbc.nhb.cost.accepted

## 4.5. Analysing which one has the highest net health benefit (NHB): with
behaviour change ####
```

```
# 4.5.1. net health benefit analysis for behaviour change intervention
####

bc.nhb <- matrix(0, nrow = dim.net, ncol = dim.mda)

rownames(bc.nhb) <- netcoverage.grid

colnames(bc.nhb) <-mdacoverage.grid

for(i in 1:dim.net){

  for(j in 1:dim.mda){

    if (nhb.grid.bc[i,j,'nhb'] <= 0) {bc.nhb[i,j] <- 0}

    else if (0 < nhb.grid.bc[i,j,'nhb'] && nhb.grid.bc[i,j,'nhb'] <=
50000) {bc.nhb[i,j] <- 1}

    else if (50000 < nhb.grid.bc[i,j,'nhb'] && nhb.grid.bc[i,j,'nhb'] <=
100000) {bc.nhb[i,j] <- 2}

    else {bc.nhb[i,j] <- 3}

  }

}


# 4.5.2. total cost analysis for behaviour change intervention ####

bc.cost <- matrix(0, nrow = dim.net, ncol = dim.mda)

rownames(bc.cost) <- netcoverage.grid

colnames(bc.cost) <-mdacoverage.grid

for(i in 1:dim.net){

  for(j in 1:dim.mda){

    if (nhb.grid.bc[i,j,'cost'] <= (nhb.grid.bc[11,1,'cost']))
{bc.cost[i,j] <- 1}

    else {bc.cost[i,j] <- 0}

  }

}

bc.cost


# 4.5.3. nhb under budget constraints analysis for behaviour change
intervention ####

bc.nhb.cost.accepted <- matrix(0, nrow = dim.net, ncol = dim.mda)

rownames(bc.nhb.cost.accepted) <- netcoverage.grid

colnames(bc.nhb.cost.accepted) <-mdacoverage.grid

for(i in 1:dim.net){

  for(j in 1:dim.mda){

    if (bc.cost[i,j] == 1 & bc.nhb[i,j] > 0) {bc.nhb.cost.accepted[i,j] <-
nhb.grid.bc[i,j,'nhb']}

    else {bc.nhb.cost.accepted[i,j] <- 0}

  }
```

```
}


bc.nhb.cost.accepted


# CHAPTER 4: PLOTTING
############################################################

##########################################################################
######


library(pacman)
p_load(deSolve, tidyverse, gridExtra, readxl, ggplot2)


# model preparation for plotting ####
# 1.1. setting up parameters for each scenario ####
scn <- c("scenario 3", "scenario 2", "scenario 1", "baseline", "reverse
1", "reverse 2")
date <- seq(as.Date("2011/12/1"), as.Date("2021/12/1"), "month")
ncov3 <- c()
mcov3 <- c()
ncov2 <- c()
mcov2 <- c()


# indexing which combination of net coverage and mda coverage has maximum
# net health benefit under budget constraint
for(i in 1:dim.net){
  for(j in 1:dim.mda){
    if(nbc.nhb.cost.accepted[i,j] == max(nbc.nhb.cost.accepted)){
      ncov3 <-parms['net.coverage'] <- netcoverage.grid[i]
      mcov3 <-parms['mcov'] <- mdacoverage.grid[j]
    }
  }
}


# indexing which combination of net coverage and mda coverage has maximum
# net health benefit without budget constraint
for(i in 1:dim.net){
  for(j in 1:dim.mda){
    if(bc.nhb.cost.accepted[i,j] == max(bc.nhb.cost.accepted)){
```

```
      ncov2 <-parms['net.coverage'] <- netcoverage.grid[i]
      mcov2 <-parms['mcov'] <- mdacoverage.grid[j]
    }
  }
}

ncov <- c(ncov3, ncov2, 1, 1, 0.5, 0)
mcov <- c(mcov3, mcov2, 0, 0, 0, 0)

# 1.2. seting up time ####
t_start<- 0
n <- 10
t_end <- n*360
step <- 30

times <- seq(t_start, t_end, step)

# 1.3. create empty data frames for combining data frame of each scenario
####
date.df <- data.frame('date' = date)
pop.check.all <- data.frame()
all.cases.all <- data.frame()
clinical.cases.all <- data.frame()
treated.cases.all <- data.frame()
death.all <- data.frame()
incidence.all <- data.frame()

# 1.4. running all scenarios
for(i in 1:length(scn)){
  # defining net and mda coverage for each parameter in each scenario
(scn)
  parms['net.coverage'] <- ncov[i]
  parms['mcov'] <- mcov[i]

  # running the output
  if(scn[i] == "scenario 3" | scn[i] == "scenario 1"){
    out <- ode(times=times, y=start,
func=behaviour_change.model,parms=parms)
```

```
  }
  else (out <- ode(times=times, y=start,
func=no_behaviour_change.model,parms=parms))


  # binding date data frame into output
  out <- cbind(out, date.df)


  # mutate the output
  out.df <-as_tibble(as.data.frame(out)) %>%
    mutate(P =
Sf+Ef+Af+Cf+Ctf+Sev+Tf+H+Rf+Rpf+Sfm+Tfm+Rfm+Hm+Sfh+Rfh+Efh+Afh+Cfh+Ctfh+Se
vh,
           P_total = P + Death,
           C_total = Cf + Ctf + Cfh + Ctfh + Sev,
           T_total = Tf + Tfm + H + Hm,
           Deathf = c(0, diff(Death)),
           MDA = c(0, diff(CMDA)),
           Snap = c(0, diff(CSnap)),
           Hosp = c(0, diff(Chosp)),
           Test = c(0, diff(Ctest)),
           Incf = c(0, diff(Cinc)),
           Trtf = c(0, diff(Ctrt))) %>%
    pivot_longer(names_to = "variable", cols = !c(1,32))%>%
    mutate(model = "clinical",
           Scenario = scn[i])


  # population check preparation
  pop.check <- out.df %>%
    filter(variable %in% c("P_total"), time > 0)


  pop.check.all <- rbind(pop.check.all, pop.check)


  # all cases plot
  all.cases <- out.df  %>%
    filter(variable %in% c("Cf", "Ctf", "Sev", "Af")) %>%
    group_by(variable) %>%
    filter(time > 360*4)
```

```
  all.cases.all <- rbind(all.cases.all, all.cases)

  # clinical cases
  clinical.cases <- out.df %>%
    filter(variable %in% c("Cf", "Ctf", "Sev", "C_total")) %>%
    group_by(variable) %>%
    filter(time > 360*4)

  clinical.cases.all <- rbind(clinical.cases.all, clinical.cases)

  # treated cases
  treated.cases <- out.df  %>%
    filter(variable %in% c("Tf", "H", "T_total")) %>%
    group_by(variable) %>%
    filter(time > 360*4)

  treated.cases.all <- rbind(treated.cases.all, treated.cases)

  # deaths
  death <- out.df  %>%
    filter(variable %in% c("Deathf")) %>%
    group_by(variable) %>%
    filter(time > 360*4)

  death.all <- rbind(death.all, death)

  # incidence
  incidence <- out.df %>%
    filter(variable %in% c("Incf")) %>%
    filter(time > 360*4)

  incidence.all <- rbind(incidence.all, incidence)
}

## 2. Disease Dynamics plot ####
# 2.1. population check ####
ggplot(pop.check.all) +
```

```
  aes(x = date, y = value) +
  geom_line(colour = "#112446") +
  labs(x = "year", y = "population", title = "Population check") +
  theme_minimal() +
  facet_wrap(vars(Scenario))

# 2.2. all cases ####
ggplot(all.cases.all) +
  aes(x = date, y = value, colour = variable) +
  geom_line() +
  scale_color_hue(direction = 1) +
  labs(x = "year", y = "population", title = "All Cases") +
  theme_minimal() +
  facet_wrap(vars(Scenario), scales = "free")

# 2.3. clinical cases ####
ggplot(clinical.cases.all) +
  aes(x = date, y = value, colour = variable) +
  geom_line() +
  scale_color_hue(direction = 1) +
  labs(x = "year", y = "population", title = "Clinical Cases") +
  theme_minimal() +
  facet_wrap(vars(Scenario), scales = "free")

# 2.4. treated cases ####
ggplot(treated.cases.all) +
  aes(x = date, y = value, colour = variable) +
  geom_line() +
  scale_color_hue(direction = 1) +
  labs(x = "year", y = "population", title = "Treated Cases") +
  theme_minimal() +
  facet_wrap(vars(Scenario), scales = "free")

# 2.5. Incidence ####
# 2.5.1. All monthly incidence ####
ggplot(incidence.all) +
  aes(x = date, y = value, colour = variable) +
```

```
  geom_line() +
  scale_color_hue(direction = 1) +
  labs(x = "year", y = "population", title = "Incidence") +
  theme_minimal() +
  facet_wrap(vars(Scenario), scales = "free")


# 2.5.2. Baseline and reverse monthly incidence ####
baseline.intervention_plot <- incidence.all %>%
  filter(Scenario %in% c("baseline", "reverse 1","reverse 2")) %>%
  ggplot() +
  aes(x = date, y = value, colour = Scenario) +
  geom_line() +
  scale_color_manual(
    values = c(baseline = "#2A778E",
               `reverse 1` = "#404385",
               `reverse 2` = "#440154")
  ) +
  theme_minimal() +
  labs(title = "Monthly Falciparum Malaria Incidence: Reverse Scenarios vs
Baseline", x = "date", y =("population"))


baseline.intervention_plot


# 2.5.3. Baseline and intervention monthly incidence ####
baseline.reverse_plot <- incidence.all %>%
  filter(Scenario %in% c("baseline", "scenario 1", "scenario 2", "scenario
3")) %>%
  ggplot() +
  aes(x = date, y = value, colour = Scenario) +
  geom_line() +
  scale_color_manual(
    values = c(baseline = "#2A778E",
               `scenario 1` = "#27A882",
               `scenario 2` = "#7BD04F",
               `scenario 3` = "#FF9800")
  ) +
  theme_minimal() +
```

```
  labs(title = "Monthly Falciparum Malaria Incidence: Intervention
Scenarios vs Baseline", x = "date", y =("population"))


baseline.reverse_plot


# 2.5.4. combine plot ####
grid.arrange(baseline.intervention_plot, baseline.reverse_plot)


# 2.6. deaths ####
ggplot(death.all) +
  aes(x = date, y = value, colour = variable) +
  geom_line() +
  scale_color_hue(direction = 1) +
  labs(x = "year", y = "population", title = "Deaths") +
  theme_minimal() +
  facet_wrap(vars(Scenario), scales = "free")


## 3. Contour Plot for Model fitting ####
# 3.1. contour plot ####
par(mfrow = c(1,2))
contour(NLL.grid, nlevels = 250,x = S0.grid, y = ppn.grid,
        xlab = "Initial susceptible individuals", ylab = "Person per net",
        main = "Contour Plot: Grid Search for Maximum Likelihood")
points(x = best.fit.S0, y = best.fit.ppn, pch= 20, col = "red", cex = 2)
points(x = S0.fit, y = ppn.fit, pch= 20, col = "green", cex = 2)


# 3.2. heat plot ####
image(S0.grid, ppn.grid, -log(NLL.grid), col = heat.colors(10000),
      xlab="Initial susceptible individuals",ylab="Person per net",
      main = "Heat Map: Grid Search for Maximum Likelihood")
points(x = best.fit.S0, y = best.fit.ppn, pch= 20, col = "red", cex = 2)
points(x = S0.fit, y = ppn.fit, pch= 20, col = "green", cex = 2)


# 3.3. daily incidence and data ####
plot_incidence.fit


## 4. Economic Sensitivity Analyses ####
# 4.1 No Behaviour Change ####
```

```
par(mfrow = c(2,3))

image(netcoverage.grid, mdacoverage.grid, nbc.nhb, col = hcl.colors(4,
palette = "YlOrRd"),

      xlab="Net Coverage",ylab="MDA Coverage", main = "Net Health Benefit:
No Behaviour Change")


image(netcoverage.grid, mdacoverage.grid, -nbc.cost, col = hcl.colors(2,
palette = "greens"),

      xlab="Net Coverage",ylab="MDA Coverage", main = "Cost: No Behaviour
Change")


image(netcoverage.grid, mdacoverage.grid, -nbc.nhb.cost.accepted, col =
hcl.colors(10, palette = "blues"),

      xlab="Net Coverage",ylab="MDA Coverage", main = "NHB and Cost: No
Behaviour Change")


# 4.2. With Behaviour Change ####

image(netcoverage.grid, mdacoverage.grid, bc.nhb, col = hcl.colors(4,
palette = "YlOrRd"),

      xlab="Net Coverage",ylab="MDA Coverage", main = "Net Health Benefit:
With Behaviour Change")


image(netcoverage.grid, mdacoverage.grid, -bc.cost, col = hcl.colors(2,
palette = "greens"),

      xlab="Net Coverage",ylab="MDA Coverage", main = "Cost: With
Behaviour Change")


image(netcoverage.grid, mdacoverage.grid, -bc.nhb.cost.accepted, col =
hcl.colors(10, palette = "blues"),

      xlab="Net Coverage",ylab="MDA Coverage", main = "NHB and Cost: With
Behaviour Change")


Sys.time() - start.time

##########################################################################
######

# END
##########################################################################
```