Exploring Economic Health Valuations for Malaria

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To ensure the completeness of this report and its compatibility with health economic reporting standards, we follow the CHEERS checklist. This is appended to the end of the report. Clicking on a number in the ***where*** column brings you to the appropriate part of the document.

I Modelling Health Economic Evaluation for Malaria

This report covers the cost-effective control for a malaria outbreak in the country X with a population of $100,000$ people. Currently, country X's GDP per capita is \$500 and has no malaria interventions. We understand little about the country's exact demographics; however, given the GDP per capita, we can assume the members of the population are of lower incomes when compared with the global population. And given we are modelling malaria, we assume we are in a tropical or subtropical area of the world. We take the model dynamics for our outbreak to be the following. Note the dynamics for humans (left) have subscript h and mosquitoes (right) have subscript v:

$$\frac{dS_h}{dt} = B_h - ap\frac{S_h I_v}{N_h} + \omega R_h - \mu_h S_h \qquad \frac{dS_v}{dt} = B_v - ap\frac{S_v I_h}{N_h} - \mu_v S_v$$
$$\frac{dI_h}{dt} = ap\frac{S_h I_v}{N_h} - (\gamma + \mu_h) I_h \qquad \frac{dE_v}{dt} = ap\frac{S_v I_h}{N_h} - (\sigma + \mu_v) E_v$$
$$\frac{dR_h}{dt} = (1-\delta)\gamma I_h - (\omega + \mu_h) R_h \qquad \frac{dI_v}{dt} = \sigma E_v - \mu_v I_v$$

where $B_h = \mu_h N_h + \gamma\delta I_h$, and $B_v = \mu_v K\left(1 + 0.5\cos\left(\frac{2\pi t}{365}\right)\right)$. The explanation for the model parameters is shown in Table 1 below.

Parameter	Description	Value
B_h	Total birth rate of humans	See equation
μ_h	Per capita natural mortality of humans	$\frac{1}{(50\times365)}$ days^{-1}
p_h	Probability of a person becoming infected per infectious bite of a mosquito	0.5
a	Biting rate of mosquitoes on humans	Fitted days^{-1}
ω	Waning immunity rate (R to S)	$\frac{1}{365}$ days^{-1}
γ	Inverse of time spent infected	Fitted days^{-1}
δ	Probability of a person dying following infection	0.05
B_v	Total emergence rate of adult female mosquitoes	See equation
μ_v	Mortality rate of mosquitoes	$\frac{1}{14}$ days^{-1}
p_v	Probability of a mosquito becoming infected per bite on an infectious human	0.1
σ	Inverse of the extrinsic incubation period (incubation period in mosquitoes)	$\frac{1}{7}$ days^{-1}
K	Uncontrolled carrying capacity of (female) mosquitoes	Fitted

Table 1: Model Parameters

Furthermore, we take the perspective of the direct cost to the government of country X, taking into account a higher level perspective, considering the effects on the country as a whole rather than a more localised social perspective. Whilst we consider the country as a whole, this does mean no details on different sub-demographics and subgroups are considered. To take these considerations into account, one could model the human population separately, such as in rural or urban areas. Despite these limitations, we aim to give the policymaker a recommendation on intervention strategies to use for X.

Our time horizon is modelled to be 10 years with a discounting rate of 3%. These are suitable since they allow us to model the long-term effects of the outbreak whilst taking into account the priority now rather than later. Note that the parameters given as fitted are taken from a .csv file to introduce uncertainty and variability into our model. First, we assume that no interventions are in place, however we are researching various considered interventions including a drug which speeds up recovery by 10% and reduces probability of death by 10%, and also indoor residual spraying (IRS), which increases the mortality rate of mosquito's by 1.6 times. The costs for each intervention are outlined in Table 2 below:

Intervention	**Unit cost ($)**	**Unit**
Drug	$X \sim \Gamma(6, 0.5)$	per person treated
IRS	$X \sim \Gamma(16, 0.5)$	annually per person in the population

Table 2: Cost of Interventions.

Finally, the disability weighting for the time infected 0.2 and the discounted years of life lost for death is 25. We perform a cost-effectiveness analysis comparing various strategies, which are implementing no interventions to using the Drug, using IRS, and using them in conjunction. **NB** For the following report, we will use the following acronyms. Daily Adjusted Life Years (DALYs), Incremental Cost Effectiveness Ratio (ICER), Cost Effectiveness (CE), Cost-Effectiveness Acceptability Curves (CEACs) and Cost-Effectiveness Acceptability Frontier (CEAF).

As our outcome to measure the benefits/harms of each strategy, we will be predominantly considering deaths due to malaria in country X. To quantify these effectively, we focus on DALYs as a measure for these outcomes. DALYs are defined as:

$$\text{DALYS}(i) = \text{Disability Weighting} \times \text{Person Years}(i) + \text{Discounted YLL} \times \text{Deaths}(i)$$

For our model, since we are using R, to calculate the integrals for Deaths(i), and Person Years(i), we use the *trapz* function.

To model this system, we use the *deSolve* package in R and a deterministic ODE method modelling two compartments as shown in equation (1), which we have defined ourselves. While this model is not publicly accessible, it is defined in the accompanying R document. Our rationale for using this model is that we can efficiently and quickly model many simulations. Additionally, given the model dynamics of two intertwined populations, using ODE methods significantly reduces the computation required. Furthermore, to account for the unpredictable nature of diseases, we use values for a, K and γ fitted to

real-life data from outbreaks. In our case, we use $1,000$ different instances and run our simulations on this.

Compartmental Diagram: The compartmental diagram for the model is shown below:

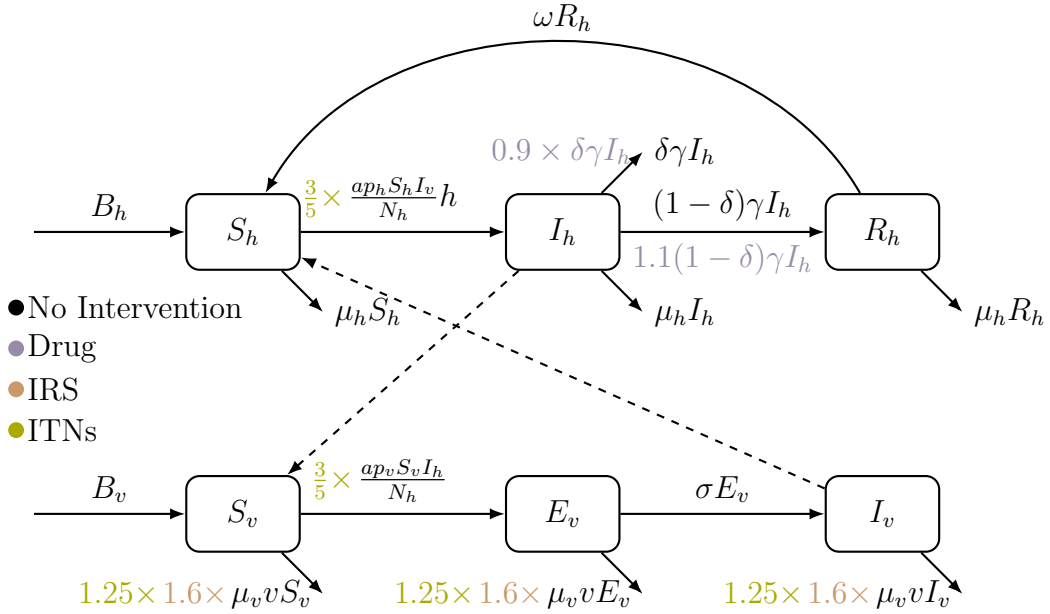

Figure 1: Compartmental Diagram for Equation (1)

Infection Dynamics: The infection dynamics (for humans) for each strategy are shown in Figure 2 below. Note that these dynamics are plotted with $1,000$ iterations of varying initial parameters, and this model dynamics plot shows the 95% confidence intervals for those dynamics:

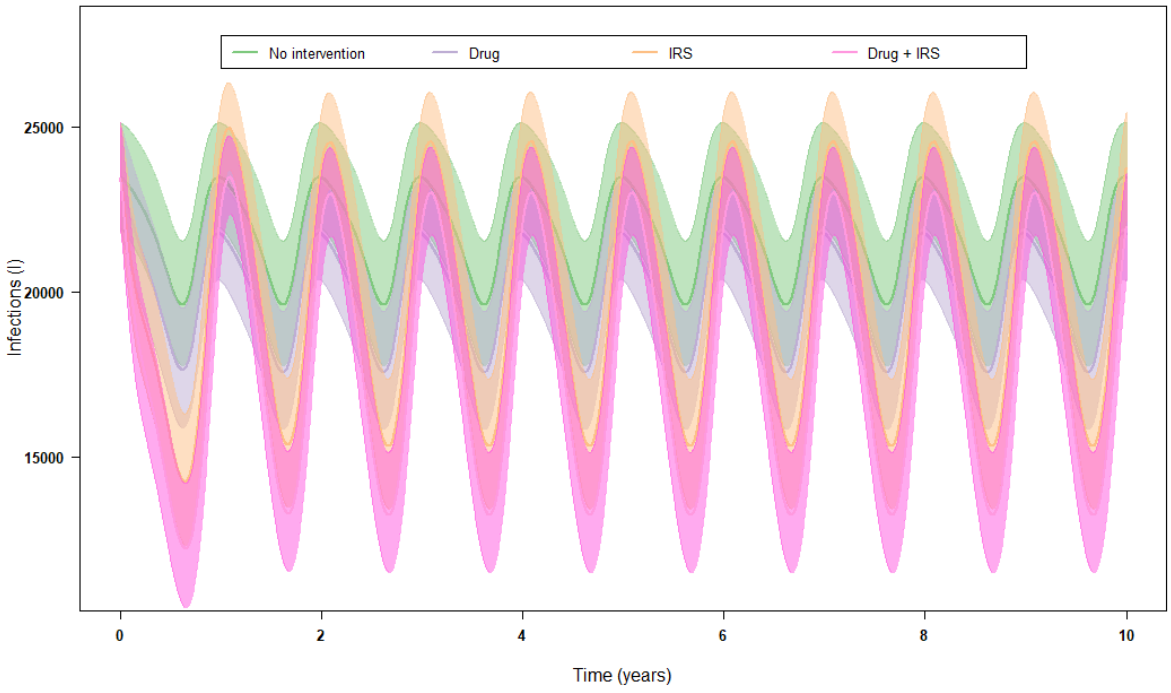

Figure 2: $I(t)$ Infection Dynamics - For Each Strategy

Undiscounted Mead DALYs and CPYs: Figure 3 shows the plot for the DALYs averted and the additional costs in Thousands.

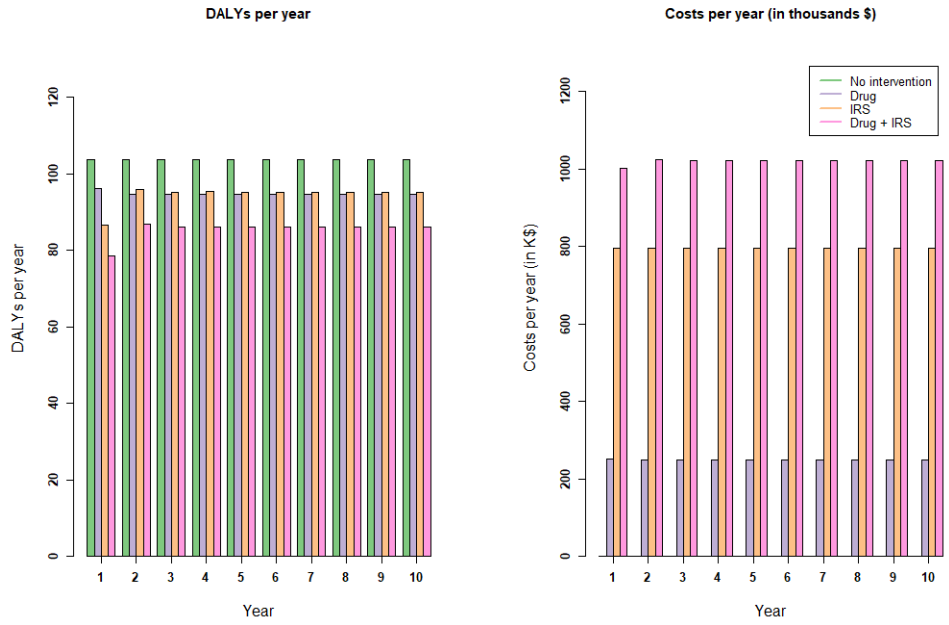

Figure 3: Undiscounted Mead DALYs and CPYs

Reporting Discounted Mean ΔCosts, Mean ΔDALYs, and corresponding ICERs: Table 3 shows the metrics for each of the Interventions.

Intervention	Mean ΔCosts	Interval	ΔDALYs	Interval	ICERs
No Intervention	0	0	0	0	Referent
Drug	2,815	[764.2, 4,334]	77,790	[74,600, 81,000]	28.87
IRS	6,987	[4,015, 10,840]	81,820	[73,120, 91,440]	W. Dom
Drug & IRS	8,956	[5,635, 13,120]	160,500	[148,600, 173,200]	81.90

Table 3: Model Parameters

CE - Plane: Figure 4 below shows the CE plane for the three different interventions. Whilst there is significant variability across the different simulations, it is clear that purely using IRS is far behind this plane. Figure 5 shows the **CEACs and CEAF**s for the four strategies, as an overview as well as scaled to view probabilities in greater detail.

Our Recommendations: We split our recommendations into three categories, giving the policymakers a range of possibilities according to their budget and preferences. These recommendations are shown in Table 4, from Figure 4, it is clear that IRS alone is far behind the CE plane, and Table 3 shows the weak domination of using IRS alone. Moreover, Figure 5, and Table 3 show that at $81.90, the Drug + IRS strategy becomes the most cost-effective.

There are some assumptions we are taking when considering the costs of the methods. For example, when spraying using IRS, we take the population at the start of the year. The rationale for this is that throughout the year, any new births will live in the same household as their parents - meaning they, in theory, don't need that applied, and also,

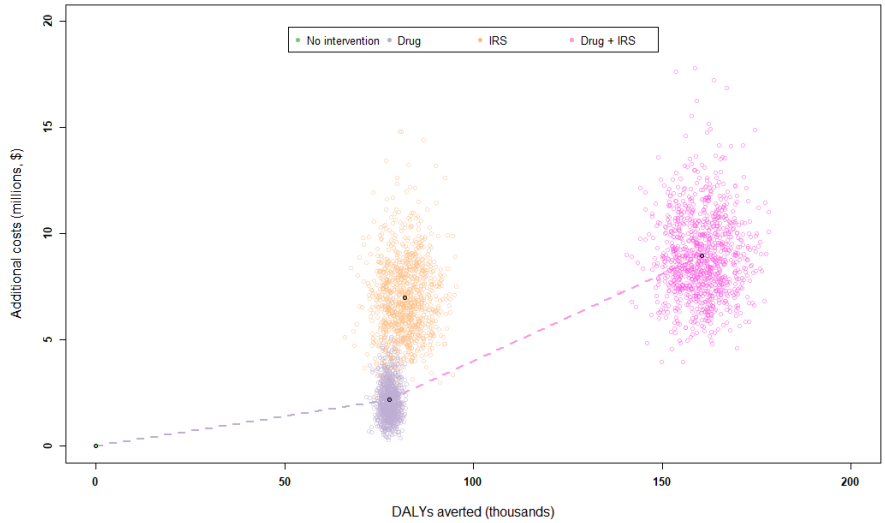

Figure 4: Cost Effectiveness Plane

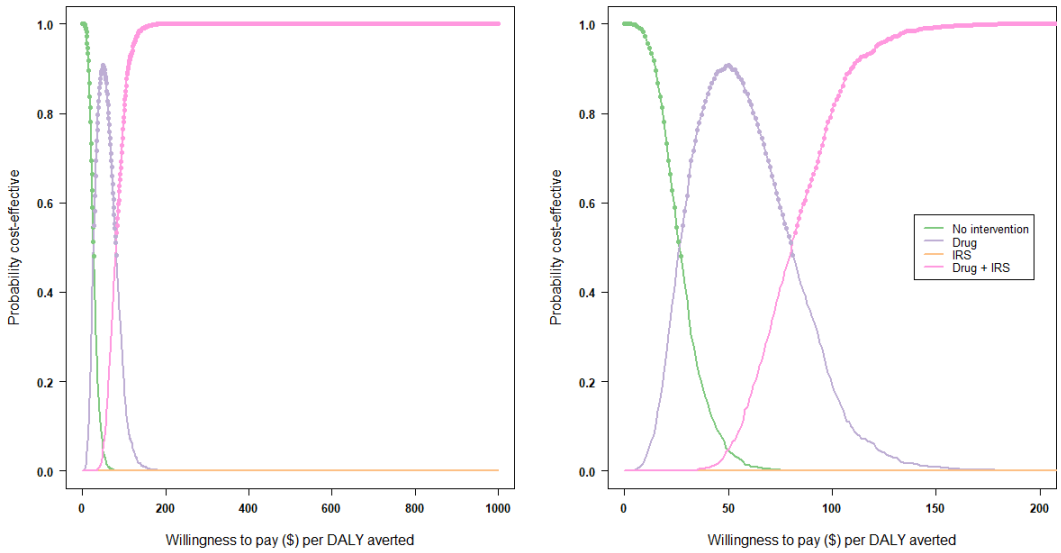

Figure 5: CEACs and CEAF for the 4 Strategies Using 1,000 Iterations

WTP Range	**Recommendation**
Less than 29	No Intervention
Between 29 and 82	Drug Only
More than 82	Drug and IRS

Table 4: Recommendation Table

anyone who dies in the year will already have had the treatment. Whilst these impacts may be minimal, the policymaker should consider them.

One fundamental limitation of our model is that it does not necessarily consider the general population's availability to purchase the intervention methods. Given the GDP

per capita of X, depending on the source of funding - governmental or from the member of the public. There may be a lack of ability to purchase the interventions. This means different subgroups will have different reproductivity rates of mosquitoes, for example, impacting the model's overall accuracy. The policymaker should consider this when considering the findings presented.

II Implementing Additional Measures

Introducing Mosquito Nets: As specified by the WHO, insecticide-treated nets (ITNs) are a key intervention in preventing the spread of malaria. They are a simple yet effective intervention, which is also very accessible. Additionally, since they are inert - not a medical drug or a chemical, they will not go off or require specific conditions for transport or storage. Furthermore, as defined by the WHO, they have an average lifespan of three years (between 18 months and seven years). Therefore, the comparatively low cost per person means these nets could be an excellent option. Regarding updates to our model parameters, we adjust a to $a \times 3/5$ since we assume that people will spend 8 hours a day in the nets to sleep and at dusk and dawn - where mosquitoes are more prevalent. Finally, we increase μ_v to $1.25\mu_v$ since the insecticide on the mosquito nets may increase their death rate. The compartmental diagram in Figure 1 shows the updated model parameters for this intervention.

Intervention Cost: According to Scates. Et. Al,ITNs typically have a financial cost of $\$8 - \$20$, and therefore price these with $X \sim Gamma(40, 0.25)$ where the second parameter is Scale. Additionally, they typically have a lifespan of around $2 - 3$ years; therefore, we assume every second year, every member of the population buys a mosquito net. With this additional intervention method, we add the intervention strategy of purely using mosquito nets, and using a combination of Drug + IRS + ITNs. Whilst this measure is more expensive, the compounding effects of multiple measures may have a much higher impact.

Updating our CEA Results: With these updated strategies, we re-ran our model for the $1,000$ iterations, which gave us exceeding insight into the effectiveness of the new strategies implemented. Table 5 shows how our combined strategy dominates all other strategies, with an ICER which is lower than that of purely using strategy one coming in at \$21.67, which is far lower than \$28.87.

Intervention	Mean ΔCosts	Interval	ΔDALYs	Interval	ICERs
No Intervention	0	0	0	0	Referent
Drug	2,815	[764.2, 4,334]	77,790	[74,600, 81,000]	Dominated
ITNs	4,306	[3,107, 5,683]	134,400	[120,200, 150,000]	Dominated
IRS	6,987	[4,015, 10,840]	81,820	[73,120, 91,440]	Dominated
Drug & IRS	8,956	[5,635, 13,120]	160,500	[148,600, 173,200]	Dominated
Drug, IRS & ITNs	11,960	[8,614, 15,770]	552,000	[697,100, 612,600]	21.67

Table 5: Updated ICERs, Mean ΔDALYs, and Mean ΔCosts

However, there is one consideration for this strategy: it is, of course, more expensive than the other strategies. Considering that each person is required to buy a mosquito net every other year, members of the population with dependents will be required to expend a significantly more considerable amount than those without.

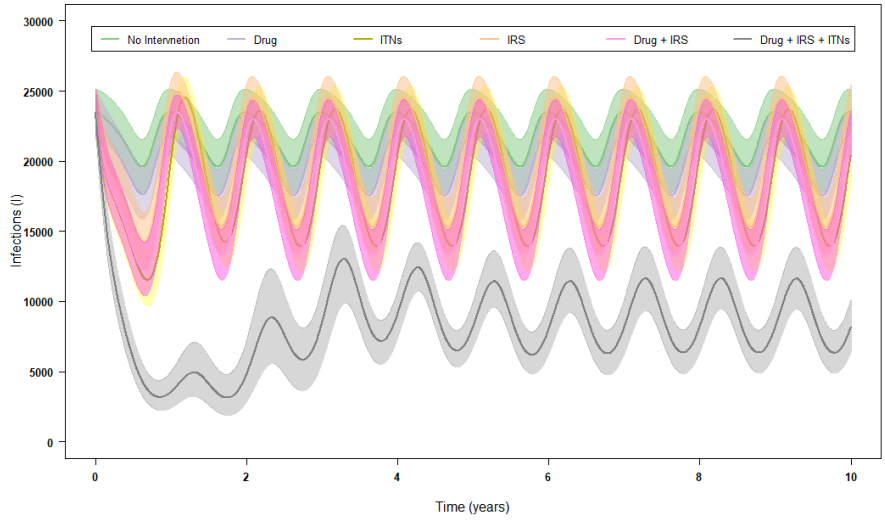

Figure 6: Complete Model Dynamics for All Interventions

Figure 6 shows the significantly decreased infections using the combined strategy, which additionally means that costs due to human life, reduction of a functioning workforce and strain on medical services will be significantly decreased.

By following the grey dashed line across the plot, we see that the CE plane cuts off all the strategies modelled, reinforcing the domination of that over the other strategies.

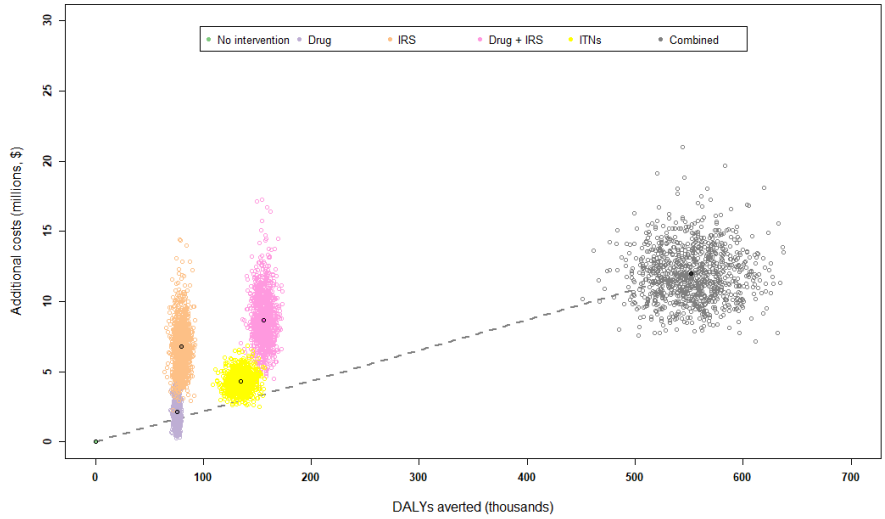

Figure 7: Updated Cost Effectiveness Plane for Updated Strategies

Concluding our Analysis and Updating our Recommendation: Whilst it is clear that a combination of the three strategies has an increased cost, it becomes apparent

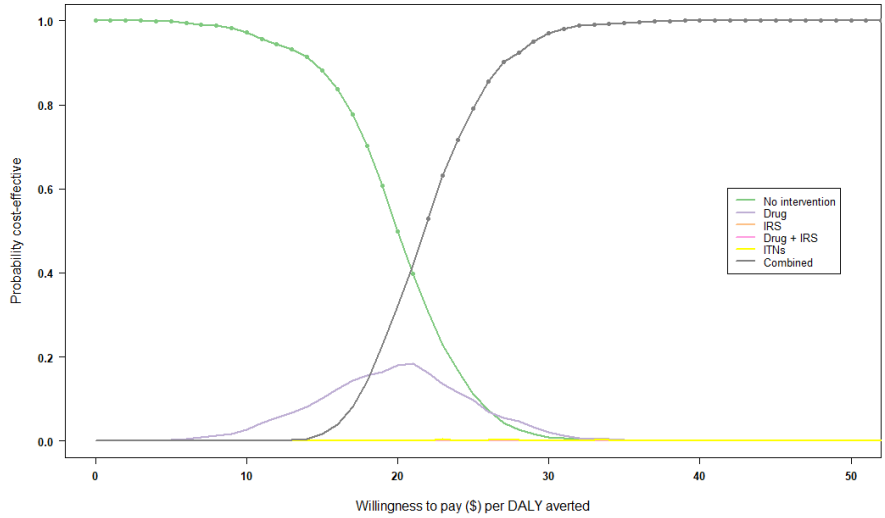

Figure 8: CEACs and CEAF for the 6 Strategies Using 1,000 Iterations

very quickly that this strategy dominates the other strategies very significantly. We see this most prominently with the DALYs averted; this far outweighs the other strategies used. Notably, we see from our compartmental diagram that when both IRS and ITNs are used, the death rates of mosquitoes increase significantly $1.25 \times 1.6 = 2$, showing the combined strategies compounded the death rates and amplified each other's effect. Moreover, the WHO states that IRS + ITNs combined are typically very effective strategies in conjunction with one another.

Below, we update our recommendations, shown in Table 6. These recommendations are based on the plots shown above, showing where the combined approach is likely to have a high probability of being cost-effective. However, though our model shows the combined strategy is strongly dominant, it should be noted that to examine this further, a wide number of parameter updates should be implemented for the ITNs to discover, at which point it results in such a strongly dominant combined strategy.

WTP Range	**Recommendation**
Less than $22	No Intervention
Greater than $22	Combined Strategy of IRS & ITNs & Drug

Table 6: Updated Recommendation Table

In conclusion, whilst the strategy we recommend is strongly dominant over the others, as well as outperforming them in many other metrics, if the economic cost is too high, then as stated earlier. Using an IRS + Drugs strategy was weakly dominant over just using the IRS; therefore, this could still be feasible. However, it does have a far lower probability of being cost-effective than other measures implemented. Furthermore, more research should be done using IRS + ITNs and ITNs + Drugs alone to give a more in-depth analysis of effectiveness.

Item	Guidance for Reporting	Where
1	Identify the study as an economic evaluation and specify the interventions being compared.	1
2	Provide a structured summary that highlights context, key methods, results, and alternative analyses.	NA
3	Give the context for the study, the study question, and its practical relevance for decision-making in policy or practice.	3
4	Indicate whether a health economic analysis plan was developed and where available.	NA
5	Describe characteristics of the study population (age range, demographics, socioeconomic or clinical characteristics).	5
6	Provide relevant contextual information that may influence findings.	6
7	Describe the interventions or strategies being compared and why chosen.	7
8	State the perspective(s) adopted by the study and why chosen.	8
9	State the time horizon for the study and why appropriate.	9
10	Report the discount rate(s) and reason chosen.	10
11	Describe what outcomes were used as the measure(s) of benefit(s) and harm(s).	11
12	Describe how outcomes used to capture benefit(s) and harm(s) were measured.	12
13	Describe the population and methods used to measure and value outcomes.	13
14	Describe how costs were valued.	14
15	Report the dates of the estimated resource quantities and unit costs plus the currency and year of conversion.	15
16	If modelling is used, describe in detail and why used. Report if the model is publicly available and where it can be accessed.	16
17	Describe any methods for analysing or statistically transforming data, any extrapolation methods, and approaches for validating any model used.	17
18	Describe any methods used for estimating how the results of the study vary for sub-groups.	18
19	Describe how impacts are distributed across different individuals or adjustments made to reflect priority populations.	19
20	Describe methods to characterize any sources of uncertainty in the analysis.	20
21	Describe any approaches to engage patients or service recipients, the general public, communities, or stakeholders in the design of the study.	NA
22	Report all analytic inputs (e.g., values, ranges, references) including uncertainty or distributional assumptions.	22
23	Report the mean values for the main categories of costs and outcomes of interest and summarize them in the most appropriate overall measure.	23
24	Describe how uncertainty about analytic judgments, inputs, or projections affect findings. Report the effect of choice of discount rate and time horizon if applicable.	24
25	Report on any difference patient/service recipient, general public, community, or stakeholder involvement made to the approach or findings of the study.	NA
26	Report key findings, limitations, ethical or equity considerations not captured and how these could impact patients, policy, or practice.	26
27	Describe how the study was funded and any role of the funder in the identification, design, conduct, and reporting of the analysis.	NA
28	Report authors' conflicts of interest according to journal or International Committee of Medical Journal Editors requirements.	NA

Table 7: CHEERS Checklist