MA4M1 Epidemiology By Example Assessed Worksheet 4

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Introduction

In this report we provide a health economic analysis to control soil transmitted helminths (STH). The model used is a deterministic ODE that describes the evolution of mean worm burden in children and adults, M_c and M_a respectively, and the infectious source l.

$$\begin{aligned}
\dot{M}_c &= \beta_c l - \sigma M_c \\
\dot{M}_a &= \beta_a l - \sigma M_a \\
\dot{l} &= \frac{R_0 \sigma \mu}{\beta_c \rho n_c + \beta_a (1-\rho) n_a} \times \\
&\quad [\varphi(M_c) f(M_c; k, z) n_c \rho + \varphi(M_a) f(M_a; k, z) n_a (1-\rho)] - \mu l
\end{aligned}$$

With

$$f(M;k,z) = \frac{M}{(1 + M(1-z)/k)^{k+1}} \qquad \varphi(M) = 1 - \left(\frac{1 + M(1-z)/k}{1 + M(2-z)/k}\right)^{k+1}$$

Where a full description of parameters is given in TABLE. In addition to splitting the population into children and adults, we also have three classes of infection. The equations above describe mean worm burden which, along with shape parameter k, inform a negative binomial distribution for how many people have a specific number of worms:

$$\pi(x) = \text{NegativeBinomial}(x, M, k)$$

We define a high-intensity worm infection as for ≥ 30 worms and has disability weighting of 0.15. Medium for $15 - 29$ with disability weighting 0.01 and low intensity for $0 - 14$ with disability weighting 0.

In Country X, there is a population of 100,000. We have 4 strategies which we call $S1, S2, S3$ and $S4$ respectively with S1 being our comparator strategy of no intervention. For each strategy we assume the drug removes $h = 0.95$ or worms and is given to a proportion g people. We then assume that the drug instantly reduced M by this factor ($M \mapsto (1 - gh)M$). k is unchanged. In $S2$, we give the drug to children each year, and use $g = 0.85$. In S3 we give the drug to children twice a year using $g = 0.85^2$. In S4 each year we do S2 and also provide the drug to adults with their separate $g_a = 0.2$. Therefore in S4 each year:

$$M_c \mapsto (1 - 0.85 \times 0.95) M_c \qquad M_a \mapsto (1 - 0.2 \times 0.95) M_a$$

The cost of the drug for children is modelled by a $\Gamma(4.5, \frac{1}{3})$ distribution and for adults we use a $\Gamma(45, \frac{2}{30})$ distribution.

Infection Level	Children	Adults
Low	21,800	62,800
Medium	5,280	6,150
High	2,900	1,070

Table 1: Comparison of mean and standard deviation of each chain shows good agreement between chains.

Initial Conditions

To begin with, we ran the model for sufficient time to find endemic equilibrium of around $M_c = 11.5, M_a = 5.6$ and $l = 5.6$, which we start at before further evolving with a new parameter set to find the endemic equilibrium for that parameter set. Plugging the above values into our negative binomial distribution, we see the initial number of worms in a given person has the distribution of figure (1).

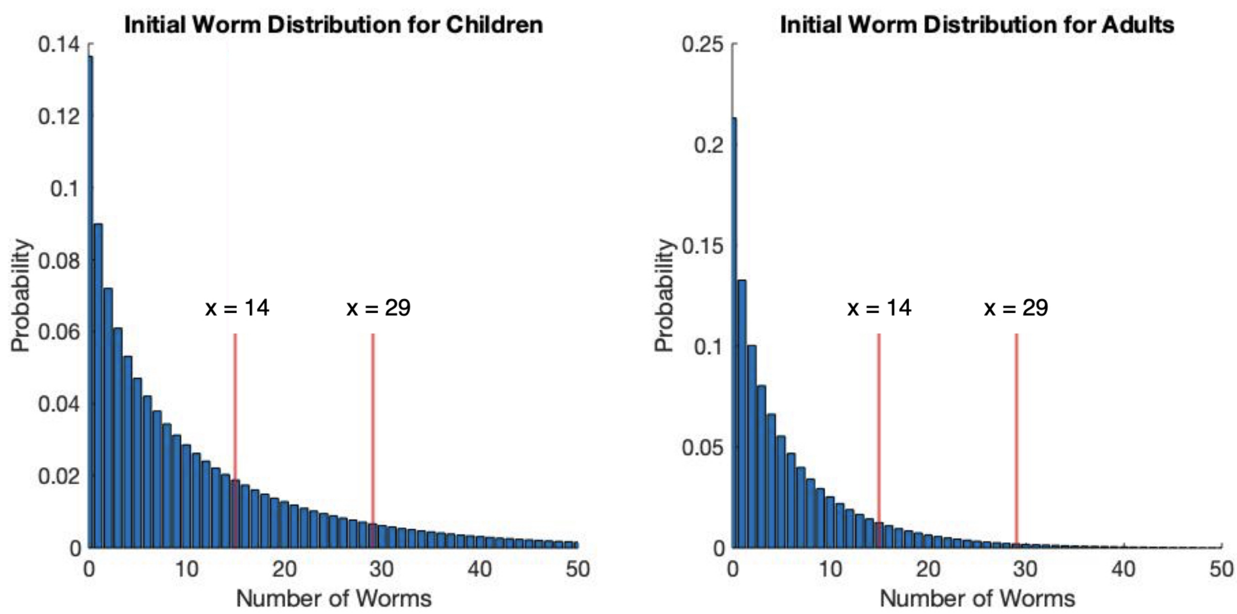

Figure 1: Initial distribution of number of worms a person carries. The cut off for each infection level is marked.

To calculate the number of children in the low section we compute $\alpha_a = \sum_{x=0}^{14} \pi(x)$ for a given M_c and then have $L_a = \alpha_a \times n_a \times N$. A similar method works for all other cases and we summarise results in table 1.

Infection Dynamics

In figure 2, see the plotted infection dynamics. The graph shows the endemic equilibrium before introducing a strategy at day zero. The dashed lines are adult numbers and full lines children numbers. In each case there is a typical saw tooth pattern where the drop

Strategy	Delta Costs	Delta DALYs	ICER
1	0	0	0
3	5.012+05	1759	285
4	1.233e+06	1923	4457

Table 2: ICER Table for each strategy. Strategy 2 was dominated and so was removed.

in mean burden causes a drop in infections, before climbing back towards endemic equilibrium and this correlates which how often a population is given the drug. Interestingly, the long term trend is not to decrease over time, but instead have yearly cycles which peak at around 3700 for medium infections, and 500 for highly infected. Hence none of these strategies lead to eradication.

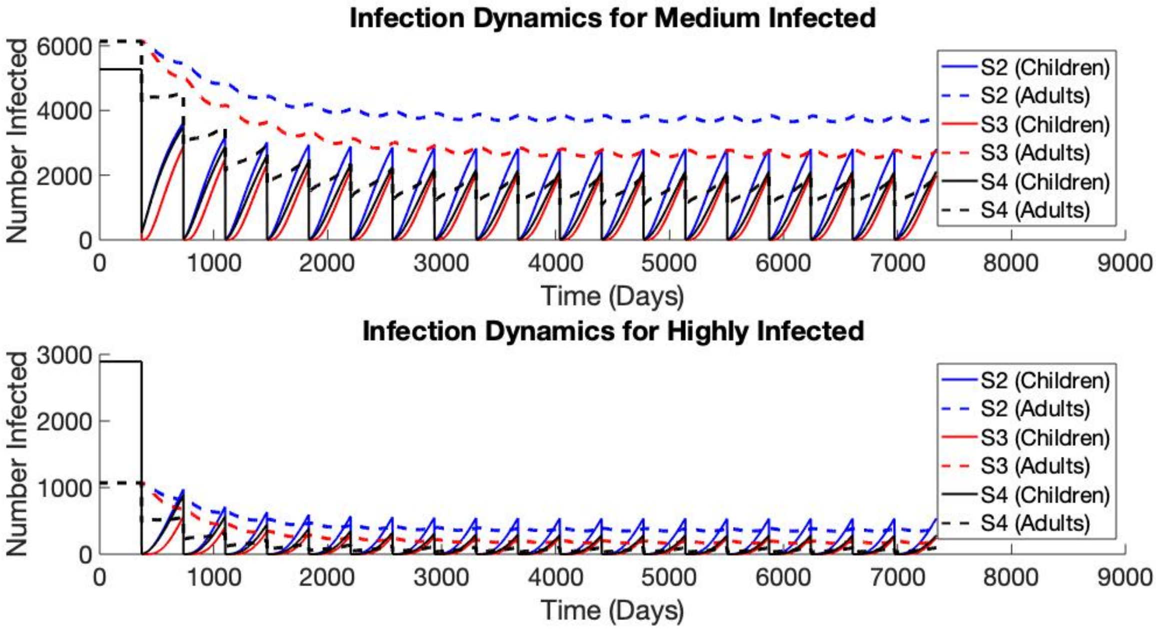

Figure 2: Infection dynamics for medium and highly infected. Each plot shows the dyanmics of each strategy for children and adults. In most cases we have sudden drops which then seek to return to endemic equilibrium

Cost Analysis

The DALYs lost and costs per year is shown in figure 3. Each strategy respectively decreases the number of DALYs lost but interestingly strategy 3 costs less than strategy 2 despite averting more DALYs. This is likely because in strategy 3, costs double, but the number of worms is reduced by a further factor of 0.85, so overall it is more cost effective for a biannual strategy. That said, the ideal strategy is S4, as this also targets the adult population, allowing a more global reduction of cases.

Based on the information in table 2, we see a country with a Willingness to Pay Threshold (WTP) of $400 would choose strategy 3. However, if WTP was $100, they would choose the comparator strategy, strategy 1 no intervention.

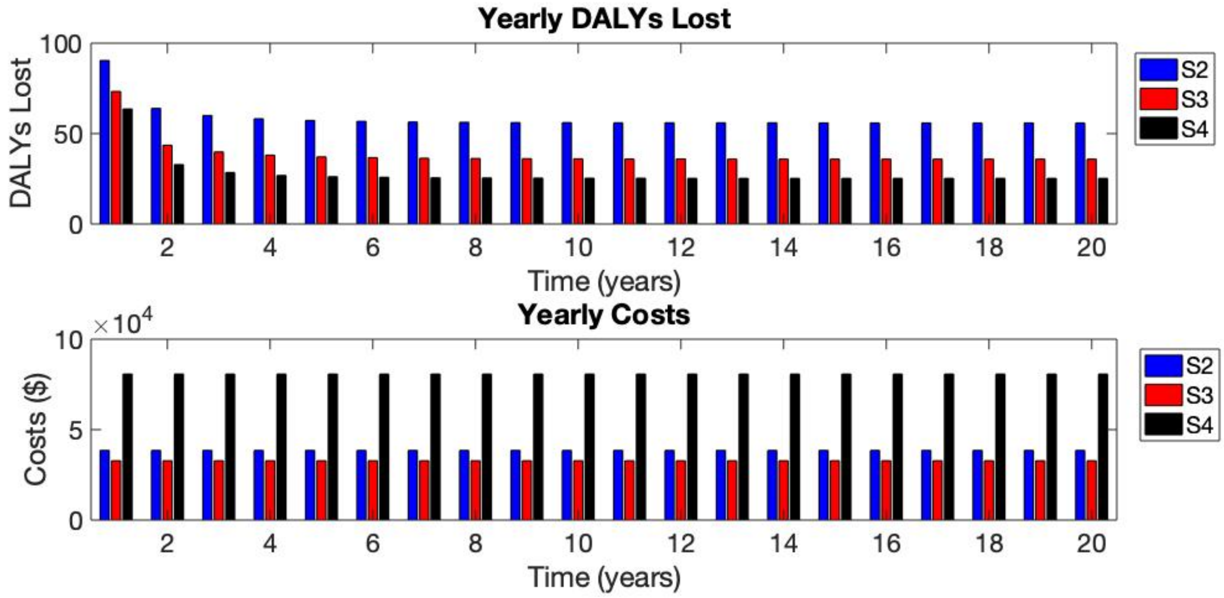

Figure 3: DALYs lost and costs each year for each strategy.

Plotting the CE plane in figure 4 we can see S4 is better than S3 which is better than S1. We have also marked on S2. We see it costs more and averts less DALYs.

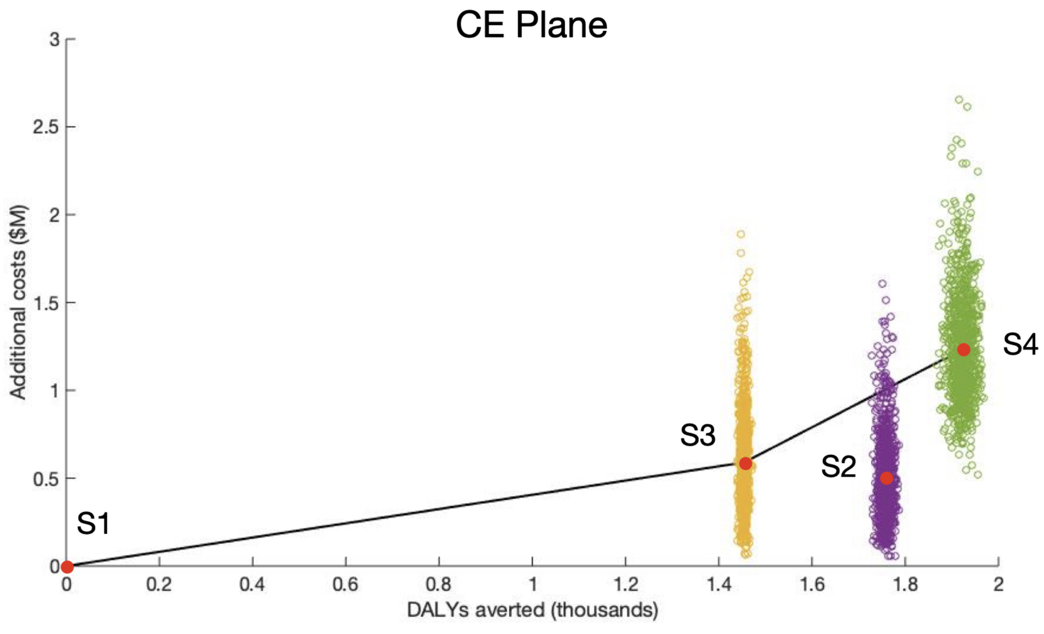

Figure 4: Change in DALYs averted against change in costs.

The Cost Effective Analysis Curves (CEACs) in figure 5 back up what we saw in the table. S1 is ideal until WTP crosses around $280 and then S3 dominates. S4 is far too expensive and it is only at the tail end of the plot that S4 becomes favourable to S1. This is due to the substantial added costs of treating adults, but the minimal benefit as not enough adults are treated to significantly reduce the disease dynamics.

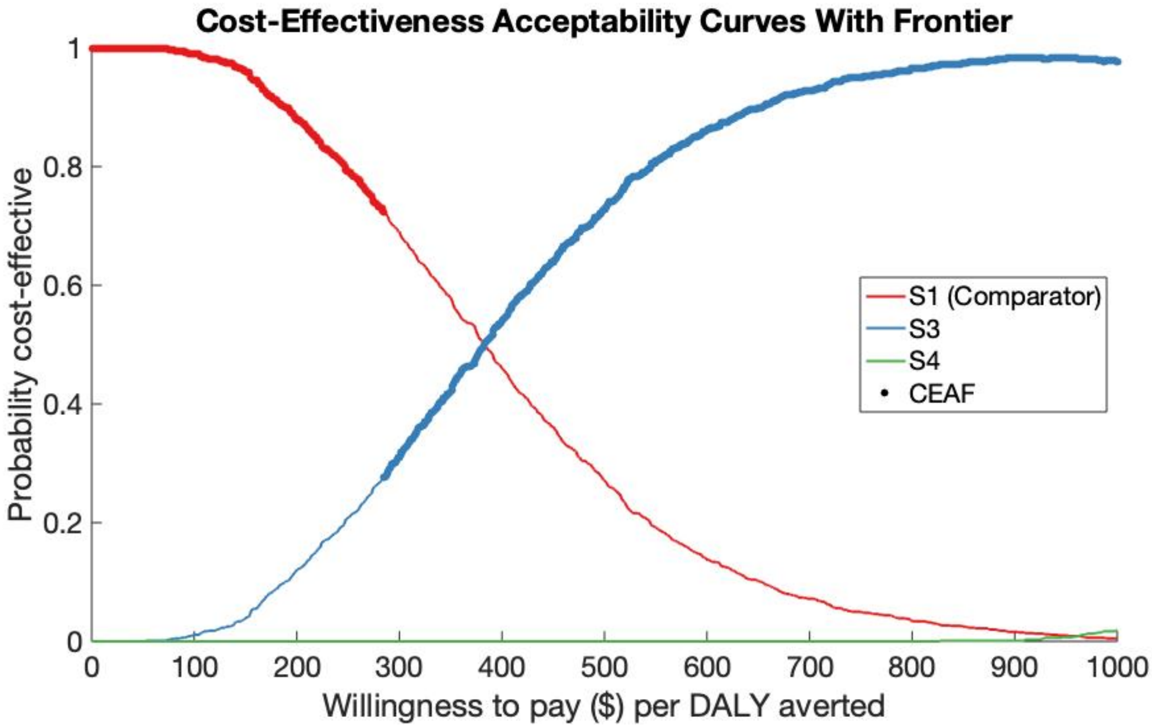

Figure 5: CEAC Curve for S1, S3 and S4. WTP against probability of cost-effectiveness.

Considering Extra Strategies.

As mentioned by WHO, a leading cause of infection is contaminated water and unclean food. Hence we may introduce interventions that seek to reduce β_c and β_a via cleaning. Define S5 to be a simple ad campaign encouraging people to clean their food. We model this as reducing β_c and β_a both to $\frac{3}{5}$ their original value. This policy is cheap with an average cost of \$0.5 [1], and Cost distribution modelled by Gamma$(4.5, \frac{1}{9})$.

Next we have a policy that is more financially intensive but more far reaching; cleaning all water in schools. Here, we have $\beta_c \mapsto \frac{1}{4}\beta_c$ as only children will be effected. As all the water is clean however, children will definitely drink clean water, compared to S5, where there is no enforcement of cleaning food. Water treatment is more expensive with an expectation of \$2 per person[2]. Hence we model cost distribution by a Gamma$(18, \frac{1}{9})$ distribution.

Plotting these new infection dynamics we have figure 6. We see by altering βs the endemic equilibrium isn't really changed. As endemic equilibrium is not reduced, and we are no longer removing worms via a drug, STHs persist in the population. Therefore, in figure 7 we see these strategies carry substantially more DALYs. Furthermore, these policies require a fixed amount of spending (we pay for everyone, not just those who have the disease). Therefore S6 in particular has a high cost, as each year we clean water for *all* students. That said, despite S5 not leading to a massive reduction in prevalence and also having fixed costs, as the costs are so cheap, S5 turns out to be the cheapest strategy.

However, computing ICERs, strategy 5 is weakly dominated. So table 3 appears much as before in table 2. As Strategy 6 is so expensive and averts so few DALYs it is also

[1] https://www.wordstream.com/blog/ws/2017/07/05/online-advertising-costs

[2] https://washmatters.wateraid.org/sites/g/files/jkxoof256/files/Water%20%20At%20What%20Cost%20%20The%20State%20of%20the%20Worlds%20Water%202016.pdf

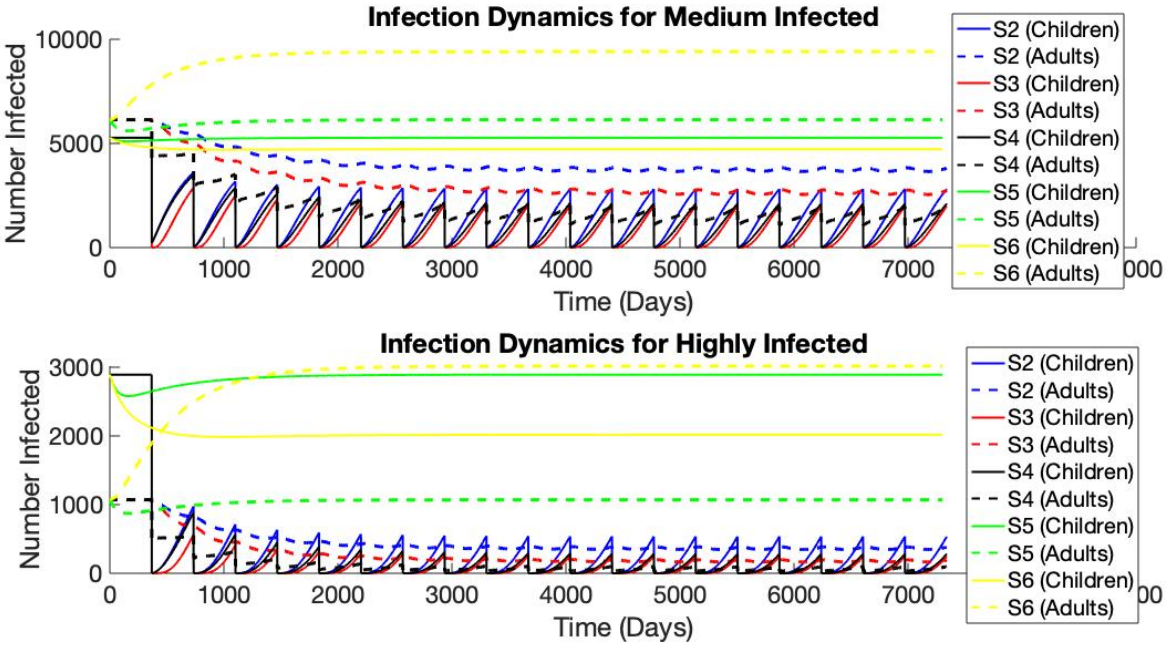

Figure 6: Infection Dynamics including strategies 5 and 6

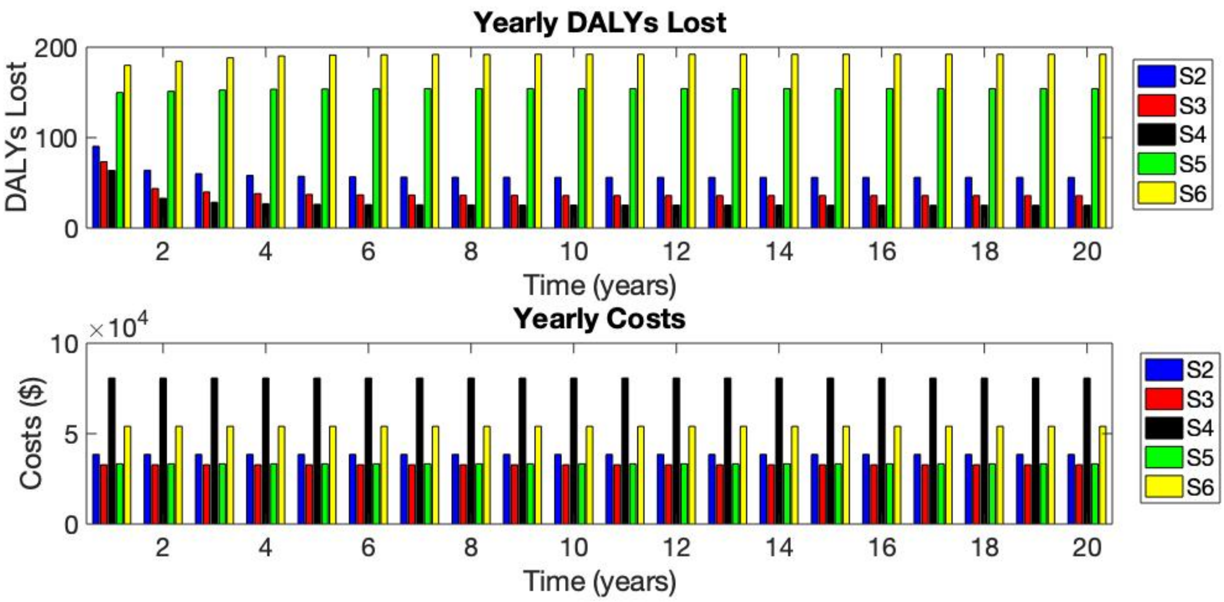

Figure 7: DALYs lost and costs each year for each strategy.

dominated. Hence we gain a similar table to that seen before.

Indeed, plotting on the CE plane in figure 8 we see a similar picture. The exception is which side of the ICER curve S2 lies changes. As S5 was the cheapest strategy, that changes some of the initial orderings and so the positions of strategies on the CE plane. However it is clear that S5 and S6, both being closer to S1 but costing more, are in effect very poor strategies.

The CEAC curves are also similar, again showing a cross over from no intervention to bi-annual drug administration about $280.Here we extend the range to $2000 to show

Strategy	Delta Costs	Delta DALYs	ICER
1	0	0	0
3	5.013e+05	1759	285
4	1.233e+06	1923	4457

Table 3: ICER Table for each strategy after removing those dominated or weakly dominated.

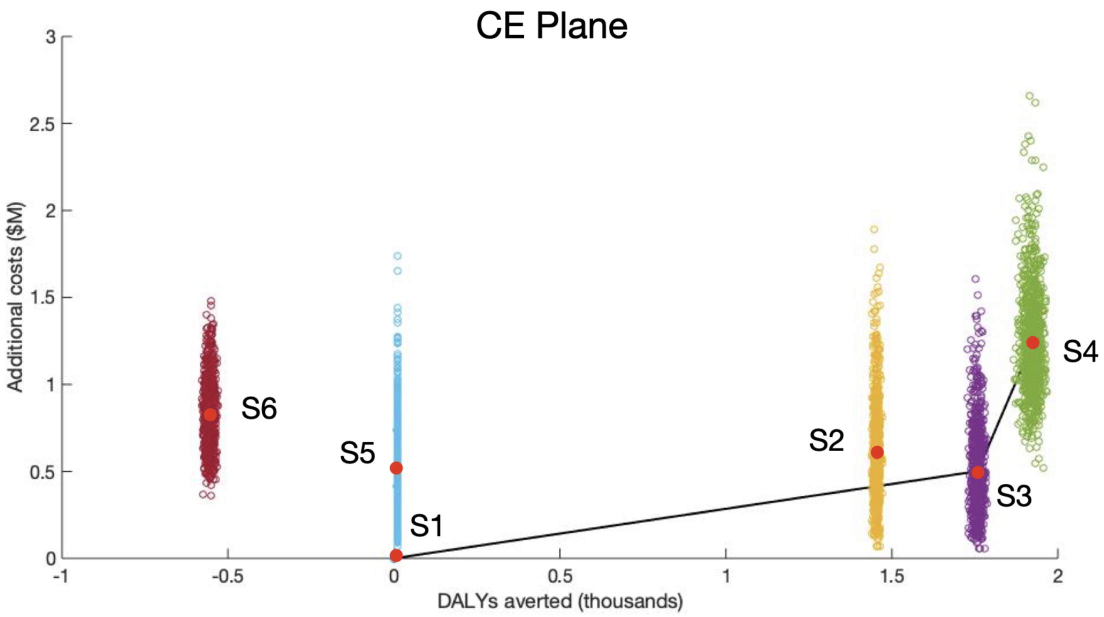

Figure 8: Change in DALYs averted against change in costs.

that eventually S4 does become viable, but only after extreme expenditure.

We have seen bi-annual administration to be the best strategy. It is fairly cheap and averts a large amount of DALYs. However, this is considering all infected individuals. If a government purely wanted to tackle a subset of infected cases, say those highly infected who may not be able to live with the disease, a similar result can be reached for cheaper, if annual instead of bi-annual drug administration is used. Equally, strategy depends on the type of helminth. The hookworm is mainly transmitted to people via skin contact, not eating or drinking. Hence, the reduction in β, and thus the viability of strategies S5 and S6 depend on type of helminth, not just cost-effectiveness.

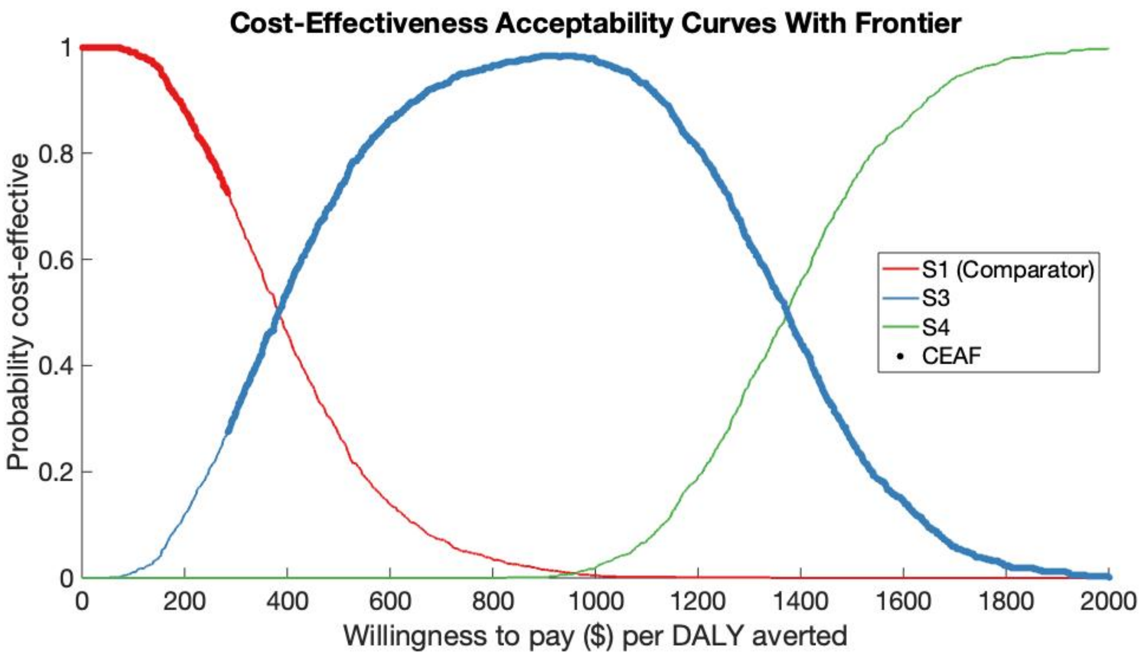

Figure 9: CEAC Curve for S1, S3 and S4. WTP against probability of cost-effectiveness.