Worksheet 4: Health economic evaluation

Due in noon Wednesday Week 9

This example sheet is for credit. Example sheets 7 and 8 can help you. Please make sure code is well commented and shows your working for these answers. Code must be uploaded alongside your pdf solutions.

20 marks will be awarded for presentation (including LaTeXed solutions and clarity of answers). Your write up (including figures) should be no more than 8 pages using size 12 font and 2.5cm margins. You do not have to copy out the questions asked, but the solutions must make sense as a stand alone document. 15 marks will be given for appropriate use of code with comments.

In this worksheet we will consider the cost-effective control of soil transmitted helminths (STH, intestinal worms), specifically for the species *Ascaris lumbricoides* (round worm). Before starting this worksheet please watch these videos:
`https://www.youtube.com/watch?v=xo0iGoe_r9Y`
and
`https://www.youtube.com/watch?v=LQYzhBSzQKs`
and read this webpage:
`https://www.who.int/news-room/fact-sheets/detail/soil-transmitted-helminth-infections`

The model

We will use a deterministic model to describe the transmission of STH between children and adults via an infectious source. The ODEs describe the mean worm burden in children (M_c) and adults (M_a) and the infectious source (l):

$$\text{Humans} \quad \begin{cases} \dfrac{\mathrm{d}M_c}{\mathrm{d}t} &= \beta_c l - \sigma M_c \\ \dfrac{\mathrm{d}M_a}{\mathrm{d}t} &= \beta_a l - \sigma M_a \end{cases}$$

$$\text{Infectious source} \quad \begin{cases} \dfrac{\mathrm{d}l}{\mathrm{d}t} &= \dfrac{R_0\sigma\mu}{(\beta_c\rho n_c + \beta_a(1-\rho)n_a)} \times \\ & \quad [\varphi(M_c)f(M_c;k,z)n_c\rho + \varphi(M_a)f(M_a;k,z)n_a(1-\rho)] \\ & \quad -\mu l \end{cases} \tag{1}$$

Worms are assumed to be distributed in people according to the negative binomial distribution – with means $M \in \{M_c, M_a\}$ and aggregation parameter k – so that the proportion

of people in one age class with exactly x worms is given by:

$$\pi(x) = \frac{\Gamma(k+x)}{x!\Gamma(k)} \left(\frac{M}{M+k}\right)^x \left(1+\frac{M}{k}\right)^{-k},$$

where $\Gamma(i)$ is the gamma function, taking value $\Gamma(i) = (i-1)!$ for integers. Egg production rate is also affected by this worm distribution in hosts with the function:

$$f(M;k,z) = \frac{M}{(1+M(1-z)/k)^{k+1}}$$

describing the mean egg production rate based on host worm distribution and a density-dependent egg production parameter, z.

Finally, in order for eggs to be fertile (sexual reproduction of the worms) there is a need for at least one male worm in the host, therefore the function

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

describes the fraction of total eggs from the host population that are fertilized, assuming density dependent effects: $\varphi(M)$ is almost 1 for large M, but for low mean worm burdens such as $M \leq 1$ the probability of eggs being fertilized, $\varphi(M)$, is much smaller.

A description of model parameters and their values in given in Table 1.

Parameter	Description	Value
β_c	Strength of infectious contact rate for children	2 days^{-1}
β_a	Strength of infectious contact rate for adults	1 days^{-1}
n_c	Proportion of the human population who are children	0.3
n_a	Proportion of the human population who are adults	$1-n_c$
σ	Inverse of average worm lifespan	1 year^{-1}
ρ	Relative contribution of children to infectious source	$\frac{2}{3}$
μ	Inverse of average egg survival time	5 years^{-1}
k	Aggregation parameter	Fitted
z	Density-dependence parameter for egg production	0.93
R_0	Basic reproduction number	Fitted

Table 1: Model parameters. Fitted posterior parameters R_0 and k can be found in the `Posterior.mat` file in Moodle

The disability weighting during a "high-intensity" worm infection ($\geq$30 worms) is assumed to be 0.15, and a "moderate-intensity" worm infection (15–29) is 0.01. We will assume that "low-intensity" worm infections (<15 worms) do not accrue DALYs and that mortality is also negligible.

Interventions

Assume, that up until now, no interventions have been in place, however now the ministry of health in Country X is considering mass drug administration (MDA) of mebendazole in a region with 100,000 people. The drug is assumed to be given to a proportion g of people and kills a proportion $h = 0.95$ of worms in the treated person, yielding a total net effectiveness of gh. For simplicity we will assume that the mean worm burden is *instantaneously* decreased by this factor but the aggregation parameter k remains the same as before control.

They plan to give the drug in one of the three scenarios:

- Once per year (annual) to children through schools. Since there is around 85% school attendance, $g = 0.85$ for children per MDA round
- Twice per year (biannual) to children through schools. $g = 0.85$ for children per MDA round
- Once per year (annual) to children through schools and adults in the community. $g = 0.85$ for children per MDA round, but targeting adults is harder and $g = 0.2$ for adults per MDA round.

We will assume that the expected cost per dose of the drug administered in a school is \$1.5 but that we have uncertainty described by the distribution $\Gamma(4.5, \frac{1}{3})$ (using shape and scale parameterisation). If the drug is given to adults there is an additional scaling for the doses administered to adults due to difficulties of community administration. The scaling parameter is described by $\Gamma(45, \frac{2}{30})$ (using shape and scale parameterisation).

Analysis

1. (a) Use this deterministic model – with uncertainty in posterior parameterisation and costs – to perform a cost-effectiveness analysis (CEA) comparing doing no interventions (comparator) with a strategy using annual MDA for children, a strategy using biannual MDA for children, and a strategy with annual MDA for children and adults. Use 3% discounting and a 20-year time horizon. [36 marks]

   [Hint: Assume that the system is initially at endemic equilibrium - you might want to run an initial simulation for a few years to check what to use for your initial conditions for running the strategies.]

   Make sure that your report covers each of the areas below:

   - A plot of the pre-control worm burden distribution in children and adults and numbers of individuals in the "moderate" and "high" intensity infection categories.
   - A plot of the infection dynamics of each strategy and brief summary of differences between strategies.
   - A plot of *undiscounted* mean DALYs and costs per year for each strategy (showing your working to convert from mean worm burden to numbers of high- and moderate-intensity infections to DALYs)

- A table reporting your *discounted* mean ΔCosts, mean ΔDALYs and corresponding ICERs
- A plot of your cost-effectiveness (CE) plane
- A plot of your cost-effectiveness acceptability curves (CEACs) and frontier (CEAF)

(b) Make a recommendation to a policy maker in Country X which has a per capita GDP of $400. [3 marks]

(c) If it is discovered that the willingness-to-pay threshold is actually $100 for Country X, how does this impact your recommendation? [3 marks]

2. (a) Describe another plausible intervention (other than mass drug administration) which could be used to control STH and modify your model equations accordingly. [3 marks]

(b) Find a justifiable cost from the literature to assign to this intervention. Include a citation to the source (webpage or article) as a reference. *[Do not spend a lot of time finding "the best" cost].* [3 marks]

(c) Define two new strategies which include this new intervention and update your CEA using all five strategies (two new and three original). What is your new recommendation? [15 marks]

(d) What other factors could influence a policy maker's decision to implement your new intervention other than cost-effectiveness? [2 marks]