Model to estimate expected QALYs and Costs

Let

$q_{i,j}$ = EQ-5D-5L for individual i at time j, $i=1,..,n;\ j=1,2,3$

$c_{i,j}$ = total cost for individual i at time j $i=1,..,n;\ j=2,3$

k_i = treatment arm for individual i, $k=1$ advice; $k=2$ physio

Model for EQ-5D-5L, accounting for baseline EQ-5D-5L

First we estimate the distribution of baseline (month 0, $j=1$) EQ-5D-5L scores:

$$q_{i,1} \sim Normal(\mu_{q,1}, \sigma^2_{q,1}) \qquad (1)$$

At 4 and 7 month follow-up ($j=2,3$) we assume a normal distribution, where the change from baseline interacts with baseline EQ-5D-5L (centred around m):

$$q_{i,j} \sim Normal(\mu_{q,i,j}, \sigma^2_{q,j}) \qquad j=2,3$$

$$\mu_{q,i,j} = q_{i,1} + \alpha_{q,j,k_i} + \beta_{q,j,k_i}\ q_{i,1} - m$$

Interpretation: $\alpha_{q,j,k}$ is the mean change in EQ-5D-5L for an individual with month 0 ("baseline") EQ-5D-5L of $\mu_{q,1}$, and $\beta_{q,j,k}$ the increase in mean change in EQ-5D-5L per unit increase in baseline EQ-5D-5L.

Estimating QALYs: Assuming that EQ-5D-5L changes linearly on each of the two time intervals (0-4months and 4-7 months), an individual with baseline EQ-5D-5L of q_1, the area under the curve method gives expected QALYs of:

$$QALY(q_1) = q_1 + q_1 + \alpha_{q,2,k} + \beta_{q,2,k}\ q_1 - m\ \ \frac{1}{2}.\frac{4}{12}$$

$$+\ q_1 + \alpha_{q,2,k} + \beta_{q,2,k}\ q_1 - m\ + q_1 + \alpha_{q,3,k} + \beta_{q,3,k}\ q_1 - m\ \ \frac{1}{2}.\frac{(7-4)}{12}$$

which can be shown to equal

$$QALY(q_1) = A + Bq_1$$

where

$$A = \frac{7}{24}\alpha_{q,2,k} + \frac{3}{24}\alpha_{q,3,k} - \frac{7}{24}\beta_{q,2,k}m - \frac{3}{24}\beta_{q,3,k}m$$
$$B = \frac{14}{24} + \frac{7}{24}\beta_{q,2,k} + \frac{3}{24}\beta_{q,3,k}$$

Forming a weighted average over the population of baseline EQ-5D-5L scores, we obtain the average QALY by integrating of over the distribution of baseline EQ-5D-5L obtained in (1) giving:

$$Q = A + B\mu_{q,1}$$

This can be evaluated at each iteration of the Markov chain Monte Carlo simulation and summarised with the posterior mean to obtain expected QALYs.

Model for Total Costs, accounting for baseline EQ-5D-5L

At 4 and 7 month follow-up:

$$c_{i,j} \sim LogNormal(\mu_{c,i,j}, \sigma^2_{c,j}) \qquad j = 2,3$$
$$\mu_{c,i,j} = \alpha_{c,j,k_i} + \beta_{c,j,k_i}\ q_{i,1} - \mu_{q,1}$$

Interpretation: $\alpha_{c,j,k}$ is the total log-cost over 0-4month ($j = 2$) interval and 4-7month ($j = 3$) interval for an individual with month 0 ("baseline") EQ-5D-5L of $\mu_{q,1}$, and $\beta_{q,j,k}$ the increase in mean log-cost per unit increase in baseline EQ-5D-5L.

Estimating Total Costs: For an individual with baseline EQ-5D-5L of q_1, assuming all costs have been covered in the 2 time-periods ($j = 2,3$), the expected total costs are:

$$C(q_1) = \exp\ \alpha_{c,2,k} + \beta_{c,2,k}\ q_{i,1} - m\ \ + \exp\ \alpha_{c,3,k} + \beta_{c,3,k}\ q_{i,1} - m$$

Forming a weighted average over the population of baseline EQ-5D-5L scores, we obtain the average total cost, C, by integrating of over the distribution of baseline EQ-5D-5L obtained in (1) giving:

$$C = \int \exp \ \alpha_{c,2,k} + \beta_{c,2,k} \ q_{i,1} - m \ + \exp \ \alpha_{c,3,k} + \beta_{c,3,k} \ q_{i,1} - m \ dq_1$$

The evaluates to

$$C = \exp\left(\alpha_{c,2,k} + \frac{1}{2} \beta_{c,2,k} \sigma^2_{q,1} \right) + \exp\left(\alpha_{c,3,k} + \frac{1}{2} \beta_{c,3,k} \sigma^2_{q,1} \right)$$

This can be evaluated at each iteration of the Markov chain Monte Carlo simulation and summarised with the posterior mean to obtain expected total costs.

Priors

We assume flat normal priors on all a and b parameters and $\mu_{q,1}$. Uniform(0,5) priors are assumed for the standard deviations parameters for EQ-5D-5L and Uniform(0,10) priors for the standard deviations for log-costs. We checked that the priors were sufficiently wide so that the posteriors for the standard deviations were not being constrained by the priors.