Calculating Markov transition probabilities when treatment effects are reported as Relative Risks with a different cycle time

Authors: Malcolm J Price, Nicky J Welton, AE Ades
University of Bristol

University of BRISTOL

Introduction

Problem

• Most common approach for estimating Markov models in health economic evaluations:
  ➢ Government statistics or a cohort study used to inform an underlying transition probability model
  ➢ Underlying model adjusted to estimate the transition probabilities under an intervention using relative risk, odds ratio, or hazard ratio statistics estimated from published RCT(s).
• Relative risk (RR) (and Odds ratio) statistics are a ratio of the probabilities that an event of interest occurs in each of two trial arms:

$$RR_{1,2}(\cdot) = \frac{risk\ in\ treatment\ group}{risk\ in\ control\ group} = \frac{p_{B,1,2}(\cdot)}{p_{A,1,2}(\cdot)}$$

• Where s is the length of the study, and $p_{k12}(\cdot)$ are the transition probabilities from the pre-event state 1 to the post event state 2 in arm (k = A or B) of the trial, defined over an elapsed time period s equal to the follow-up period of the study :
• The transition probabilities are non-linear functions of time
• Even if the hazard rate is constant, the RR is specific to the time period for which the event probabilities are defined.
• If the length of the trial reporting the RR is different to the cycle length of the CEA then direct use of the RR to adjust the transition probabilities will give incorrect estimates.

Objective

• To show how a reported relative risk estimate can be adjusted to the required cycle length for an economic model.

• To compare the magnitude of the error to that introduced by not using the 'half-cycle' correction.

• To demonstrate the impact that different factors have on the magnitude of the error.

Methods

Adjustment to the Relative Risk

The relative risk can be estimated for the correct cycle time as follows:

$$RR_{i,j}(\cdot) = \frac{1-(-p_{B,i,j}(\cdot))^{s}}{1-(-p_{A,i,j}(\cdot))^{s}}$$

Where c is the cycle length of the economic model.

Methods cont:

Half-cycle correction

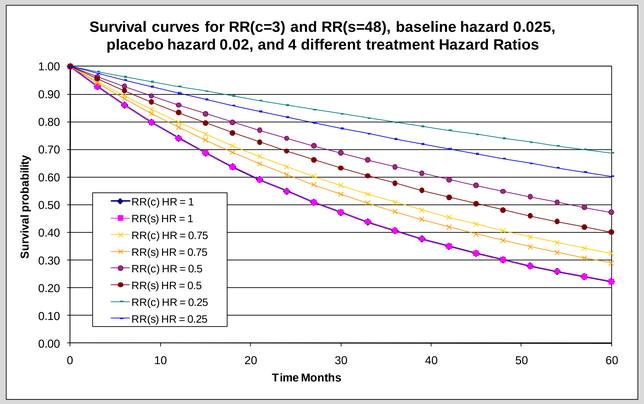
Consider a simple two-state model where interest focuses on the length of time spent in state 1, denoted t_1. If the economic model is run for H cycles and a half cycle correction is not used then:

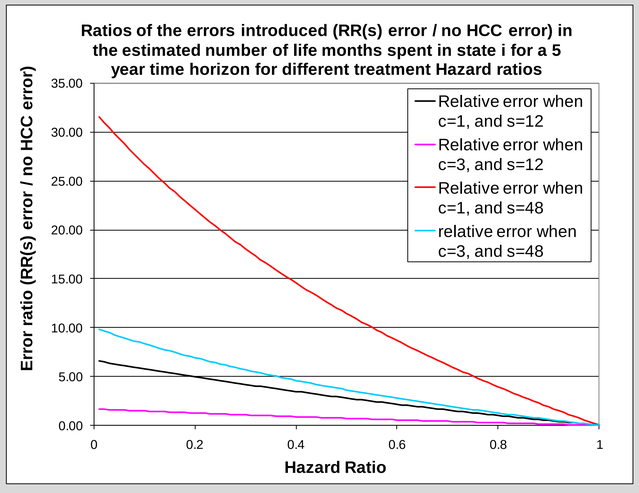
$$t_1 = 1 + \sum_{h=1}^{H-1} p_{B11}(\cdot)^{h}$$

If a half cycle correction is used then:

$$t_1 = 0.5 + \sum_{h=1}^{H-1} p_{B11}(\cdot)^{h} + 0.5 \times p_{B11}(\cdot)^{H}$$

Results





Discussion

Factors affecting the magnitude of the error

• The magnitude of the error introduced by using a RR defined over a period of time other than the cycle length of the study is dependant on the following:
  ➢ Principally the absolute and relative sizes of the event rates in the trial arms.
  ➢ The difference between the study duration and the cycle length.
  ➢ The time horizon of the study and the size of the baseline transition probability.

Reasons to use the adjustment

• The adjustment is no more difficult to implement than the half-cycle correction
• It is likely that in most situations the adjustment will have at least as large an impact on the results as the half-cycle correction.
• In some cases the size of the error introduced by not adjusting the relative risk may be far larger than the half-cycle error and could plausibly be sufficient to alter the conclusions about which intervention is the most cost-effective.

Models with competing risks

• In the presence of competing risks, it is not possible to accurately adjust individual transition probabilities because of the complicated negative correlations that exist between them.
• The relative risk estimate must be converted into a hazard ratio and the adjustment for treatment effect is then performed on the rate (more likely log-rate) scale.
• The transition probabilities for the required cycle length may then be estimated using Kolmogorov's forward equations.

Conclusions

• The Error Introduced by not adjusting reported RR estimates to the cycle length of the economic model will often have a larger impact than the half cycle correction and is just as simple to implement.

Correspondence

Malcolm Price
Department of Community Based Medicine, University of Bristol,
Cotham House, Cotham Hill, Bristol BS6 6JL, United Kingdom.
Tel: +44 (0)117 331 0641 E-mail: Malcolm.Price@bristol.ac.uk