Reviewer’s report

Title: Adapting a Markov Monte Carlo simulation model for forecasting the number of Coronary Artery Revascularisation Procedures in an era of rapidly changing technology and policy

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Reviewer: Gil L’italien

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General comments:

The authors propose a methodology to improve the predictive accuracy of a markov model developed to predict CARPs in the context of rapid changes in technology and patient management over time.

Markov model performance is heavily dependent on the choice of appropriate transition probabilities to track hypothetical cohorts through various health states over time. The authors propose methods to revise existing transition probabilities based on published trends in therapies and incorporating extrapolation of transition probabilities using mean (ie moving) average for 3 years or linear interpolation of transition probabilities over 3 years with greater weight given to recent years. The choice of method is based on the anticipated direction of trends (ie no change in level or change in level at constant rate)in event rates. The published information provides the means with which the authors modify the extrapolated probabilities. I have several major concerns regarding this approach, and with the manner and order in which the analyses have been described.

MAJOR COMPULSORY REVISIONS

1) Given that the datasource for the development of the model and its component transition probabilities is available up to 2001, why use transition probabilities from 1992-1994, extrapolated to 1995-1999 via the standard and modified methods? Why not derive new transition probabilities directly from the later data (eg from 1995-1999 or 1995-2001)? It makes much more sense to ignore the earlier (1992-1994)data since it is no longer relevant due to technology and policy changes and develop the model using the latest data available, particular since the authors main goal is forecasting of future CARP rates, not a retrospective trend analysis. One would obviously expect the performance of the predictive model to decay over time, particulary in the context of procedural and policies changes, so reporting this is not novel or unique. Thus the authors should revise the model using the latest 3 or 5 year window.

2)The method used to derive transition probabilities is not ideal, particularly since the authors admit that the transition probabilities are dependent on more than age/gender but also on a number of extraneous factors, which they have identified but not adjusted for. I recommend a method described in Hypertension.
2003;42:885-890. by Sesso et al entitled, "Blood Pressure Lowering and Life Expectancy Based on a Markov Model of Cardiovascular Events". I participated in this study and we used Cox proportional hazards regression models to estimate transition probabilities for both primary and secondary CVD events, adjusted for several relevant covariates. The ejournal version of the paper also contains a detailed supplement describing the methodology. The advantages of using this method are: a) as stated, it permits estimation of transition probabilities which a dependent on a range of ancillary covariate effects, b)it avoids the need to choose an interpolation method based on anticipated trends (page 5, para 2), which in my opinion, is biased, c) one can still re-adjust these probabilities up or down based on external published evidence, d)one can estimate conditional probabilities (as we did for secondary CVD) by restricting the analysis set to patients with the precondition, e)one can incorporate time dependent covariates (eg changes in CVD risk factor levels over time)into the model.

3)The order of data presentation is counter-intuitive. Please present the derived transition probabilities over time first, then the estimated and observed event rates and goodness of fit statistics. Applying recommendations 1&2, these tables will be simplified since fewer models would be developed (one for each gender and one for each type of event (CABG or PCI), and a shorter time window (eg 1995-1999, or 1995-2001)is considered. Please describe the validation results in more detail, including the reasons for observed model performance.

In summary, the authors should make use of the considerable data at hand to revise the models using the latest data, ignoring the earlier data; they should use cox regression adjusted for covariates to estimate the transition probabilities; they should present the results in logical sequence with component transition probabilities first, then model outputs vs observed results plus goodness of fit metrics.

I can provide the reference article and supplement to the authors if they are unable to access these.

What next?: Unable to decide on acceptance or rejection until the authors have responded to the major compulsory revisions

Level of interest: An article of importance in its field

Quality of written English: Acceptable

Statistical review: No, the manuscript does not need to be seen by a statistician.

Declaration of competing interests:

Employee of Bristol Myers Squibb, a manufacturer of pharmacologic cardiovascular therapies