Author’s response to reviews

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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Version: 2 Date: 10 March 2008

Author’s response to reviews:

Dear Editor

Thank you for the opportunity to revise our manuscript. We believe we have addressed the concerns of the reviewers and hope that the manuscript is now acceptable for publication. All changes in the paper are made using track changes option in MS Word so that the reviewers can see the actual changes made to the original paper sent earlier.

We thank the reviewers for their time and effort in reviewing our paper. Their comments show that a number of aspects of the manuscript relating to the rationale and methods were not clear. We have responded to their concerns as follows:

Reviewer 1 (L’italien).

1) The reviewer suggests using actual transition probabilities from 1995-1999 to obtain forecasts for 1995-1999. The aim of our paper is not to see if the model with actual transition probabilities from 1995-1999 gives good predictions for 1995-1999. Doing this is a check on model validity and this was done in our first paper (Mannan et al., 2007, Annals of Epid, 17(12), 964-975) which shows that the model is valid. The point of the current paper is to examine the (potential) use of the model for forecasting, that is, if it were now 1995 and we wanted forecasts for 1995-1999. We have chosen the 1995 cohort to examine the forecasting potential of the model because we know the actual event numbers for 1995-1999 and can thus evaluate the forecasting performance. We have amended the paper to make this clearer (What changes did you make?)

2) The reviewer recommends the approach of Sesso et al. (Hypertension, 2003;42:885-890) as perhaps a better method for extrapolating the transition probabilities. The Sesso et al method is a cohort study-derived risk model for primary and secondary CVD events that includes BP, cholesterol, diabetes,
smoking as well as age as covariates and then applies risk estimates from them to a hypothetical cohort of people with high blood pressure. This is an entirely different type of model from our population-based model. Our CHD/CARP model avoids having to model risks from cohort studies and simply uses population data. Our model has 96 risk estimates for each sex/age group and it would be impractical to find cohorts and develop a model for each one of these (with or without including risk factors). Furthermore, our model is not applied to hypothetical cohorts to ascertain the effect on outcomes of a particular intervention or of change in a particular risk factor. Our model is applied to the actual population cohort to forecast future event numbers. In order to apply cohort-based risk models with risk factors to our population cohort we would need risk factor data on the entire population of Western Australia. Unfortunately, this information is unavailable. We have now incorporated the Sesso et al. paper in the reference list of our paper and have specifically discussed the differences in the Discussion section.

We have demonstrated that when the standard extrapolation methods are carefully modified to incorporate changes in effectiveness of PCIs and shifts between CABGs and PCIs due to changes in health policy, our model can forecast the requirements of CARPs very well. This was achieved by changing only a few (16 for each age-sex group) associated risks of CARP events although the model includes many (96 for each age-sex group) risks of various CHD/CARP events.

3) The reviewer has suggested a change in the order of presentation of results. We believe that once the reviewer has fully understood the context and approach of the present study based on the points 1 and 2 mentioned above, this point is no longer relevant.

Reviewer 2 (Lyratzopoulos)

1. The level of statistical jargon is now reduced or better explained. The abstract is now better structured based on the journal style/format.

2. We agree that changes in all the CHD/CARP event risks might be due to a number of factors not just the particular factors we evaluated (eg, changes in CARPs due to advancement in surgical technology for CARPs). One of the primary aims of developing the CHD/CARP model was to forecast the CARP event numbers. The current paper was written with that aim in mind. Because of that we only altered the risks of certain CARP events which were likely to be influenced by advances in CARPs. Also, our illustration was not given in an attempt to prove that the changes in CARP event risks were the main drivers of CARP events over this period (as the reviewer seems to be suggesting). The illustration was provided to show how such a model can examine how much forecast event numbers change if changes (eg increase in facilities for PCI or improvements in PCI technology) that are anticipated are included. We chose sensible and realistic changes and demonstrated that, if properly incorporated, can improve forecasts.
Finally, the model could also be used to produce forecasts for other anticipated changes such as those mentioned by the reviewer.

Reviewer 3 (Bonneux)

We believe that the reviewer has misunderstood the point of the paper. It is not 'a retrospective forecast' that uses 'posterior knowledge'. The point of the paper is to illustrate how forecasts from such a model may be improved if ANTICIPATED changes are incorporated. We chose the 1995 cohort to illustrate the approach and to demonstrate that changes that would have been anticipated in 1995, could be incorporated to improve the forecasts. By demonstrating that the model can be successfully applied in this manner it therefore encourages the use of this type of model and method for real time forecasting for future years.

The first paper is now published (Mannan et al., 2007, Annals of Epid, 17(12), 964-975). The current paper is indeed a follow-up of the first paper where the model is described and validated.

We have amended the aims and context/rationale to make them clearer.

The reason for considering mean and linear extrapolation methods is that they are STANDARD extrapolation approaches and in some situations might work well. For example, we showed for a later WA population cohort (1998) that the extrapolated risks based on these standard approaches can project the event numbers very well (this is not shown in the current paper). This occurred because the shifts between CABGs and PCIs stopped by 1998 while in our paper these shifts started from 1995 when stents were introduced in WA. The point of our paper is that the standard extrapolation approaches do not work well in situations when there is rapidly changing technology, policy, etc. We have shown how in such situations the standard approach can be modified to achieve better forecasts.

Our approach does NOT assume future event numbers are determined by need. Indeed this is highly pertinent to the aim. If needs based on standard extrapolated risks are used then our paper shows that the forecasts are not good. Indeed, one of our modifications is precisely about "offer and demand" as it involves an expansion of facilities to do PCIs.

This model is a form of "time series" model for the (individual) transition probabilities that need to be extrapolated into the future. However, it is not a simple time series model for the annual event numbers, as it involves a disaggregated approach based on event risks for people in different health states, classified by age and sex.

The reviewer is incorrect in stating that our model treats all CHD history as the same. The model subdivides people with CHD history into groups according to history of CHD without and with CARPs which is the most important distinction at least from a health services viewpoint. Although it is true that all CHD admissions without CARPs have been amalgamated to a same history category, this was
done because the objective of developing the model was NOT to predict/forecast the numbers of acute AMI, non-acute AMI or angina etc. Our model does not distinguish STEMI from non-STEMI as these cannot be done from the computerised hospital admission data.

We acknowledge the point about drug eluting stents (DES). We have included this as a possible change or scenario that might be incorporated if forecasts for today’s population cohort are being performed. However, the manner in which DES should be incorporated should reflect the likely benefit on event rates AND the likely uptake of DES at the population level.

sincerely,
Haider Mannan