Reviewer’s report

Title: Estimation of Progression of Multi-state Chronic Disease Using the Markov Model and Prevalence Pool Concept

Version: 1 Date: 18 May 2006

Reviewer: Timothy Hofer

Reviewer’s report:

General

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Major Compulsory Revisions (that the author must respond to before a decision on publication can be reached)

A common method to assess the impact of healthcare interventions over time involves using multistate markov models to track the changes in incidence, prevalence and costs of disease states and survival. The biggest challenge in using these models is to obtain reasonable estimates for transition probabilities between states from existing data sources that often represent partially observed cohorts at 2 or 3 cross sectional time points.

This is an interesting paper that presents a fairly technical discussion of a method for calculating transition rates based on both complete and partially observed data at several follow-up times. The authors argue that their approach using a E-M algorithm based on prevalence pools and Markov process models is simpler than previous parametric methods that they cite.

General points:
I would be interested in them expanding a bit on the conceptual differences between their approach and the others cited in the introduction. Also in some reading I did to try to better understand what they were doing, I came across another cite that seems like it would be worth commenting on. (Welton N, 2005, Medical Decision Making 24:633-645)

While I have in fact published some markov models using much cruder approaches to derive transition probabilities from cohort data, this is not my primary area of interest or expertise and it is difficult for me to evaluate the mathematical details of their approach. I trust that they are correct. However, I would suggest that despite my lack of expertise specific to their question, I am still probably among the more numerate members of any audience that the authors are likely to find and I nevertheless found this article hard to follow.

It is not that it is badly written, and in fact both the introduction and conclusion are very well set up in terms of trying to set out the rationale and motivation for the approach and listing and discussing some of the advantages over the existing approaches. It is just that for someone who is not a population epidemiologist or specialist in Markov modeling, the mathematical descriptions of the likelihoods are too long and the conceptual explanations are too terse and ask for too much effort from even an interested and motivated audience from other fields.

For example, the introductory paragraph "Firstly, time to pre-clinical screen-detectable phase for prevalent screen-detected cases (identified in the first screen) is more uncertain than that for incident screen cases (identified in later screens) because prevalent screen-detected cases are left-censored whereas incident screen-detected cases are interval-censored. The latter usually provides more information on occurrence rates than the former." It needs another sentence or two to explain how the terms apply to the cohort data used (it does become clearer later) and to expand on the statement that "The latter usually provides more information on occurrence rates than the former"

Or this statement in the discussion, "In addition, simultaneous estimation of lambda 1 and lambda 2 may encounter a collinearity problem due to a high correlation between two parameters. This phenomenon may be observed when there is no data on interval cases, which are sometimes unavailable for unregistered conditions such as Type 2 diabetes." is just slightly too opaque. I think it is simply saying that if you don’t have much information on the intermediate states then it is hard to disaggregate the overall rate into distinct
rates for each individual state transition. Another sentence to that effect would make it more accessible.

I think some of the technical details might be moved to an appendix and even expanded so that it would be easier to replicate their methods (in some of the Welton cites they actually include BUGs code for their examples) and more time then spent on conceptual explanations.

Obviously, if the authors picked a journal whose audience was composed primarily of quantitative population epidemiologists this might not be necessary, and that might be one approach to follow as I am not really sure that this article belongs in BMC Family Practice. It does not fit with the type of articles that have been published there as I look through the last few issues and is way too technical for most clinical audiences. The fact that a diabetes example is used to illustrate the technique is almost completely incidental the way the article is written at present. This is a technical methods piece.

If the authors want to publish in an open source journal, Why wouldn't they publish in Population Health Metrics? There are some other related articles that are in that journal (e.g. Patten SB, Lee RC. Describing the longitudinal course of major depression using Markov models: data integration across three national surveys. Popul Health Metr. 2005 Nov 15;3:11) and I think they would have an audience that would be much better suited to the the material. BMC HSR is another possibility although not as good a fit I would think. Obviously places like Medical Decision-making would be another possibility.

But for a clinical or even a general health services journal they are going to have to go through the piece and add a more accessible conceputal explanation of what they are doing and why.

Now there were a few aspects of the models they were examining that seemed to raise some questions for me. First, for example, given the perceived increase in population rates of type two diabetes throughout the world, is a prevalence pool approach justified? Second, in the mortality model why would the only path to death be through the symptomatic state of diabetes? Type two diabetes occurs in older populations and death is a significant competing risk and I would think you would want a model where both persons without disease and with asymptomatic disease might die.

Specific points

p15 top- Is the OGTT sample random or selected based on history or other lab tests.

Minor Essential Revisions (such as missing labels on figures, or the wrong use of a term, which the author can be trusted to correct)

p16 top "lambda 1 was estimated as 0.0107594" is this a typo, in the estimate for lambda 2, lambda 1 is referred to as 0.107594

p19 top fragment "These could be expected to have 5-year cumulative death rate from the, of"

Discretionary Revisions (which the author can choose to ignore)

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

Level of interest: An article whose findings are important to those with closely related research interests

Quality of written English: Needs some language corrections before being published

Statistical review: No

Declaration of competing interests:

I declare that I have no competing interests