Reviewer’s report

Title: Validation of a new predictive risk model: measuring the impact of the major modifiable risks of death for patients and populations

Version: 1
Date: 15 July 2014

Reviewer: Matthew C Stiefel

Reviewer’s report:

1. Is the question posed original, important and well defined?
   Yes. My understanding of the research question: Is the proposed risk prediction model a valid and useful tool for use by individuals and clinicians to compare interventions and ACO’s to identify and track pop health risks.

2. Are the data sound and well controlled?
   Yes. The manuscript provides a very creative use of large public datasets and the literature to construct a risk prediction model. The review of the literature in Annex 1 used to derive relative risks represents an extensive undertaking and is itself a major contribution to the literature. However, it is given very little attention in the manuscript. For example, the causes of death in the model are not mentioned in the article, only in Annex 1. I recommend highlighting it (I may have missed, but can’t find a reference in the manuscript to Annex 1).

3. Is the interpretation (discussion and conclusion) well balanced and supported by the data?
   Yes, in general. However, I believe there are important issues that need further discussion.
   • I believe the tool has important limitations for individual clinician and patient use. The 12 risk factors included in the model are an important but limited subset of factors affecting future mortality. The authors note that chronic conditions, geographic, racial and socioeconomic factors affect underlying risk. In addition, factors included in other predictive models (e.g., Archimedes, DxCG) such as clinical history, self-perceived health and functional status are known to affect risk of mortality. This model, in combination with these other factors that are readily available and already included in mortality prediction models, would be enhanced for use in individual prediction. As examples, issues such as multiple chronic conditions, paralysis, amputations, or diminished self-perceived health and functional status are likely to yield different mortality risks, even with the same risk profile among the 12 risk factors in this model.

   • The model doesn’t include morbidity risk, which is important to people and can be very different from mortality risk (the important distinction between dying from and living with conditions). Many conditions, such as asthma and amputations, which may be influenced by the risk factors in the model, have a much more significant impact on morbidity or functional status than on mortality. Quality of
life can be as or more important than length of life. In fact when the baseline mortality risk is less than 10 years, 10-year mortality risk is not a relevant measure. This has important policy implications for end-of-life care, and is worth noting in the discussion.

• The 12 risk factors are a mixture of behavioural risk factors (diet, alcohol use, physical inactivity, smoking, seat belt use) and physiological risk factors (glucose, cholesterol, blood pressure, BMI). Although the authors say that they have appropriately adjusted for correlations and mediation among the risk factors to support assumptions of independence among the risk factors to justify a multiplicative model, more discussion of the implications of using these different types of risk factors is warranted. Most of the behavioural risks impact mortality through the causal pathway of the physiological risk factors. This is especially relevant in the individual applications. For example, diet, smoking, and exercise all affect blood pressure.

• Hazard changes from reduction of the risk factors may also not be straightforward. For example, people who don’t wear seatbelts may drive more recklessly than those who don’t, and wearing seatbelts may not cause people to drive less recklessly. Or reduction of risk factors may increase other risks. For example: overcontrolled blood pressure may increase fainting; or aspirin use may increase bleeding.

• Also, while the notion of a “background” mortality risk, defined in the paper as the risk associated with a person not exposed to any of the risk factors, is clear for the behavioural risk factors, it is less clear for the physiological risk factors. For example, what level of blood pressure was used as the “background” risk? The optimal level of blood pressure, beyond which no additional benefits would be conferred, is not stated, and not obvious.

• I like the discussion of the measure of predicted risk as a potential quality measure, with significant advantages over existing quality measures, is especially important (no changes).

4. Are the methods appropriate and well described, and are sufficient details provided to allow others to evaluate and/or replicate the work?

• I’m not qualified to judge the appropriateness of the adjustments for correlations and mediation among the risk factors to support assumptions of independence among the risk factors to justify a multiplicative model, and additional statistical review is warranted. That said, the contribution of the model and methods to the public domain is laudable, and will enable further public scrutiny of the model and methods.

• The model shows excellent discrimination and calibration attributes.

5. Can the writing, organization, tables and figures be improved?

Many of the references are very general and it is difficult to know where in the reference is support for the specific point in the manuscript (for example, 16 and 17).
6. Are there any ethical or competing interests issues you would like to raise?
The only ethical issue I would raise is a positive one. Kudos to the authors for contributing the model, methods, and extensive review of the literature to the public domain.

**Level of interest:** An article of outstanding merit and interest in its field

**Quality of written English:** Acceptable

**Statistical review:** Yes, but I do not feel adequately qualified to assess the statistics.

**Declaration of competing interests:**

I declare that I have no competing interests