Reviewer’s report

Title: Asking or Measuring? Self-perceived Quality of Life Predicts Mortality Risk Better than a Panel of Biomarkers, but the Combination of Both Does Best

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Reviewer: Luis Rosero-Bixby

Reviewer’s report:

The paper addresses the problem of predicting prospective death in a population of adults from a region in Germany. More specifically: whether a set of ten quantitative biomarkers affect the “predictive performance” on mortality of a set of subjective self reported health (SRH) indicators. The study is based on a ten-year prospective mortality study. If I understood correctly, biomarkers and SRH indicators are measured at baseline. In this way, the paper is suggesting that SRH indicators and biomarkers can predict mortality after one, five or even nine years. It is a population–based study in a sample of about 4,000 adults (aged 20-79), from West Pomerania, Germany.

The objectives of the study are clearly stated, the design and statistical methods seem sound and well explained, the data look robust, and the report is well written and follows scientific standards.

I recommend publishing the manuscript after some revisions, mostly additions.

In my view the design has two major limitations that are not properly addressed in the discussion and presentation of results.

(1) That the analysis uses predictors measured at baseline only (the ideal design would be to have predictors varying over time; i.e. measured every two years or so). The discussion should justify the use of predictors five or nine years old… A useful exercise to discuss this point would be to estimate Cox models for, say, years 0-2, 3-5, and 6-9 (or 0-4 and 5-9). Related to this point, the legend in Figure 1 should say “baseline” instead of “current” health status.

(2) The possibility that individuals in the sample are contaminated with the information regarding lab’s results. I am guessing that for ethical reasons the study gave back that information to participants, and some of them modified their behavior or started taking medicines to control the condition revealed by the biomarker… This point should be discussed, even though I recognize there is not an easy answer to the problem.

Another sort of important issue I would like to see addressed in the discussion is that of causality. Although the authors are careful and they talk only about “associations” it is possible that some readers misinterpret results are “causal”. So, authors should address this possible interpretation.
A minor issue is regarding the use of ROC curves and the C-statistics. I like the use of ROC curves in this paper. But I think an explanation of the C-statistic is required. It is the area under the ROC curve, which can vary between 0.50 and 1.00. Readers unfamiliar with ROC curves may believe that the C varies between 0 and 1, and, consequently, that the Cs in the study of about .88 are very high. I prefer to use the Gini coefficient, which varies between 0 and 1, and it shows the area between the ROC curve and the no-discrimination diag as a proportion of the upper triangle. In this case the Gini would be in the order of 0.76. The authors’ report that mortality prediction measured by the C-statistics improves from 0.883 to 0.887 when selected biomarkers are added to model 1 that included demographic and SRH (or that improves from 0.873 to 0.887 when SRH are added to demographic and biomarker variables). They inform us that the difference in this numbers is significant and conclude that the best prediction is achieved by including both SRH and biomarker indicators in the model. This conclusion is right, but it is a bit misleading. The improvement of 0.004 in the C-statistic seems small to me (even though is statistically significant). Moreover I would like to know the C-statistic for a model with just the demographic variables. If it is about 0.8 it would show how little SRH indicators and biomarkers improve prediction above what we already know from mortality rates by age and sex and it will put things in a right perspective.

Another issue I would like to see addressed is how the variable age was included in the models. We know that in the age bracket studied the death hazard follows approximately an exponential or Gompertz function. This should be taken into account when authors are including their age adjustments (I think Cox regression does it). Actually I would like to see the estimated effect of age on the death hazard (I would expect an increase of about 9% or 10% in the death hazard with each year of age).

Finally, I strongly suggest authors present in annexes the complete results of the regression models they estimated (I mean the regression coefficients and SE for each of the explanatory variables in the equation). Given that this is an electronic journal, there are no costs associated to including such annexes. And this information can be extremely useful for the accumulation of knowledge.

My comments suggestions can be taken as sort of discretionary revisions, which the authors can choose to ignore them, but I’d like to see a justification to ignore them.

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:
I declare that I have no competing interests