Reviewer's report

Title: Choice of relative or cause-specific approach to cancer survival analysis impacts estimates differentially by cancer type, population, and application: evidence from a Canadian population based cohort study

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Reviewer: Paul Dickman

Reviewer's report:

This is an interesting paper that makes a useful contribution to the body of literature in this area.

The authors compare four approaches to estimating net survival, 2 in a cause-specific framework and 2 in a relative survival framework. As the authors state, the relative survival framework is a de facto standard for cancer registry data but it may not always be the most appropriate choice. In particular, relative survival methods may be problematic when interest is in ethnic sub-populations, the focus of this study, since ethnic-specific population life tables are not always available. I suggest the authors emphasise this point in the introduction and discussion - at the point where they write that relative survival is standard - since the question of which approach to use is of great interest to researchers interested in estimating survival for sub-populations (whether defined by ethnicity, social class, geography, or some other factor). The authors are fortunate to have access to ethnic-specific population life tables, and are able to compare relative survival estimates using both ethnic-specific and general population life tables. In addition, their comparison of cause-specific survival using the narrow and broad definition of death due to cancer is also of large general interest, for both the first nations and non-aboriginal populations.

The description of methods on page 5 states (or at least strongly implies) that relative survival was estimated using flexible parametric models. On page 6, however, we read that the Ederer II approach was used, which suggests actuarial methods were used. Which approach was used?

The models were adjusted for age and sex. What about an age*sex interaction and time-varying effects of age and sex? Were these considered? What statistical tests were used to support the decision not to include these terms?
Page 7: "The RS-GLT approach slightly but consistently resulted in overestimates of survival among non-Aboriginals compared to RS-ELT. This is because the cohort is somewhat healthier than the average Canadian(16)." Is the cohort healthier because First nations women have been excluded or because of selection to screening?

Page 8: "Breast and prostate cancers displayed the greatest differences across methods between relative and cause-specific survival overall, and were also the only two cancers with notable differences in the estimates of disparities in survival between populations." As written, this paragraph belongs in results rather than discussion. Expand or explain! Is it due to selection to screening?

Page 8: "we restricted cases to those diagnosed in 2001 and later, by which time evidence had accumulated that PSA testing should not be routinely used as a screening test.(27,28)" The existence of such evidence does not necessarily imply that PSA testing is no longer performed (and is more likely to be performed among the more socially advantaged and healthier). A recent study in Stockholm showed that two-thirds of men aged 50 years or more had undergone a PSA test in the last 9 years (PMID: 23083803).

Page 9: "This assumption is likely to have been violated for other cancers, but for prostate cancer, where censoring was most common, it is likely to have had the largest impact." Why? What's the purported mechanism.

Table 1: Power depends on number of deaths. There are as few as 15 deaths for First nations, and the number of cancer-specific deaths will be even lower. Is this sufficient to conduct an analysis and report results?

Relative survival is considered by many to be an outdated approach for estimating net survival in a relative survival framework; many experts in the field recommend using the Pohar Perme approach instead. See "Analysing population-based cancer survival - settling the controversies" (PMID: 27912732) for a balanced discussion and "Cancer net survival on registry data: use of
the new unbiased Pohar-Perme estimator and magnitude of the bias with the classical methods." (PMID: 22961565) for an ill-informed and sensationalist point of view. The analysis performed by the authors is perfectly fine, but I suggest the authors modify their text slightly to reflect contemporary views on methodology. Specifically, write "estimating net survival in a relative survival framework" and emphasise the fact that a model-based approach is being used. The criticism of "relative survival" applies to the life table approaches; Phar Perme and colleagues made this clear in their original paper where they wrote that model-based approaches are also valid.

Paul Dickman

21 January 2017

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