Reviewer's report

Title: Relative mortality in soft tissue sarcoma patients: a Danish population-based cohort study

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Reviewer: Michael Schaapveld

Reviewer's report:

This manuscript assesses relative and cause-specific mortality in soft tissue sarcoma (STS) patients in Denmark. The paper is interesting, exploring an alternative method for estimating expected mortality compared to the widely used life table methods, by establishing a general population comparison cohort matched to the STS patients on age, sex and region who were alive at date of STS diagnosis. The paper again shows the strength of having an unique identifier for follow-up and linkage within the Danish population as well as the availability of good quality health care databases. The paper is well written.

The strength of the method in this paper is that the authors are able to estimate relative survival accounting for the level of comorbidity (and SES if that would have been available). This method may also be preferable if the cause of death under study is not rare.

Major Compulsory Revisions

I do have a methodological issues however, which is the following: the purpose of relative survival and cause-specific survival analysis is to estimate net-survival, i.e. the (hypothetical) survival which might occur if all risks of dying of other causes than the cancer of interest were removed thus studying the proportion of patients dying directly from cancer or indirectly from its consequences. Competing risks theory allows to calculate "real world" probabilities where a patient is not only at risk of dying from their cancer but also from any other cause of death using cumulative incidence functions. The cumulative incidence function will always be lower than cause specific mortality (1 minus the Kaplan-Meier survival estimate) in the presence of competing risks. In this paper Maretty-Nielsen et al. estimate relative mortality, which attempts to estimate net-survival and does not account for competing risks, and compare this to a "cancer-specific" mortality estimate. However for this latter estimate deaths due to other causes were treated as competing events. This alone may fully explain their finding that the "cancer-specific" mortality estimates are lower than the relative mortality estimates. I therefore do not agree with the conclusion of the abstract and the paper. I (strongly) suggest not to estimate "cancer-specific" mortality as a cumulative incidence function.

Discretionary Revisions

Table 3 presents mortality rates and crude/adjusted MRR. The second part of the
table actually presents MRR conditional on surviving up to 5 years. However, the mortality rates are cumulative mortality rates and have no direct relation with the MMR shown in the left columns. I would suggest to present the cumulative mortality from 5 years of follow-up (i.e. for age-group 0-39 this conditional mortality would be 6.0% and the expected mortality 0.7%, the ratio of which (8.6) much better reflects the MMR shown in the column to the right than is currently the case).

Minor comments:

Abstract, line 1 "Cancer-specific survival estimates" instead of “Cancer-specific estimates”

Statistical analysis page 9: line 13 should read either “… and the observed survival in the age- and sex matched…” OR “and the expected survival based on the observed survival in the age- and sex matched ….”

Statistical analysis page 10: line 3 “violation of” instead of “contradiction to”

Discussion, page 16: with regard to using life tables. Although I agree that technically life tables are indeed rarely free of deaths due to the disease of interest, in case of a rare cause of death, such as death due to STS, the bias this may introduce will be negligible. And as life tables are derived from mortality in the total population there is no sampling bias (so no confidence interval needs to be estimated for the expected survival) which needs to be accounted for in the design chosen in this study. The benefit of good internal comparability in this study may be fully countered by the sampling variability introduced. This is worth mentioning.

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

**Quality of written English:** Acceptable

**Statistical review:** Yes, and I have assessed the statistics in my report.

**Declaration of competing interests:**

I declare that I have no competing interests