Author's response to reviews

Title: Delivery of Health Care at the End of Life in Cancer Patients of four Swiss Cantons a retrospective database study (SAKK 89/09)

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Author's response to reviews: see over
1) Please clarify in the Methods section whether the Helsana database is publicly available and if not, who granted permission to use the data. Included at the end of the section “Helsana insurance claims”:

"The Helsana database is not publicly available and permission to use the data was given by the Helsana directorate and approved by the above-listed ethics committees and expert committee."

2) Please move the full names of the Ethics committees who approved the study to the Methods section.

\[\text{Changed from: "The study was approved by the ethics committees of the participating cantons ..." into:}\]

"The study was approved by the ethics committees of the cantons BL/BS (Ethikkommission beider Basel), TI (Comitato etico cantonale), VS (Commission Cantonale Valaisanne d'Ethique Médicale) and ZH (Kantonale Ethikkommission Zürich) ..."

3) Please include author’s contribution section after competing interest.

Included in the revised manuscript.

Referee 1:

- Discretionary Revisions (which are recommendations for improvement but which the author can choose to ignore)

1. There is no standard definition for end-of-life care for cancer patients.

Published studies used various inclusion or exclusion criteria to define study populations and outcome variables. I am curious why the current study focused on the cancer related therapies during the last 30 days before death. Why not 3 months which was used in some published studies? Will it make a difference in the results if 3 month is used to define the outcome variable?

The time horizons used for assessments of end-of-life care in cancer patients vary indeed between 3 months and 2 weeks before death. We had two main reasons for using one month before death. The first was to achieve comparability of our results with some key papers, namely:

The second reason was that analyzing the last 3 months before death would have required extracting in-patient information for all patients hospitalized during the last 3 month before death. The number of patients hospitalized during the last month before death already brought us to the possible limit in terms of available resources and time. For these reasons, no related changes were made to the manuscript.

2. It would be helpful to include data such as stage at cancer diagnosis.

These data were not available to us.

or time from date of cancer diagnosis.

The table below shows this information by cancer type. These results are in accordance with what we would expect for these cancer types. As these times and cancer type represent related information (time as a continuous variable, cancer type as a class variable) we only used cancer type in our multivariable analyses.

<table>
<thead>
<tr>
<th>Cancer diagnosis</th>
<th>Mean time from first diagnosis until death in years (95%CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Colon</td>
<td>4.26 (3.68 - 4.83)</td>
</tr>
<tr>
<td>Hematol</td>
<td>3.46 (2.84 - 4.08)</td>
</tr>
<tr>
<td>Lung</td>
<td>1.96 (1.54 - 2.38)</td>
</tr>
<tr>
<td>Mamma</td>
<td>7.58 (7.07 - 8.10)</td>
</tr>
<tr>
<td>Other</td>
<td>3.88 (3.65 - 4.10)</td>
</tr>
<tr>
<td>Prostate</td>
<td>5.66 (5.16 - 6.16)</td>
</tr>
</tbody>
</table>

In Table 1, information on time from first diagnosis to death has now been included. These data will provide better understanding of health care delivery if they are available and shed lights whether the treatment was given with curative or palliative intent.

Information on the intention of the given cancer therapy was not available from the insurance data and difficult to extract from the information contained in the patients’ chart data.

In the discussion we state: “Unfortunately, we cannot differentiate between ACDT or RT given with a curative or a palliative intent.”

No additional changes were made to the manuscript.

3. Cancer therapy is directly connected with cancer type and stage. In my opinion, it would be a cleaner analysis to analyze each cancer separately.

There are two reasons why we did not analyze cancer types separately.

1. The major objective of the analysis was to assess the magnitude and significance of effects of demographic, geographic and insurance coverage-related factors, cancer type as such was treated as a co-variable in the analyses.

2. Sample size was calculated for all cancer patients, analyzing cancer types separately would have decreased the power considerably.

No related changes were made to the manuscript.
- Minor Essential Revisions (such as missing labels on figures, or the wrong use of a term, which the author can be trusted to correct)

4. Throughout the manuscript, the 1000 separator appeared as ‘ instead of , .

This has been corrected.

5. Discussion, paragraph 2

One of the reasons why lower percentages reported for Belgium or the Netherlands was due to different selection criteria. Sudden deaths (35% of total death) were excluded in the referred study.

In the study in question it is stated that:

“Patients dying as a result of cancer were identified by a question about the underlying cause of death. Those who had died totally unexpectedly and suddenly, as judged by the GP, were excluded from further analysis since our focus was on those patients with cancer for whom the provision of end-of-life care was a relevant consideration.”

In the discussion we changed the sentence

“The percentage of patients dying while hospitalized (61%) was much higher than the percentages reported for Belgium (29%) or the Netherlands (19%) [1] or in the USA (38%) [2].”

Into

The percentage of patients dying while hospitalized (61%) was much higher than percentages reported for Belgium and the Netherlands (29% and 19%, respectively, excluding patients suffering sudden death) [1] or the USA (38%) [2].

6. Supplementary table 1 multivariate logistic regression. The table is confusing. What are the meaning of spline 1a, 1b, 2a and 2b? Better notations or notes are needed.

We have reworked the left column of Supplementary table 1 and hope the notation and descriptions are now clearer.

Referee 2:

Major Compulsory Revisions

The population of interest is the population of deceased for cancer between 2006 and 2008 in the participating Swiss cantons. The actual sample derives from a complex system of merging from different databases. The degree the study population reflects the “true population” is not clearly reported in the methods section, and in the results section. This point should be commented in the Discussion.

We state at the beginning of the results section: “The distribution of patients over the four cantons differed slightly from the expected distribution the cause of death statistics (www.bfs.admin.ch) and the percentage Helsana insured population (BL/BS=9.8% expected 12.2%, TI=23.8% expected 17.2%, VS=9.4% expected 8.8%, ZH=55.3% expected 61.8%, see Error! Reference source not found. 1).” In the discussion we address the degree to which our study population reflects the “true population” in detail starting with “In addition, these
findings are not generalizable to all of Switzerland for several reasons. The study is based on data from only one insurance company (albeit one of the largest in Switzerland with a market share of about 20%) ...”

We were not sure what to add to the information already provided. Currently, no changes were made to the manuscript.

The analyses were performed on different populations as some information were not available. This point should be clarified in the results section.

The first series of analyses includes: the description of the overall study sample (N=3809; table 1) and the description of the hospitalised study sample with clinical information (N=2494; table 2). The overall hospitalised study sample is reported in Figure 1 (N=2608). According to that, table 1 is not useful, as all the analyses have been performed on the smaller study sample (1201 not hospitalised + 2494 hospitalised with clinical information).

This is a misunderstanding that may have been caused by Figure 1. All analyses were performed on the 3809 patients. In table 2, patient numbers are now provided to avoid confusion. Figure 1 has been re-organized to better distinguish the study population and the information available on this population and the title changed to “study patients”.

I would suggest: - a table reporting for each independent variable: total sample (N),; number and proportion (with 95%CI) of each of the dependent variables (hospitalisation, CT, RT, CT+RT). In my opinion the cantons should be reported as independent variables. This table should include age, although the results are also reported in figure 2. - a second table where the relationship between the independent variables (all those reported in the previous table) and the dependent variables (the four previously reported) are analysed in terms of univariate and multivariate association.

Table 2 has been amended to meet the first request of the reviewer.

We feel that presenting the univariable analyses would imply the addition of a lot of material but not contribute very much. Many of the univariable results are substantially confounded by other covariates and not very meaningful. In this observational study, the multivariable findings are clearly of primary importance. However, we will be happy to provide the univariable results in supplementary files if the Editorial Office advises us to do so.

The multivariable associations are provided in the supplementary table nr1.

The OR was correctly used by the authors. In the table, for each variable, the referent strata should be clearly identified.

We trust that this is now also clearer.

Minor Essential Revisions

In Figure 1 should be reported the number of patients used in the analyses (patients with clinical information). The flow-chart is correct, but this number is missing.

Please see new figure.

I do not find informative (and for a lesser extent a possible source of misunderstanding) reporting the means in figure 2.
The mean is the overall mean over the total study population. By showing the mean one can easily see which part of the age groups are above or under the mean.

We included the following legend for figure 2:
Legend: •••=proportion of patients with indication, dark grey area= 95% confidence interval on proportion, light grey bars= number of patients per age group, ----= mean proportion across all age groups

The results of the interaction analyses are interesting. Was there a statistic plan for analysing the interactions? If so, this point should be included in the methods section.

It was always clear (as a part of good practice) that we would test for all possible interactions but this is not explicitly stated in the protocol. Therefore, we regard the current phrasing in the methods section as the most appropriate: “In addition, all possible interactions between these variables were tested.” It was planned as it was to be expected that interactions would occur.

The percentage of hospitalization is rather high. I’m not sure that the availability of PC wards might explain these figures. Do you have any statistics about the use of these palliative care wards in the four cantons? Do you have any information about place of death of the patients from this sample?

We agree that the percentage of hospitalizations is rather high. As Switzerland has no specific “hospice” institutions, patients are often admitted in acute care hospitals. It was also often seen that patients were transferred from home or nursing home to a hospital because their clinical situation could no longer be handled.
We only know if patients died in hospital or not. Whether or not on a PC ward is not visible from the insurance data. Furthermore, as it was not intended to be a variable in the analysis we did not record this information from the patient’ charts. In reality we then found that even if hospitals had a specific PC ward, from the chart data it was not consequently available on what ward the patient was while dying.
This was reflected in the discussion and we have amended the text slightly to say: “One reason for this finding may be a low availability of hospice care facilities in Switzerland. On the other hand, many acute-care hospitals have palliative care wards to which end-of-life patients may be transferred. We were not able to distinguish the types of wards where patients stayed and therefore the percentage of patients who died in a true acute-care setting may be substantially lower than 61%.”