Reviewer's report

Title: Increased health care utilization by survivors of childhood lymphoblastic leukemia is confined to those treated with cranial or total body irradiation: a case cohort study

Version: 2 Date: 28 March 2014

Reviewer: Corina S. Rueegg

Reviewer's report:

Minor and Major Essential Revisions

The authors have answered most of my comments satisfactory and I think the revised manuscript has improved. Besides some minor formal comments, I only have some more little concerns left regarding structure and understanding of the analysis they performed.

1. Abstract; Results: You have added the unit “days during study period”. However, we don’t know the length of the study period. Could you either indicate these in the methods section or add it to the unit to give the reader an idea about the absolute burden of these hospital contacts.

2. Methods; Paragraph 5: Add the comparison of irradiated and non-irradiated survivors in your aims, because this is a main objective of your article (even stated in the title).

3. Methods: Please add a paragraph with subtitle where you describe all your exposure variables: which one did you assess, how did you code them, why did you choose selected cut-offs, how do you name them etc. You can take all the description of the exposure variables from the analysis part and move them to this paragraph.

4. Methods, Outcome variables: I would include here the information you wrote at the end of the first paragraph of the statistical analysis where you describe the cut-offs/recoding of your outcome variables. Please argument also shortly, why you chose these cut-offs.

5. Methods, Statistical analysis, Paragraph 1: At the end of this paragraph, you wrote that you will display continuous variables as median and interquartile range. In effect you show later median and range. Adapt either of the two things. I would prefer to keep the range and just delete the word “interquartile”.

6. Methods, Statistical analysis, Paragraph 1: Here you have to mention everything you did for your descriptive analysis, i.e. all the analysis to get the results of Table 1, Table 2, Table 3 and Table 4. Please expand that all your steps are clear to the reader.

7. Methods, Statistical analysis, Paragraph 2+3: I still think it is very difficult to
follow exactly what different models you did to investigate your risk factors. I would organize your analysis steps based on your tables. For Table 5 (to assess the risk of treatment) you performed 3 multilevel multivariable models, one logistic and two ordinal. State the outcome and exposure for each model and for what you adjusted additionally. In addition you did a dose-response analysis for cranial irradiation dose. Here again, how was cranial irradiation dose exactly included in the model (describe in the paragraph on exposure variables), for what did you additionally adjust? For Table 6 (to assess socio-demographic risk factors) you performed again 3 multilevel multivariable models. Explain again your outcome, exposure and confounding factors you used in each model.

8. Results, Rate of hospital contacts: Like for the abstract, state how long the study period was to give us an impression on the absolute burden.

9. Results, Rate of hospital contacts: At the end of this paragraph you show results on an analysis without TBI patients but you never mentioned this in the analysis part or show any results in the tables. Why did you analyse this only for TBI? How are the results without cranial irradiated patients? Or without relapsed patients?

10. Results, Risk factors for hospital contacts: I would divide this paragraph into two parts. One for the treatment risk factors compared to controls and one on socio-demographic risk factors comparing survivors and controls.

11. Results, Risk factors for hospital contacts: At the end of paragraph two, you state your results on relapse. I would report these results in the paragraph “rate of hospital contacts”, because it’s only the results from your stratified proportions and you did not really test the risk in a multivariable model.

12. Results, Risk factors for hospital contacts: You analyse the influence of radiation dose on the hospitalization risk. Why did you not make a real dose-response analysis with the two continuous outcomes? You could show a nice graph if a dose-response relationship really exists. Is this OR you report univariable or have you adjusted for other variables? Please state as that in the results part/methods part.

13. Results, Risk factors for hospital contacts: Please distinguish better in reporting between a) risk factors for hospitalization in survivors and controls, b) differences in risk factors between survivors and controls (interaction term and different directions if present). Was socio-economic status dropped during your backwards model building approach? Or why did you not show this results in your table? Please state what variables you all tested and whether or not they were associated and whether the association differs between survivors and controls.

14. Discussion, Paragraph 2: For the CCSS and BCCSS you only state relative information (ALL more at risk than others). If available in the literature please state also absolute proportion of hospitalization (like for the Canadian study) and explain possible differences.
15. Table 5: Report in the title (survivors compared to controls), footnote or table itself what the reference is (controls). Report in the footnote for what other variables this model is adjusted. You have * and # in your table that are not explained in the footnote. I think this should be 2 and 3.

16. Table 6: As mentioned in the results section, state in the footnote which factors were tested but not included in the final model because not associated. What age did you take for the controls when you have age at diagnosis for the survivors? Please indicate this in the methods part when describing the model and perhaps also in the footnote of the table.

**Level of interest:** An article of importance in its field

**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.