Reviewer's report

Title: Childhood cancer mortality in Japan, 1980-2013

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Reviewer: Danny Youlden

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This paper uses data compiled by the Japanese Ministry of Health, Labour and Welfare to describe mortality trends for the period 1980-2013. Geographical differences according to Prefecture were also examined.

My comments and suggestions are as follows:

Major Compulsory Revisions

1. Methods, Paragraph 4 – Could the authors please clarify whether the analysis by Prefecture is the place of residence at diagnosis or death? If the latter, a comment needs to be included as to how this might affect the results reported in this study. In particular, given that a family may move following a diagnosis of cancer to be closer to treatment facilities etc., the geographical distribution at the time of death may be skewed in comparison to the geographical distribution at the time of diagnosis.

2. Methods, Paragraph 3 – It is not clear as to why the AAPC for the period 2000-2010 would be used to compare results between countries, particularly if there was a significant change in the trend during this period. Rather, it would be preferable to make any comparisons based on the actual joinpoint trends. I would therefore suggest omitting the AAPC data from Tables 1 and 2 and comment on the APC rather than the AAPC in the Results section, as swapping between the two measures could also be somewhat confusing for readers.

Minor Essential Revisions

3. Methods, Paragraph 1 – Is any information available on the quality of data contained in the Vital Statistics? Are cancer deaths considered to be complete, and what percent are histologically verified?

4. Methods, Paragraph 4 – It would be useful to include some general summary information on the Prefectures for readers who are not familiar with the geography of Japan.

5. Results, Paragraph 1 – The average mortality rate due to CNS appears to be higher than 0.7 per 100,000 in the other countries as shown in Figure 1, particularly among boys.

6. Results, Paragraph 2 – It would be useful to mention the significant APCs in this paragraph eg. “Mortality of all cancer combined for Japanese boys decreased significantly by an average of 3.9% per year from 5.5 to 2.0 per
100,000 population from 1980 to 2003…”.

7. Results, Paragraph 7 – It would be helpful to readers if the elevated SMRs for the Prefectures listed were inserted into the text. Also, were there any Prefectures where the SMR was significantly lower than expected?

8. Discussion – The following statements require references:
Paragraph 2: “Early diagnosis and progress in therapies for childhood cancer over recent decades have greatly improved prognosis among pediatric cancer patients.”
Paragraph 3: “Standardization of the applied protocol and the expanded use of chemotherapeutic agents and combination regimens have contributed to the improvement of treatment, resulting in a dramatic increase in survival of childhood leukemia.”

9. Discussion, Paragraph 4 – What is meant by the statement that “The mortality rates of CNS tumors in Japan remained unfavourable during 1980 through 2013…”? However, in Paragraph 1 of the Results section, the authors state that “Mortality rates of CNS tumors in Japan were low relative to those in other countries…” These two comments appear to be contradictory without further explanation.

10. Discussion, Paragraph 6 – Apart from the analyses conducted using the WHO mortality database to evaluate the results for Japan against other countries, it would be worthwhile to include other published data on childhood cancer mortality for comparison. For example, see http://www.ncbi.nlm.nih.gov/pubmed/22739323.

11. Figure 1 – Why were 5-year averages used here instead of showing trends based on annual data? The latter approach would probably give a clearer picture of the differences between countries. It would also be preferable if the data shown for Japan were consistent in Figures 1 and 2.

12. Table 2 – If a minimum of 4 observations are required between joinpoints (i.e. 6 observations including the joinpoints), why are trends shown for 2008-2010 for all cancers and leukaemia for girls in Italy, from 1980-1983 for lymphoma among girls in Japan and 2007-2010 for malignant bone tumours among girls in the UK? This might also affect the corresponding information reported in the Results section.

13. Figure 3 – The highest SMR category is labelled as >100, but this appears to be incorrect.

Discretionary Revisions

14. Methods, Paragraph 2 – The standard coding system for reporting childhood cancers is the International Classification of Childhood Cancers (third edition). If at all possible, deaths should be recoded from ICD-9 and ICD-10 to ICCC-3 to allow direct comparisons with other studies.
15. Methods, Paragraph 3 – I would suggest increasing the minimum number of observations allowed between joinpoints to at least 6 or 7. With the small numbers involved for specific types of cancer, using only 4 observations between joinpoints could result in some dubious trends being reported.

16. Discussion, Paragraph 9 – The second sentence regarding inaccuracies in trend analysis by considering only the first and last years of a data series is not necessary and should be deleted. It is also a bit confusing because changes in both incidence and mortality are mentioned.

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 have authored a paper on childhood cancer mortality trends in Australia, and have suggested that the authors consider these results in the Discussion section of their paper. Other than that, I declare that I have no competing interests.