Reviewer’s report

Title: Childhood cancer mortality in Japan, 1980-2013

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Reviewer: Amy Linabery

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General comments:

The authors have examined mortality rates and trends in childhood cancers (i.e., in children and adolescents <15 years of age), overall and for specific cancer morphologies/sites, in Japan during the period 1980-2013. They additionally compare the trends in Japan in 1980-2013 to those in four other economically developed countries in 1980-2010. Their analysis showed a reduction in mortality rates over time for all cancers combined and for most specific cancer diagnoses. The authors speculate that the incidence rates are unlikely to have changed by a comparable amount during the time period examined, and thus reason that the reductions in mortality are ascribed to improvements in treatment. The one notable exception was a slight, but significant increase in CNS mortality rates that seems to have arisen in the most recent observation period.

Overall, the paper would be strengthened if the authors could clarify a few sections of the paper (mentioned below) and add some additional interpretation of the data.

Major Compulsory Revisions

1. After reading this paper twice, it seems that the authors have not adequately addressed the fact that the mortality rate for CNS tumors in Japan is lower than that seen in 4 other economically developed countries, but has increased in recent years while the rate has decreased in 3 of 4 the other countries examined. This is especially puzzling given that the CNS treatment regimens used in the other countries are published and, according to the authors on page 11 of the Discussion, similar treatment achievements have been made in Japan. On the other hand, given the rarity of CNS tumors in childhood and early adolescence, perhaps it is a statistical anomaly (i.e., a higher rate due to random fluctuations in the data), that will not be evident after more time has passed. Importantly, it seems that this observation alone would warrant an active nationwide surveillance program.

2. In the second paragraph of the Background spanning pages 3-4, the authors should mention that there are local childhood cancer registries (as mentioned in the Discussion – references 12 and 14), but no nationwide registry in Japan.

3. Throughout the Methods section, the authors should be mindful to specify which countries’ data are included in which analyses and which years are being examined.
4. The Results section seems to jump around a bit. In the first paragraph, the first and third sentences refer strictly to the Japanese data. The second, fourth and fifth sentences mention data from all of the countries. The second paragraph refers to Japan only. I suggest describing the overall rates/trends within Japan first, and then comparing the overall and cancer-specific rates in Japan to rates in the other countries.

5. The value of the comparison of mortality rates across the 47 prefectures is unclear, given the relatively small number of cases diagnosed with cancer during the period 2005-2013 and given the high survival rate during this same period. In addition, in the last paragraph of the Results on page 9, the authors indicated that mortality rates were higher for a few prefectures for boys and for a few different prefectures for girls, however, the authors do not interpret these results further in the Discussion on page 12. Are the prefectures listed for boys and girls different in notable ways (i.e., measures of socioeconomic status, SES) from the other prefectures? Are there differences in access to care in Japan based on SES?

6. On page 9 of the Discussion, the authors speculate that the incidence rates have not changed by a comparable amount to account for the observed reductions in mortality: “Changes in the incidence of childhood cancer[s] are likely to be small and limited, so the declines in childhood cancer mortality in the 1980s and 1990s appear to be mostly due to improved outcome[s].” Do the authors have any data to substantiate this claim? (Please provide references.)

Minor Essential Revisions

7. Throughout the manuscript: Due to the rarity of childhood cancers, it is standard practice to describe rates per 1,000,000 persons (instead of rates per 100,000 persons as is commonly done for adult cancers).

8. In the first paragraph of the Background on page 3, it was surprising to read that cancer was the most common cause of death in Japanese children aged 1-14 years, given that the authors’ prior paper from 2009, they indicated that cancer deaths were the fourth leading cause of death for children 0-14 years. Could the authors verify or comment on this?

9. What proportion of deaths due to childhood cancer are captured using Japan’s death certificate data? (The authors’ prior publication from 2009 indicates 100% ascertainment of deaths.)

10. The year of the World Standard Population (e.g., WHO 2000-2025), as well as a reference, should be included in the first paragraph of the Methods section on the bottom of page 4.

11. In the Methods section on pages 4-5, the authors should provide a bit more information regarding the nature of the data used from the other 4 economically developed countries and obtained from the WHO mortality database.

12. Throughout the Methods section, the authors should be mindful to specify which countries’ data are included in which analyses and which years are being examined.
13. At the top of page 13 in the Discussion section (line 218), remove the words “… incidence or …”, since incidence rate changes were not examined in the current paper.

Discretionary Revisions
14. In the Conclusions paragraph on page 14, suggest replacing “address” on line 243 with “improve surveillance of”.

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

Quality of written English: Needs some language corrections before being published

Statistical review: No, the manuscript does not need to be seen by a statistician.

Declaration of competing interests: I declare that I have no competing interests