Author's response to reviews


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Author's response to reviews: see over
POINT-BY-POINT RESPONSES TO REVIEWERS’S COMMENTMENTS

Reviewer: Archie W Bleyer

• Response to Major Comments

(1.) **Abstract:** The incidence rates are now presented separately in the results section for ages 0-14, 15-29 & 30-39.

(2.) **Nomenclature:** The incidence rates are now expressed as “per million persons per year”. The text has been changed throughout the manuscript.

(3.) **Background:** The rates are for all ages and have been standardized to the world population. This is now stated in parentheses at the end of the second sentence, paragraph 1.

(4.) **Methods and Table 2:** We disagree with the reviewer’s comment concerning the appropriateness of standardizing incidence rates to the world population. World standardized rates are used extensively in the literature and provide an easy way to make comparisons between different studies.

(5.) **Methods:** Exact cause of death was not available for this dataset. However, we estimate that only 5 cases would be expected to have died from other causes during the study period. Therefore, analyses using relative survival would give similar results.

(6.) **Discussion, para.2:** We have deleted the words “and chondrosarcoma” from this sentence.

• Response to Minor Comments

(1.) **Abstract:** The regression in the Methods section is now plural.

(2.) **Sarcoma** in Ewing sarcoma is now lower case on page 7.

(3.) **Page 12:** We have changed the word “highlighted” to “indicated” on page 12 (2 occurrences).

(4.) **Table 3:** Age group is now specified as “0-39 year olds”.

(5.) **Data:** Survival rates are now expressed as whole numbers (changes made in text and Table 3).

Reviewer: Sean Scully

• Response to Comments
(1.) We agree that the data presented are consistent with the data contained in the NCI SEER database (references included in first sentence of third paragraph of Discussion).

(2.) We agree that the word “older” may be misleading and have changed the wording throughout the text.

(3.) The group of other tumours is now omitted from all analyses, although the number of such cases is still stated in Results, paragraph 1.

(4.) The basic case data were accurately recorded by the registry, but clinical data were deemed inaccurate. Therefore, the analyses of incidence and survival were reliable.

(5.) We agree that the grouped results for all bone cancer may not be useful. We now only present separate disease specific analyses for osteosarcoma, Ewing sarcoma and chondrosarcoma.

Reviewer: Piero Picci

• Response to Comments

(1.) We agree with the reviewer that there is a lack of epidemiological data regarding rare tumours such as bone tumours. Data provided from the regional registry (analysed in this study) is highly reliable.

(2.) There was a mistake on page 9. Survival for chondrosarcoma was better than for osteosarcoma. The sentence has been corrected to read: “Significantly better survival rates were found for chondrosarcoma compared with osteosarcoma ($P = 0.001$) …………”

(3.) We have re-worded the statement at the bottom of page 9, which now reads: “For osteosarcoma there was a non-statistically significant improvement in survival during the study period (HR per annum = 0.98; 95% CI 0.95 – 1.01; $P = 0.18$)”.

(4.) We have included the new reference (Mirabello et al, Cancer 2009) and added the following sentence: “Another recent study from the USA analysed data from the Surveillance, Epidemiology and End Results Program and has found that there has been no statistically significant improvement in survival from osteosarcoma (at all ages) from 1984 to 2004”. (Discussion, 4th paragraph from the end).

Reviewer: Dae-Geun Jeon

• Response to Comments
(1.) **Introduction:** We have analysed temporal changes in incidence and survival in 0 – 39 year olds. The reviewer is correct. Older ages (>40 years) is beyond the scope of this study.

(2.) **Discussion, 3rd paragraph from the end:** We recognize that differences between our study and the US study may be due to age of patients. We now include the following sentence: “However, better survival of osteosarcoma compared with the US study is likely to be due to the exclusion of patients aged >40 years from the present study.”

(3.) **Discussion, penultimate paragraph:** We have added the additional reference (Harting *et al*, *J Cancer Res Clin Oncol* 2009) and the following sentence: “However, most of these studies have found worse survival in cases of osteosarcoma aged >40 years and it is very well recognized that age is a prognostic factor [26].”

**Other Issues**

(1.) We now outline the advance of our present study over our previous article. Specifically, our present submission analyses data on 0 – 39 year olds, whereas our previous article included only data on 0 – 14 year olds. It is important to analyse this age-range as the incidence of both osteosarcoma and Ewing sarcoma peak after childhood (in those aged more than 15 years). The final paragraph of the Background section has been amended.

(2.) The background section of the abstract has been revised.