Author's response to reviews

Title: Birth characteristics and the risk of childhood leukaemias and lymphomas in New Zealand: a case-control study.

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Author's response to reviews:

Eratxe Puebla
Senior Assistant Editor
BMC-series journals

Dear Eratxe Puebla,

Thank you for sending us the comments of the reviewers. We are grateful for these, and have amended the manuscript to take account of them. The changes and our responses are detailed below:

REVIEWER: CHARLES A STILLER

Thank you for your positive comments about the design and usefulness of this study.

1. We have added a paragraph to the Discussion about Hodgkin's disease (our findings, aetiology and possible relevance of exposures at the time of birth).

Parity derived from the birth records is within existing marriage, so there is missing data on parity in this study if the parents were not married. Those with Hodgkin's disease, having an older age range, were more likely than those with other diagnoses to be born in earlier years. Marriage rates declined over time during the birth years studied. Consequently, proportionately more of the Hodgkin's disease parents were married. We tested this assumption in a logistic regression analysis and showed that it was correct. Once birth year was adjusted for, the apparent difference between Hodgkin's disease and the other conditions studied relating to missing data disappeared. This issue is now summarised in the Discussion.

2. We've now quoted the papers by Reynolds et al. and Ma et al. where relevant in the Discussion.

3. In the Background we've made revisions to give a good description of who and when we were referring to with unemployment, low income, and unmarried status.

4. The point at which we excluded cases born outside NZ is now specified in the Methods. A new paragraph there gives the relevant numbers for those who were ineligible or who could not be included for other reasons.

5. We have added a definition of urban/rural status to the Methods, and given the relevant reference.

6. The controls were matched to cases by sex, and birth year and quarter (Jan-Mar, Apr-Jun...). This is now clarified in the Methods. Because it is somewhat difficult to describe in a concise way, we are still using the shorthand concept of age matching but have explained exactly what we mean by this. Let us know if you'd rather have us put this in a different way.

REVIEWER: RICHARD JQ McNALLY

Major Compulsory Revisions
1-4. We have rewritten the Abstract to take care of of these points.
5.6. We have made the suggested amendments in the Background

7. You are right in saying that we could not answer such a large question as the one we have posed. We have rewritten the relevant sentences to make this clear.

8. We assigned urban/non-urban status on the basis of the relevant statistical boundaries used in the 1971 New Zealand Census; this is now stated in the Methods and the relevant reference is cited and included in the References.

9. The basis for extending the age range of Hodgkin's disease is now given in the Methods.

10. The Elley-Irving scale is now described in the Methods, cited, and referenced. See point 8. above for urban/non-urban status.

11. The penultimate paragraph of the Methods has been altered to deal with the issue raised about plausible confounders.

12. The p value of 0.10 from the ALL trend analysis for paternal age is now mentioned in the text.

13. On the basis of the p value above, one cannot reject the null hypothesis, so although we have now mentioned the finding in the Discussion, we do not feel comfortable speculating about this result. The other reason that we think it is likely to be due to chance is that the direction of this non-significant effect (a reduction in risk with increasing paternal age) is the opposite of the direction found elsewhere. For example, the very large study by Dockerty et al. in England and Wales (our reference #7) found a highly statistically significant trend of increasing ALL risk with higher paternal age (p=0.002).

14. The relevant biases in some earlier studies are now listed.

15. The specific limitations of interview-based and record-based (eg linkage) studies are now outlined in the Conclusions.

Minor Essential Revisions

1. We agree that the word 'overseas' is confusing internationally. We no longer use the word in the paper. Its use is something of a habit for New Zealanders as our whole country is surrounded by ocean.

2. We've solved this issue by changing the sentence in the results section of the Abstract.

3. We've rewritten this.

4. We've added a reference to back up the statement about feline leukaemia virus.

5. We now say 'were analysed' as suggested.

6. Thank you for pointing this out. We have made it clearer.

The paper is now much improved, and we hope that you will now find it suitable for publication in BMC Blood Disorders.

With best wishes,

Yours sincerely,

John D Dockerty and Donny IM Wong.