Reviewer’s report

Title: Ethnicity and incidence of Hodgkin lymphoma in Canadian population

Version: 3 Date: 9 January 2009

Reviewer: Marie-Claude Rousseau

Reviewer’s report:

Summary: The authors investigated, using data from a population-based case-control study conducted in six provinces of Canada, the association between ethnicity and incidence of Hodgkin’s lymphoma (HL) adjusting for medical history and pesticide exposure. They reported that compared to North Americans descendents, the risk of HL was significantly greater among the Eastern European and Western European descendents.

General impression: Although the revised manuscript was improved, some specific issues remain to be addressed before publication. Also, the discussion needs to be more thorough with respect to the main exposure studied.

Major Compulsory Revisions

Justification for medical conditions as risk factors for HL

1- The two sentences that the authors have added are not quite sufficient justification for the extensive list of medical conditions that they have considered. What made them all pertinent? Is there a postulated biological mechanism in general, or a few mechanisms specifically for subgroups of conditions? If the purpose is to adjust for the association between ethnicity and HL for confounders, this list should be restricted to the conditions for which there is reasonably convincing evidence of an association.

Explanation of matching strategy and use of conditional regression analysis

2- In response to questions from both reviewers on the matching and choice of conditional regression as the analytical technique, the authors reiterated that their study was matched and thus that conditional regression should be used. They have added information in the Methods section explaining in more details how the control selection and matching was performed. However, some further clarifications may be necessary. It is not clear whether the sentence “The study had approximately three matched controls for each HL case.” refers to the original study or to the current analysis. It should be clear that the current analysis uses all controls. The ratio of controls to cases seems to be approximately 5:1 rather the 3:1. More importantly, the conditional analysis uses strata defined on “cross-classifying 5-years age intervals and province of residence”, as mentioned by the author in response to the other reviewer. This needs to be mentioned in the statistical analysis section, as it is not clear with the current description how the matching strata were defined for analysis.
Definition of ethnicity

3- In the definition of ethnicity given on p.8 of the manuscript, the authors should specify, as in their response to our previous comment, that any individual who had less than 3 grandparents from the same ethnic group was also classified in the “other” category. Since this catch-all category is quite prevalent (28% of cases and 27% of controls overall), I would recommend showing in Table 3 the breakdown into all specific groups. This would include the ethnic groups for which presumably numbers are too low for separate analyses (African, American Indian, Central American, etc.), those with unknown ethnicity because of adoption, and those with mixed ethnicities (< 3 grandparents from same ethnic group). The grouped category “Other” could still be used for the analysis, but at least the distribution of ethnicities within it would be known.

Definition of exposure to pesticides

4- Although informative, Table 1 should rather be presented as an Appendix to the manuscript. If I understood well, this variable is used for adjusting and not the main focus of the analysis. Was exposure to Dichlorprop defined as “ever vs. never”? This is still unclear from the manuscript. It seems that those who reported < 10 hrs/yr of exposure to herbicides would be considered as never exposed. I infer that those who reported > 10 hrs/yr of exposure to herbicides but did not report Dichlorprop exposure on phone interview would also be considered unexposed, whereas those who reported such exposure, whatever the frequency, would be considered as exposed. The exact algorithm for assigning pesticide exposure should be more clearly explained in the methods.

Discussion

5- It seems to me that the discussion still needs work. The authors do not discuss their findings very much. The possible reasons of the observed increased incidence of HL within European descent populations are not explored, whereas too much emphasis is placed on medical conditions and exposure to pesticides which were supposed to be used as adjustment variables in the models. I am not clear on what the take-home message is, and on the implications of these findings.

Minor Essential Revisions

6- HD was changed to HL, however not throughout. See middle of Background paragraph and tables.

7- Repetition of the same sentence at the end of the 1st paragraph of Background (second to last), and at the beginning of 2nd paragraph of Background.

8- It is surprising that there is no section on medical conditions in the methods section. Presumably, subjects were asked in the questionnaire whether they have ever been diagnosed by a physician for these conditions. Is that so? This information should appear in the methods.
9- Please delete footnote (a) under Table 2. It does not seem to belong there.

Discretionary Revisions
10- I would suggest moving the participation rates (first 2 sentences of the discussion) to the Methods or Results section.

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

Quality of written English: Acceptable

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.