

Reviewer's report

Title: Occupational Exposures and Non-Hodgkin's Lymphoma: Canadian Case-Control Study

Version: 1 **Date:** 11 April 2008

Reviewer: Pierluigi Cocco

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Several into large multinational collaborative studies on lymphoma aetiology are currently under way, that only can achieve the statistical power necessary to test hypotheses related to rare disease entities or specific occupational and environmental exposures. However, it is this reviewer's opinion that local studies do maintain an important role, as long as they 1. suggest new hypotheses, and/or 2. are able to explore in detail associations that have been established, but not well defined for lack of detailed information in multicenter or pooled studies. Unfortunately, this paper, in its current version, does not comply with either requirement. The authors should make some additional effort to get the best from their potentially rich material. It is this reviewer's hope that the following suggestions and comments might help.

Major compulsory revisions

1. In their analysis, the authors consider two types of job entries in the individual work histories of study subjects: a. "longest" held jobs (those lasting one year or more), and b. short term employments, such as summer jobs and similar. Using the superlative adjective "longest" generates a linguistic misunderstanding that leads the reader to interpret it in relation to any other job entry in the work history of the same study subject. Such strategy might appear a non sense to the unaware reader, asking himself what convenience is out there in spending so much time and resources to conduct a questionnaire study to get complete work histories, when the longest held job during a lifetime may be more easily available from death certificates or other publicly available resources. Wording itself causes such a confusion. On the other hand, the authors should clearly explain in the methods section their rationale for analyzing short term employments as well. For instance, are these repeatedly held by the same subject over the years? If so, this reviewer sees a creative new feature in this study and encourages the authors to explain in the methods what were the minimum number of job entries to consider a short term employment for analysis. Alternatively, simply fix a minimum duration for considering a job entry (6 months – 1 year consistently with most literature) and cumulate years for the same job if repeated in the work history. Showing results for a summer job as chicken farmer that might have been held for three months as a student does not appear to convey much of a meaning. Once the criteria for selecting occupations are made clear (minimum duration, and minimum number of subjects), use an unique table to show number of cases and controls, and odds ratios for all the occupations. Negative and not significant results might be interesting for other scholars as

comparison terms with the rest of the literature.

2. Apparently, the authors used a very generic coding for occupations and did not code industries at all. Apart from the need of mentioning in the Methods what coding system, if any, was used to group the occupational titles, this is unfortunate, as the gain in statistical power is accompanied by a great loss in biological meaning of their findings. In this reviewer's view, it is preferable presenting results for a small number of well defined occupations rather than for a series of generic and bureaucratic definitions. For instance, starting from the hopefully commonly shared belief that our epidemiological work is meant for preventive purposes, how do the authors think the term "manager" can be interpreted? Bureaucratic definitions such as manager, labourer, or retired, might be helpful for socio-economic analyses, but, if alone, have not any occupational health significance. Under such perspective, even the definition of farmer and even pesticide, are too generic, but at least they can restrict the range for future studies investigating in more detail on risk factors within such broad categories. Broad definitions and variations in farming activities and type of pesticides should be discussed as sources of inconsistency across findings in different studies, which the authors address only on line 10-11 of the background section. Heterogeneity of work circumstances and exposures within such generic definitions implies that only conditions with high prevalence among subjects fitting them might account for the excess, and these are more likely to be socio-economic than occupational in nature. Alternatively, a number of different exposures/conditions might sum up their effects, which suggests the direction for future studies. To summarize: a. be more specific in defining occupations (4 digit codes are suitable); b. predefine in the methods the duration and number of study subjects criteria for considering an occupation worth of analysis; c. present odds ratios along with number of cases and controls for all occupations in one table divided in two sections: ever held (above the pre-defined minimum duration) and long held occupations (e.g. 10 years or more); and d. when and if applicable, use duration as a surrogate for cumulative exposure to calculate trends, which are helpful in the inferential process.

Minor essential revisions.

1. First paragraph of introduction. A plateau in the incidence rates has been recently shown in the U.S. and some European countries. Is anything like that going on in Canada as well?

2. Defining "soil/field" as an exposure is awkward. Inorganic dust should be the proper term. Anyway, on page 10 (discussion) the authors do not mention dust as the reported exposure in reference # 17, but the fact that " Forest and the soil conservationists are often occupationally exposed from mixing and /or applying pesticides as a part of their regular duties [17]". Organic dust including grain, wood and textile dust should be cited among the occupational exposures suspected of a role in lymphoma aetiology.

3. The classification criteria for diagnosis of non Hodgkin's lymphoma need to be clarified in the Methods section. It seems clear that HL and MM cases were not

included, but due to the frequent changes in Lymphoma classification, it would be suitable to be explicit about it to avoid confusion in the reader.

4. The response rates of for cases and controls should be reported in the methods section. The low participation rate among controls was presumably expected, considering also that a postal questionnaire was administered, and the authors properly addressed it in the discussion. However, the participation rate seems low also among cases. Reasons for not participating (death, change of address, refusal, et cetera) should be highlighted in the discussion for either study groups.

5. What were the “Statistically significant ($p \leq 0.05$) variables and important explanatory variables [that] were considered for the final multivariate model”?

6. This reviewer was quite surprised in seeing that 12 cases and 12 controls reported to radium. Can the authors explain in what occupation and industries, when and how long before lymphoma diagnosis?

7. Discussion: avoid discussing together ionizing and non ionizing radiation. Update the references on UV light and lymphoma.

8. Reorganization of the discussion, some rephrasing and some review of the typing is necessary. See for instance line 15 on page 10 “benzene exposure may increases the risk of NHL”; and lines 17-18 on page 18: “Duration of exposure as the longest held job was not significant ($p=0.088$) but it shows increased risk of NHL with longer duration of exposure”.

Minor discretionary revisions.

9. Results. Please explain what a seed cleaner is and what exposures might be involved.

10. Odds ratio for ever exposure to cutting oils was significantly lower than unity. Unless authors have any reason to suspect a protective effect, it seems a chance finding, irrelevant, and pointless. The conclusion reports: “NHL was associated with personal history of cancer, exposure to cutting oils,...” However, Table 5 shows a negative risk; and on page 7 (Odds ratio of those who were ever exposed to cutting oils was significantly lower than those who were not exposed”) and page 8 (“Exposure to cutting oils at work independently was associated with decreased risk of developing NHL, the rationale for which is unclear”) a negative result is repeatedly reported.

11. Second paragraphe on page 10. Woodworkers are not mentioned in the results nor in the tables. Either cite the finding in the results as a negative one or drop the paragraph from the discussion.

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.