Author's response to reviews

Title: Temporal trends in the frequency of twins and higher-order multiple births in Canada and the United States

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Author's response to reviews: see over
REVIEWER’S REPORT #1

Title: Temporal trends in the frequency of twins and higher-order multiple births in Canada and the United States
Version: 1
Date: 18 March 2012
Reviewer: Leanne Bricker

Reviewer’s report:
This paper reports trends in twin and higher order livebirth rates in the USA and Canada (excluding Ontario) over a 19 year period (1991-2009). It clearly sets out in the introduction why this is important (perinatal and long-term risks of multiple pregnancy) and what might affect the trends (increasing access to ART and changes in ART practices based on new guidance). It is well written and easy to understand. I am unable to comment on statistical methodology as this is not my area of expertise but it seems appropriate to the untrained eye.

A few issues which I think would enhance its value as a paper:

1. Introduction paragraph 3 mentions that new guidance for ART in terms of embryo transfer number. It would be useful if this information was enriched by providing years guidance introduced which would impact on clinical practice. For example the publication date for the USA guidance (ref 27) is 2009 – therefore it is not clear if this guidance would have embedded and had any impact at all as the data is for 1991-2009. (essential revision)

Author’s response:
We agree that the background information on guidelines for embryo transfer would be enhanced with more information on the timing of the release of these recommendations, thus, the paragraph in question has been modified (see below):

“In response to the high rates of multiple births and ever-improving implantation rates with ART, guidelines advocating limits on the number of embryos transferred during ART procedures emerged in Canada (in 2006 and 2010) [25,26] and the United States (first in 1998 [27] and most recently in 2009 [28]) in an attempt to reduce the incidence of iatrogenic triplet or higher-order gestations.”

2. The Ontario data is mentioned in some detail in discussion (and it is well explained why not included in overall Canadian data) but I think as it is data presented it should be in results section and in methodology it can be explained why this data is given separately. (essential revision)

Author’s response:
The Ontario results have been moved from the ‘Discussion’ to the ‘Results’ section of the manuscript, as requested. Additional information regarding the justification for separate reporting of Ontario data has been added to the ‘Methods’ section (see text below).
“Data from Ontario were excluded from the calculation of overall rates for Canada due to data quality issues with respect to live birth registrations. In particular, the under-registration of live births may have affected the reporting of the number and rate of multiple live births [1,32]. A more in-depth discussion of this data quality problem can be found elsewhere [1,32]. Ontario rates are described separately in the results, and figures including Ontario data are shown in an Appendix.”

3. In discussion it would be interesting if authors tackled the issue / hot potato (if you like) relating to guidance vs legislation in terms of ART practices. My personal view is that if numbers of embryos transferred were legislated (with caveats of course) that might have higher impact on absolute numbers of multiple births particularly higher orders, rather than guidance. This would be particularly effective in the private sector as my impression is that often the clinicians are pressurised to transfer higher numbers by the fee paying client. (discretionary revision)

Author’s response:
We agree that the relative impact of guidance versus legislation on the number of embryos transferred during ART procedures is of great interest. We have cited examples from two jurisdictions demonstrating the impact of legislation of embryo practice patterns (in Quebec, Canada and in Sweden, see references #38 and 39, respectively). However, it is challenging to present a comprehensive summary of the impact of guidance versus legislation within this manuscript, since embryo transfer practices appear to be influenced by myriad other factors in addition to legislation (see reference # 35), and even in the presence of legislation, there are important contextual differences in the scope and uptake of the statutes which affect practice (see reference #36). We have briefly addressed this issue in the ‘Discussion’ and now cite two international reviews which have attempted to compare embryo transfer practices against the background of legislative and other contextual factors.

Level of interest: An article of importance in its field
Quality of written English: Acceptable
Statistical review: No, the manuscript does not need to be seen by a statistician.
Declaration of competing interests: No to all
REVIEWER’S REPORT #2

Title: Temporal trends in the frequency of twins and higher-order multiple births in Canada and the United States
Version: 1
Date: 9 July 2012
Reviewer: Steve Cole

Reviewer’s report:

Major Compulsory Revisions

1. The references for the original data are incomplete. The authors only reference the 2009 US National Vital Statistics Report. I assume that the data on live births for the different time periods from both countries are derived from more than just this one report. That being the case, all published reports that have had data extracted from them should be included in the references.

Author’s response:
The data contained in this manuscript originate from 19 years of vital statistics data collection in the United States and Canada. The singular citation provided for the U.S. data (reference #2) presents not only the final data on live births for 2009, but also historical data back to 1980. The upper panel of Table 27 of the report (see page 64: http://www.cdc.gov/nchs/data/nvsr/nvsr60/nvsr60_01.pdf) contains each of the data points used to populate all of the tables and graphs in our manuscript. Given the availability of historical data in the referenced report, we do not feel it is necessary to cite additional reports for the U.S. data; however the citation itself has been revised to include the url and the table number giving rise to the data for our manuscript.

With regard to the Canadian data, the data tables containing the total number of live births, twin live births and triplet+ live births from Canada and for the province of Ontario were provided in an Excel spreadsheet directly from Statistics Canada following a data request. A new citation has been added for the Canadian data, as requested (reference #31).

2. The data from Ontario are excluded due to data quality concerns. Whilst the authors have provided a reference related to this, it would be helpful to provide a very brief explanation, as the reasons for exclusion are not immediately obvious to anyone outside of Canada, and very few readers will go to the trouble of seeking out the reference for clarification.

Author’s response:
We agree that few readers will consult original references related to Ontario vital statistics, thus a brief description of the primary concern has been added to the ‘Methods’ section (see below). See also the response to Reviewer 1 comment 2 related to Ontario data.

"Data from Ontario were excluded from the calculation of overall rates for Canada due to data quality issues with respect to live birth registrations. In particular, the under-registration of live births may have affected the reporting of the number and rate of multiple live births [1,32]. A more in-depth discussion of this data quality problem can be found elsewhere [1,32]. Ontario
Temporal trends in the frequency of twins and higher-order multiple births in Canada and the United States rates are described separately in the results, and figures including Ontario data are shown in an Appendix.”

Discretionary Revisions

The prime purpose of this report appears to be merely to document the multiple pregnancy rate in Canada and USA. The value of the report could however be enhanced by including in the discussion some attempt to contextualise these results by comparing and contrasting them with those from other countries (eg European, Australian), where the multiple birth rates are substantially lower.

Author’s response:
Indeed, our intent for this manuscript was to document and compare recent trends in multiple births in Canada and the United States, specifically, where multiple birth rates are among the highest in the world and where geographic proximity has likely cultivated similarity in practice guidelines and clinical practices in the two countries. We feel that an in-depth review of trends in multiple births in other countries is beyond the scope of this manuscript; however, we have now cited two reviews of international ART practices and have noted the global variability in practices related to number of embryos transferred (see below).

“There is tremendous variability in embryo transfer practices internationally, influenced by legislation, availability of public funding for ART, and clinical as well as social factors [35]. Reviews of international policies and practices related to ART have documented the highest rates of single embryo transfer in Sweden, Australia, New Zealand and some other Scandinavian countries, with rates in Canada and the United States among the lowest of those studied [35,36]. Further, those countries with the highest proportion of single embryo transfers also had the highest rates of singleton pregnancies following ART [36].”

Level of interest: An article whose findings are important to those with closely related research interests
Quality of written English: Acceptable
Statistical review: Yes, but I do not feel adequately qualified to assess the statistics.
Declaration of competing interests: I declare that I have no competing interests.