Author's response to reviews

Title: Maternal and perinatal factors associated with hospitalised infectious mononucleosis in children, adolescents and young adults: record linkage study

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Version: 3 Date: 17 November 2010

Author's response to reviews: see over
Reviewer's report

Title: Maternal and perinatal factors associated with hospitalised infectious mononucleosis in children, adolescents and young adults: record linkage study

Version: 2 Date: 21 October 2010

Reviewer: Sally Glaser

Reviewer's report:
The authors have been quite responsive to the critiques, and their paper is improved and more up-to-date in its consideration of the relevant literature. However, I remain concerned that the authors should make it clear throughout the paper that they are addressing a small subset of all IM cases, namely those severe enough to involve hospitalization. The paper still does not describe what the underlying pathogenesis and risk factors may be for clinically severe IM, and whether there is any indication that this reflects a different process than “regular” IM. Therefore I think it is potentially misleading to make comments about “IM” without the modifier “hospitalized”.

WE THANK THE REVIEWER FOR THE COMMENTS. WE HAVE ADDED SOME DETAIL TO THE DISCUSSION ON PATHOGENESIS AND SEVERITY OF IM. WE HESITATE TO WRITE MORE ABOUT THE DETAIL OF PATHOGENESIS AND ITS GENETIC BASIS, FOR FEAR OF STRAYING OUTSIDE OUR AREAS OF EXPERTISE. WE HAVE USED ‘HOSPITALISED IM’ THROUGHOUT THE ABSTRACT AND IN OTHER PARTS OF THE MANUSCRIPT.

Specific comments follow.
Abstract
For the Background, I suggest some rewording:

Background line 2: “Infectious mononucleosis can follow…

NOW CHANGED

Background line 3: “…and has been shown to increase risk for multiple sclerosis…”

NOW CHANGED

Background
1. Page 4, line 3: Primary EBV infection occurs in infancy and childhood throughout the world, not just in industrialized countries.

WE HAVE DELETED ‘IN INDUSTRIALISED COUNTRIES’
2. Page 4, end of first paragraph: Perhaps it would be relevant to mention the risk factors identified by reference 4.

WE HAVE ADDED SENTENCES ON THE RISK FACTORS FOUND BY THIS STUDY.

3. Page 4, paragraph 2, line 2: EBV was found in the Burkitt’s lymphoma cells themselves.

WE HAVE ALTERED THE SENTENCE TO SAY,’ EBV WAS FIRST IDENTIFIED IN BURKITT’S LYMPHOMA CELLS.’

4. Page 4, paragraph 2, line 6: In discussing risk, it isn’t necessary to say “subsequent”.

‘SUBSEQUENT’ HAS BEEN DELETED

5. Page 5, paragraph 1, lines 4-6: Is the quote from Purtilo and Sakamoto directed to the pregnant women themselves rather than their offspring?

WE HAVE NOW CLARIFIED THIS – THEY REFER TO BOTH MOTHER AND CHILD.

Results
1. Page 9, paragraph 1, line 12: I don’t see information about twins and singletons in Table 3, nor yet information relevant to IM by age at diagnosis.

APOLOGIES FOR THE ERROR, THIS SHOULD READ TABLE 4 (WHERE WE GIVE THE DATA), NOT 3. IT HAS NOW BEEN CORRECTED.

2. Page 9, paragraph 2: I would think that the multivariate analyses would justify a table, since they are really the findings that matter most.

THE ONLY FACTOR THAT WAS SIGNIFICANT AFTER MULTIVARIATE ANALYSIS WAS MARITAL STATUS (AS WE STATE IN THE TEXT), SO WE THINK THAT ADDING ANOTHER TABLE COVERING THE NON-SIGNIFICANT FINDINGS WOULD NOT ADD ANY MORE MEANINGFUL INFORMATION. HOWEVER, WE HAVE GIVEN A NEW TABLE 5, TO COVER THE STRATA OF DATA (PARITY, SOCIAL CLASS) THAT SHOW THE ASSOCIATIONS WITH MARITAL STATUS MORE FULLY. WE THINK THAT THIS IS A USEFUL ADDITION.

Discussion
1. Page 11, paragraph 1, lines 4-5: The “face validity” argument is not convincing. The association of IM with MS and HD could itself reflect misclassification of IM.

WE HAVE NOW DELETED THIS SENTENCE
2. Page 11, paragraph 2, lines 4-: I think we need something more here about clinically severe IM beyond that it represents the “strongest reactions” to infection. What is known about such patients What about their immune function? Are their significant and potentially relevant comorbidities? The work of Hjalgrim et al. (NEJM 2003) does provide support for the idea that persons with clinically severe IM are at risk for HL, since their data are based in part on hospitalized cases.

WE HAVE ADDED THE HJALGRIM STUDY HERE TO SUPPORT THE IDEA THAT IM SEVERITY MAY BE IMPORTANT. WE HAVE ALSO ADDED SOME FURTHER COMMENTS ON PATHOGENESIS TO PAGE 12, PARAGRAPH 2, WHICH ALSO ADDRESSES IM SEVERITY.

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