Reviewer's report

Title: The disparities in prevalence of neural tube defects and its subtypes at any gestational age in 2006-2008 of China: a study on the hospital-based birth defects surveillance system

Version: 4 Date: 19 July 2012

Reviewer: Marilyn Felkner

Reviewer's report:

1. Is the question posed by the authors well defined? No
2. Are the methods appropriate and well described? Additional clarification is needed.
3. Are the data sound? Pending methods clarification.
4. Does the manuscript adhere to the relevant standards for reporting and data deposition?
5. Are the discussion and conclusions well balanced and adequately supported by the data?
6. Are limitations of the work clearly stated? The authors do cover some important limitations, but additional limitations should be discussed. Specific limitations are covered below.
7. Do the authors clearly acknowledge any work upon which they are building, both published and unpublished? Literature review needs to be broadened. Based on the authors' response letter, much of the information about differences in all gestational ages vs. #28 weeks should be deleted from this article and their previous article referenced.
8. Do the title and abstract accurately convey what has been found? No, the title does not indicate the study question. It makes no mention of geographic distribution. Based on the title, the objective of the paper appears be to compare prevalence of overall NTD and NTD subtypes when cases at AGA are counted with prevalence when only cases at # 28 weeks gestation are counted.
9. Is the writing acceptable? Current English language usage is somewhat below the level expected for a scientific journal.

Discretionary Revisions (which are recommendations for improvement but which the author can choose to ignore)

Note: I counted each line of type; I did not count the skipped lines of the double-spacing.

Methods
1) Lines 21, 24, 27, 34: It would be nice to know more specifics about the credentials and training of the various staff who are involved, especially how they
differ from one another (‘Experts in relevant medical department’ “experts in the member hospitals” and "the expert in higher-level hospitals,” “staff specifically assigned,” “specialized staff.”). Are they physicians, nurses, other types of health care providers, public health outreach workers, statisticians, data entry clerks? Are they specialists? Did they have specific training related to this project?

Minor Essential Revisions (such as missing labels on figures, or the wrong use of a term, which the author can be trusted to correct)

Abstract
2) line 6: years should be 2006-2008, not 2008-2008
3) line 16: larger, not lager

Methods
4) Line 68: Pearson chi square, not Person

Results
5) Line 13: Use -, not ~ between confidence limits

Major Compulsory Revisions (which the author must respond to before a decision on publication can be reached)

Background
6) line 8: The statement “…many risk factors, such as genetic, environmental and nutritional factors…” has only four citations. Two of the cited articles do not deal with NTD risk factors. The Canfield article focuses on birth defects other than NTDs and the Milunsky article is about screening results rather than risk factors. A more thorough literature review is needed to support a statement on genetic, environmental, and nutritional factors.

Methods
7) Line 6: The authors state that the CBDMN covers “county-level-higher hospitals.” Please address if there are birth sites that are not included in the network such as smaller than county-level hospitals, birthing centers and home births. If there are, explain the rationale for not including them in the study and, in the Discussion, describe what impact the absence of these data have on the study outcome.

8) Lines 11, 12: “The monitoring subject in the CBDMN were all live births and stillbirths more than or equal to 28 week gestation age…” This seems to contradict the study’s claim to detecting birth defects at all gestational ages. There is no mention of the investigators’ method for ascertaining birth defects among fetuses less than 28 weeks.

9) Line 16: the authors state that the revised monitoring program was for “cases with major lethal malformation.” Please clarify because this would not include many cases of spina bifida, which are not typically lethal.
10) Line 20: The methods of surveillance for and ascertainment of NTDs prior to 28 weeks gestation must be included. The authors state that “every neonate is immediately examined after birth” but in the background (line 18/19) the authors explained that prior to 28 weeks most NTDs are terminated. Were all terminated fetuses also examined?

11) Line 37: I do not understand what a “statistical standard of NTDS” means. It seems to me that the ICBDSR would establish a diagnostic standard.

12) Line 49/50: Please explain the differences in provinces/autonomous regions/municipalities. These would be overlapping jurisdictions in the U.S.

13) Lines 55/56: Please define urban and rural using population numbers or some other objective standard.

Results

14) The number of results presented in this paper is overwhelming obscuring the main the study question. It would be helpful to present the text results in the same order as the tables with prevalence rates by region, by urban/rural, and by province in the first paragraph and prevalence rate ratios in the same order in the second paragraph.

15) Lines 5-11: If, as stated in the explanatory letter, the objective is to examine geographic differences, comparisons between all gestational ages and #28 weeks and trends over time should be omitted from this paper. Their previously published paper can be cited for information on gestational age differences if relevant.

16) Lines 41-51 Treating maternal age as a main variable distracts from the study question. Maternal age should be examined and reported only as a confounder and or effect modifier of geographic distribution. This section should be rewritten accordingly.

Discussion

17) Lines 1, 2: Omit discussion of differences in all ages vs. # 28 weeks.

18) Lines 8-11: Omit discussion of maternal age as a main variable.

19) Lines 12-34: Omit. This presumably would have been covered in the authors’ previously published paper and is not germane to the current study question. Once the gestational age has been defined in the methods, it merits little further mention.

20) Lines 35-60: This should be the most important part of the article. The authors cite 4 articles to cover NTD risk factors Vitamin B, cigarette smoke, drinking, taking antipyretic drugs and antibiotics. There are hundreds of articles on NTD risk factors. The authors should do a thorough literature review of NTD risk factors, select the risk factors that are most relevant to geographic disparities
in China, and discuss these selected risk factors and their relation to their findings in depth.

21) 61-64: The authors have one citation for education level, health awareness, access to preconception care, and periconceptional nutrition. Their importance as NTD risk factors should be covered more thoroughly.

22) Lines 79-92: Discussion of maternal age is outside the scope of this study.

23) The limitations of ascertaining NTDs at less than 28 weeks should be discussed. At what GA are NTDs not discernible? Would this ascertainment vary depending on the available technology or variable access to prenatal care? How would the resulting differences in case ascertainment impact the PRs?

Tables

24) Table 1 is very nicely organized. To keep the focus on geographic disparities, omit maternal age from Table 1.

25) Table 2 should be organized similarly to Table 1. The table should be understood without referring to the text. So use plain language rather than statistical symbols to label column headings. The variables should be clearly named. The referent group should be identified. Confidence intervals are preferable, but p-values are acceptable. The beta and chi square can be omitted. Omit maternal age as a main variable. Adjusting for age, as is indicated in the footnote, is sufficient.

Figures

26) Omit Figure 1. It is unrelated to the study question for this paper.

27) Figure 2. Very nice way to present these data. However, in gray shades, it is very difficult to make that number of distinctions. If the publication will not be in color, collapse some of the categories.

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

Quality of written English: Not suitable for publication unless extensively edited

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