Author's response to reviews

Title: Congenital heart disease in men - birth characteristics and reproduction. A national cohort study.

Authors:

Kristina Kernell (kristina.kernell@lio.se)
Gunilla Sydsjö (gunilla.sydsjo@lio.se)
Ann-Britt Wirehn (ann-britt.wirehn@lio.se)
Niels Erik Nielsen (niels.erik.nielsen@lio.se)
Ann Josefsson (ann.josefsson@lio.se)

Version: 2 Date: 27 September 2013

Author's response to reviews: see over
Dear Editor in chief,

Thank you for valuable comments on our manuscript “Congenital heart disease in men – birth characteristics and reproduction. A national cohort study”.

We have tried our very best to answer the questions and suggestions made by the referees, please see below. If you still think there are modifications that need to be done in order to make the manuscript publishable, please do not hesitate to contact us.

Kind regards, Ann Josefsson

Reviewer’s report

Title: Congenital heart disease in men - birth characteristics and reproduction. A national cohort study.

Version: 1 Date: 25 August 2013

Reviewer: GARY D WEBB

Reviewer’s report:

I have some difficulty understanding how you want me to submit my review.

I found the manuscript have to be of interest, and the data to be publishable. The question posed is well defined. The methods are appropriate, but have limitations as described below. The data is clearly valuable, but also has limitations. The authors have taken a very responsible approach to reporting and analyzing the data. The discussion is very appropriate. The limitations are not as fully described as I would like. English usage is excellent.

My main concern has to do with the various diagnoses attached to the males in the study, and how and when these diagnoses were made.

First of all, thank you very much for valuable comments, which we think, have helped us to improve our manuscript. As the National patient registry covers all public inpatient and outpatient care we think that all men with CHD diagnoses have been identified. The diagnoses of CHD in the population of Swedish men were made either in the neonatal period, during childhood or when signing in for Swedish military duty, or at any other visit within the Swedish health care due to problems related to the diagnosis. We have added some clarifications in the background and methods sections of the manuscript.

In table 1, the diagnoses and their frequency are documented. Tetralogy should be more common than TGA, but is not.
We do agree. When analyzing the total Swedish population (men and women) tetralogy is more common than TGA. In an earlier published study on women with CHD based on the same material, tetralogy was more common than TGA. Josefsson A, Kernell K, Nielsen NE, Bladh M, Sydsjö G. Reproductive patterns and pregnancy outcomes in women with congenital heart disease – a Swedish population-based study. Acta Obstet Gynecol Scand. 2011;90:659-665.

What is congenital aortic insufficiency? There are a lot of these patients.

We think that in Sweden, this group has a big proportion of patients with bicuspid aortic valve. But unfortunately we cannot give the exact number because we do not have access to many of the echocardiographic examinations.

There are lot of patients with congenital anomalies of the great veins. I don't know what this means.

According to the Swedish version of the ICD-8,-9 and -10 this group comprises of the total or partially anomalies of pulmonary veins.

In neonates, VSDs should be the dominant congenital diagnosis. It is not dominant enough in this series. In other words, I don't think that the patients represented in this study are truly representative of all congenital heart males.

Please see above. The diagnoses for the men are not only neonatal diagnoses.

Again, the overall incidence of CHD was 0.5%, lower than the generally acknowledged 0.8%. Also of concern is the fact that only 14.7% had complex CHD, possibly reflecting the terminology included in this group, but lower than expected.

The incidence 0.5% reflects men born in Sweden between 1973 and 1983 and who were alive and still living in Sweden at 13 years of age. This is stated in the methods section.

The limitations of the data in the registry is noted. Whether this applies to the putative parent or just to the putative offspring is not entirely clear.

The possible limitation of underreporting of congenital malformations is only valid for the offspring as their diagnoses are only based on the Medical Birth Registry. Please see Discussion where a clarification has been written.

That having been said, the data is unique enough that I think it is worth publishing. I would like to have the authors comment further on the methodology and the limitations of it.

Please see above. If the methodology still is not clear, please let us know.

Level of interest: An article of importance in its field
Quality of written English: Acceptable

Statistical review: Yes, but I do not feel adequately qualified to assess the statistics.

Declaration of competing interests:

I have no competing interests.

Reviewer's report  Title: Congenital heart disease in men - birth characteristics and reproduction. A national cohort study.

Version: 1  Date: 21 August 2013

Reviewer: Morten Olsen

Reviewer's report:

Thank you for the opportunity to review this interesting paper. Please see my comments below.

- Major Compulsory Revisions

1) Validity (positive predictive value) of data on CHD overall and in particular specific CHD types needs to be addressed in methods and discussion sections. Furthermore, it is not clear to me how specific defect types were assigned to patients with multiple defects.

We have added some clarifications in methods and discussion sections.


In this study, the results are in line with previous published studies on womens CHD. Hence, the findings in the present study can be considered reliable.

Only the main diagnoses were used when patients were divided into the two groups. Clarifications have been added in the manuscript.
2) How was single ventricle diagnoses defined in the ICD-8 period? Are there specific ICD-8 codes for this type of CHD?

Yes, in the Swedish version of ICD-8 there are specific codes as follow, 74637 and 74674.

3) The defect specific data in Table 4 are very difficult to interpret as they do not consider time at risk. I would consider omitting this table, and focus on the overall analyses based on Cox regression. Time at risk is particularly important to consider in a population with high mortality, as the CHD population.

We think that Table 4 adds important information and do not want to omit it. Maybe we do not understand your question fully but around 90% of all individuals with CHD survive childhood and reach reproductive age. Our national cohort of men with CHD born between 1973-1983 have reached the age where they can become fathers.

- Minor Essential Revisions

1) Abstract: The methods section of the abstract needs to address the data sources and statistics used in more detail.

Done. Data sources are added, however detailed statistics are described in the Methods section.

2) Abstract: Results section of abstract should display the actual main results in numbers and not described by words.

Done.

3) Table 4 and 5: It seems from table 5 that more men with complex chd had children than the 54 described in table 4.

Please see the Methods section, Study population, line 121-123, for explanation. In Table 5 we only present results where the data from the registries are complete.

4) Table 4 does not contain incidence data, as stated in results.

Changes have been made.

5) Numbers of CHD patients differ between abstract(n=2310) and main text (n=2689).

Thank you very much for noticing, we have changed the numbers.

- Discretionary Revisions
1) Methods: Would consider revising the text and combine the description of the study population and variables with the description of the various registries used to identify them.

*We think that the results of this study are of interest for clinicians in obstetrics and cardiology working with preconception counseling and patients with CHD in their reproductive ages. In order to make the paper easy accessible we have chosen the present lay-out.*

**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:** Yes, but I do not feel adequately qualified to assess the statistics.

**Declaration of competing interests:**

I declare that I have no competing interests