Author's response to reviews

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

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Author's response to reviews: see over
Dear Editor in-Chief

Thank you for the statistical review of our manuscript. The comments were very valuable. We have actually reanalysed the complete database and recalculated the statistics and found some mistakes which have been corrected.

Please see answers to reviewer Carstensen below.

We look forward to your decision concerning publication of this manuscript,

Sincerely Yours,

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Reviewer's report

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

Version: 3

Date: 24 March 2014

Reviewer: John JC Carstensen

Reviewer's report:

Statistical review of manuscript ‘Congenital heart disease in men - ...’ by K Kernell et al

This is a well written report on an important subject. The analysis is based on an excellent material which has been created by combining information from several population-based registers. However, I have some ‘problems’ with parts of this study:

1. Page 7, line 122: ‘268 men in total study population died’. Even in the age-group 13-33 years, this seems to be a very low number in 500,000 men followed 10-20 years (Also compare the corresponding information for women in ref 3, page 660: 0.38% of 494692).

Please explain and/or correct.
Answer: A total of 4405 men died during the study period of which 272 had become fathers. The revised total mortality rate among men during the study period is hence 0.84%. This has been revised in the paper.

2. Page 7, line 125: ‘Due to missing values on birth weight or gestational length of the children 29175 men were excluded ...’. This corresponds to 21% of the children of the fathers and is much higher than that given for children of mothers in ref 3, page 660 (912/189819=0.5%). Please explain and/or correct.
Answer: The number of father-offspring pairs has been miscalculated. The correct number of father-offspring pairs is 110,419 of which 251 (0.2%) have missing values on birthweight and 252 (0.2%) have missing values on gestational length resulting in a total of 491 (0.4%) cases excluded due to missing values. Numbers and analyses have been revised and corrected numbers inserted in the manuscript.

3. The crude “paternity rates” by diagnosis, presented in table 4, are potentially misleading since the observation time has not been accounted for. The statistical analysis should be based on appropriate methods like Cox regression (it has been correctly used for the whole heart disease group but not for the diagnostic sub-groups).
Answer: This table is solely to present crude estimates of the proportion of men who had become fathers, in each CHD sub-group, during the study period. The heading of the table has been changed.

4. Have twin births been excluded in the ‘next generation’ analysis (table 5)? Explain/correct.
Answer: Twins were not excluded; corrected numbers have now been inserted in Table 5.