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

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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.

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.

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).

4. Have twin births been excluded in the ‘next generation’ analysis (table 5)? Explain/correct.