Reviewer's report

Title: Does economic development contribute to sex differences in ischaemic heart disease mortality? Hong Kong as a natural experiment using a case-control study

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Reviewer: Per Wändell

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General
This is an interesting article with the attempt to study gender differences in ischemic heart disease (IHD) in relation to economic development. The methods and statistics are well described and discussed, and the authors seem to be aware of possible limitations.

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

1. The background and discussion is far too brief.
   a) The context is actually migration and health, and there are many articles published on this issue. The authors should refer to relevant studies, i.e. changes in IHD incidence and mortality associated with migration to a higher economically developed country and region (e.g. the Honolulu Heart Study, but there are a great many studies), but also in changes in risk factors for IHD or description of risk factor profiles among immigrants. In general, studies usually find higher rates of overweight, obesity, metabolic syndrome, hypertension and diabetes.
   b) The authors have also written about the situation before economic development, i.e. in more traditional societies. They could refer to e.g., studies Melanesians in Kitava by Staffan Lindeberg, to get a baseline of the situation before Westernization of a society. When looking at blood lipids, there is no sign of reduced HDL-cholesterol among Swedish men in relation to women compared to the Kitava population.
   c) When looking at life tables (accessible from the WHO), one could see small gender differences in e.g., some African countries, while in many other countries women have 3-6 years longer expected average length of life. This, however, seems to be mostly related to a high maternal mortality. When discussion gender differences in relation to economic development this is also a matter of possible importance.
   d) The authors could also discuss other risk factors, such as psycho-social stress associated with migration, as psycho-social factors were found to be of great importance in the INTERHEART Study.

2. Hypothesis.
a) The authors speculate that a better pre-adult environment increases sex-steroids at puberty, thus increasing gender differences. However, they hardly present any scientific support for this. When considering the studies mentioned above the authors should have discussed if their speculation could fit in with other studies. I doubt it.

b) As regards diabetes, Gale found a tendency over time in Western societies from a female preponderance in the early 20th century to a more equal situation in the late 20th century. Possible explanations to that could be that men are more predisposed to central fat deposition, which also is associated with reduced oxidation of fat; this could predispose to higher incidence of IHD as well as of type 2 diabetes. Thus, another hypothesis is that men are more susceptible to environmental changes by economic development due to metabolic differences.

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

The rate of IHD-deaths of all deaths is rather low. Thus, it is of value to show the greatest causes of death. Besides, the authors write that Hong Kong cause of death coding is found to be of good quality in other studies, but only one study is mentioned. This should be better supported.

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Discretionary Revisions (which the author can choose to ignore)

The heading to the tables is rather sparse, and thus it takes some time to understand the message of the tables. It would be easier for the readers if the authors proved the tables with more explaining heading text and in Table 1 also set some space between the age groups and between IHD and pneumonia cases. Besides, Tables 2 and 3 could be quicker read if the authors put in a parenthesis with (reference group, OR=1) after “women” and “migrants from Guangdong”, respectively, in the heading.

What next?: Unable to decide on acceptance or rejection until the authors have responded to the major compulsory revisions

Level of interest: An article of importance in its field

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