Reviewer’s report

Title:A comparison of risk factors for mortality from heart failure in Asian and non-Asian populations: An overview of individual participant data from 32 prospective cohorts from the Asia-Pacific Region

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Reviewer:John Atherton

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The authors use individual-participant data from 543,694 participants derived from 32 cohorts in the Asia Pacific region (namely Australia, China, Korea, Japan and Taiwan) to determine the association between cardiovascular risk factors and subsequent heart failure (HF) death.

In adjusted analyses, subsequent HF death was positively associated with baseline elevated systolic blood pressure, diabetes and cigarette smoking, and there was a U-shaped relationship with body mass index. There was no significant association with total cholesterol level. Significant interaction effects were observed for blood pressure (age) and diabetes (Australia vs. Asia).

This represents a large body of work that combines numerous cohorts with access to individual-participant data and over three million person years follow-up. The findings are interesting and appear largely consistent with other population-based cohorts (except perhaps the association with low BMI).

Major compulsory revisions:

1. I would find it helpful if more details could be provided about how individuals were identified in the various cohorts. Were these unselected, community-based cohorts? The authors indicate that selection of subjects was not consequent to pre-existing disease. However, were patients with clinical HF at baseline excluded in the current analysis?

2. Also, are the associations unchanged (esp. for BMI) if patients with prior myocardial infarction at baseline are excluded.

3. To determine the importance of cardiovascular risk factors in contributing to the future HF (and minimise the potential confounding effect of reverse causality between risk factors and outcomes in patients once they develop HF during the study), it would be informative to also report the association between cardiovascular risk factors and subsequent clinical HF (ie, incident non-fatal and fatal HF events combined). If the authors cannot do this, then they should at least acknowledge this limitation in the discussion.

Minor essential revisions:

1. In the discussion, the authors make comparisons with other studies that are not directly relevant. For example, they refer to reverse causality with low BMI
observed in cohorts comprising patients with established HF at baseline (and therefore not directly relevant to a population-based cohort). They also refer to associations with incident HF (not just HF death) in other unselected, population-based cohorts. This should be clarified in the discussion.

2. Was the association with smoking present in both diabetics and non-diabetics?

3. The authors report no association with total cholesterol. If HF deaths in the 1st 2 years were censored, was their still no association?

4. Page 5: I would generally refer to heart failure as a complex syndrome (rather than a disease).

5. Page 11, paragraph 2: The authors state, “Data from the current study, confirmed an independent association between diabetes and HF for Asians and (to a lesser extent) non-Asians.” It should be the other way around.

6. In the discussion, the authors sometimes refer to their study identifying associations with “HF”. However, they only identified associations with “HF death”.

7. Aneurism misspelt in Table 1 footnote.

Discretionary revisions:

1. In the Framingham study, low BMI was not associated with an increased risk of developing HF (although this was based on a small number of events). Could the association reported in individuals with low BMI in the current study reflect the inclusion of patients with undiagnosed HF at baseline, or the limitation of using HF death as the outcome variable?

Level of interest: An article of outstanding merit and interest in its field

Quality of written English: Acceptable

Statistical review: Yes, and I have assessed the statistics in my report.

Declaration of competing interests:

I declare that I have no competing interests.