Reviewer's report

Title: Cardiovascular risk estimated after 13 years of follow-up in a low-incidence Mediterranean region with high-prevalence of cardiovascular risk factors

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Reviewer: Maria Jose Medrano

Reviewer's report:

This is a very well written manuscript that assesses the relationship between exposure to major cardiovascular risk factors and incidence of cerebrovascular and ischemic heart disease in a population-based cohort in Murcia, Spain. Study methods are correct and generally well described, with strict endpoint diagnostic criteria and classification procedures, and special attention given to statistical methods. Some limitations of the study (e.g. self-reported diabetes status, statistical power limitations) are adequately commented in the discussion section. Moreover, the study makes two important contributions to the literature in this field:

a) It shows, for the first time, that classical cardiovascular risk factors are associated not only with coronary disease, but with cerebrovascular disease too, in a Mediterranean region, such as Murcia, with a low morbimortality from cardiovascular diseases in the international context.

b) This study shows the feasibility of conducting large prospective epidemiologic studies using cross-sectional studies as baseline, and record-linkage techniques with administrative data for event detection in follow-up.

Mayor Compulsory Revisions

The lack of effect of obesity on vascular risk found in this study is surprising. Absence of statistical association may be due to:

1) categorization of BMI in obese/non-obese: a better approach would be to consider BMI in the continuous scale, in three categories as stated in the methods section (<25, 25-29.9, >=30), or in two categories (<25, >=25) which would probably improve statistical power.

2) adjustment by intermediate variables, such as hypertension, triglycerides and diabetes. This gives an estimation of the independent effect of obesity, this is, the effect that is not mediated by these factors. In fact, data in table 2 show substantial reductions in RRs after multivariate adjustment, which probably would be more evident if considering other categories for BMI.

It is suggested that authors include these considerations in the discussion section.

Minor Essential Revisions
Results in table 3 are not included in the text (results section)

Discretionary Revisions (which the author can choose to ignore)

1. A brief but more detailed description of the recruitment methods would be desirable because the reference given in the text refers to an article in Spanish which many readers will not be able to understand.

2. It would be interesting to have a description of those subjects lost for follow-up, and also of those excluded because missing data. Can these exclusions bias the results? To what extent? In which manner?

3. It would be interesting to know the number of missing values for every risk factor.

4. Did results change substantially when using different cut-offs for risk factors (e.g., lower cut-off for BMI)?

5. During the study period substantial reduction in risk factors prevalence and improvement in their medical control have occurred in Murcia. Can these changes have affected the study results?

**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'