

MJ - Decision on
Manuscript ID
BMJ.2015.029885.R1

Body: 23-Jun-2016

Dear Prof. Corrao:

Manuscript ID BMJ.2015.029885.R1 entitled "Non-steroidal anti-inflammatory drugs and the risk of heart failure: a nested case-control study from four European countries in the SOS Project" which you submitted to BMJ,

Thank you for sending us your paper. We are pleased to say that we would like to publish it in the BMJ. The statistical reviewer, Dr. Julie Morris, has a few minor comments. We would like you to address her comments and those from the other reviewers. We are provisionally offering acceptance but will make the final decision when we see the revised version.

We are looking forward to reading the revised manuscript and, we hope, making a final acceptance decision.

Please note that the BMJ might choose to shorten content or replace or re-size images for the print issue.

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Yours sincerely

Jose Merino
jmerino@bmj.com,

REFEREE COMMENTS

Reviewer: 1

Recommendation:

Comments:

The authors have provided a very detailed and, on the whole, reasonable response to the statistical concerns contained in my review, and the paper has been revised to take account of most of the issues raised.

Specifically, more details of the harmonisation process have been provided, a more extensive discussion of the limitations of the study, in particular potential bias and confounding concerns, has been included and the Tables and Figures have been suitably modified.

There are some issues that remain, but these are not major blocks to publication as long as acknowledgement of these concerns is made.

I still have some reservations about the pooling of data from moderately diverse databases and the heterogeneity in health care provision between countries. However, there does seem a precedence set for the harmonisation process used by the authors.

Also, I do not entirely agree with the argument used to support the omission of any adjustment for multiple testing or any acknowledgment of the problem. A clear statement of the authors' approach to this matter should be included in the paper.

Additional Questions:

Please enter your name: Julie Morris

Job Title: Head of Medical Statistics

Institution: UHSM

Reimbursement for attending a symposium?: No

A fee for speaking?: No

A fee for organising education?: No

Funds for research?: No

Funds for a member of staff?: No

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Do you hold any stocks or shares in an organisation that may in any way gain or lose financially from the publication of this paper?: No

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Reviewer: 2

Recommendation:

Comments:

Thank you for the opportunity to review and to the authors for the thorough response. While the authors provide rationale for their study design choices in the response and in the manuscript, the use of an active comparator of another medication would enhance the study methodology. In addition, while the authors provide rationale for their interest in examining the 27 NSAIDs individually (and making specific inferences about their individual hypotheses), to some degree, the authors are still making generalizations from these hypotheses about the global association between NSAID use and HF, which one can see in their conclusion. Some acknowledgement of the risk for multiple comparisons may still therefore be warranted.

Additional Questions:

Please enter your name: Julie Lauffenburger

Job Title: Research Fellow

Institution: Brigham and Women's Hospital

Reimbursement for attending a symposium?: No

A fee for speaking?: No

A fee for organising education?: No

Funds for research?: No

Funds for a member of staff?: No

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g. Footnotes and statements

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