

Review Form 1.7

Journal Name:	Journal of Advances in Medicine and Medical Research
Manuscript Number:	Ms_JAMMR_114713
Title of the Manuscript:	Comparative Cardiovascular Efficacy & Safety of NSAIDs: A Systematic Review and Meta-analysis of Randomized Controlled Trials
Type of the Article	

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PART 1: Review Comments

	Reviewer's comment	Author's comment (if agreed with reviewer, correct the manuscript and highlight that part in the manuscript. It is mandatory that authors should write his/her feedback here)
<p><u>Compulsory</u> REVISION comments</p> <p>1. Is the manuscript important for scientific community? (Please write few sentences on this manuscript)</p> <p>2. Is the title of the article suitable? (If not please suggest an alternative title)</p> <p>3. Is the abstract of the article comprehensive?</p> <p>4. Are subsections and structure of the manuscript appropriate?</p> <p>5. Do you think the manuscript is scientifically correct?</p> <p>6. Are the references sufficient and recent? If you have suggestion of additional references, please mention in the review form.</p> <p><u>(Apart from above mentioned 6 points, reviewers are free to provide additional suggestions/comments)</u></p>	<p>1. Yes, it is a question not yet resolved.</p> <p>2. yes</p> <p>3. No, you have problems in the writing</p> <p>4. Yes</p> <p>5. No</p> <p>6. Some older references are missing</p>	<p>OKAY</p> <p>NOTED</p> <p>OKAY</p>
<p><u>Minor</u> REVISION comments</p> <p>1. Is language/English quality of the article suitable for scholarly communications?</p>	<p>yes</p>	<p>OKAY</p>
<p><u>Optional/General</u> comments</p>	<p>An interesting question, but the design of the work raises multiple questions.</p> <p>Why was the date range chosen specifically to search for the studies? It is striking, since one of the largest works carried out, the PRESICION and the most important meta-analysis on the subject, were just published between 2016-2017, that is, they were left out of this review; and yet the work of Brito et al. 2017 was included despite being outside the specified range.</p> <p>The combination of safety and efficacy does not seem to be adequate, because in general the studies to evaluate the effectiveness in preventing cardiovascular events are carried out primarily with aspirin, since the other NSAIDS have a secondary role, so the recommendation of both outcomes would not be appropriate. In the study by Gaziano JM et al. 2018, has a totally different objective from the other studies included, the doses used do not have an anti-inflammatory effect but rather an antiplatelet drug, so the outcomes cannot be comparable.</p> <p>The definition of cardiovascular safety used at work, uses many outcomes that are not directly linked to cardiovascular compromise, and that may be primarily associated with the underlying disease.</p> <p>A similar situation occurs with the definition of cardiovascular efficacy, since multiple outcomes are included that would not correspond to this definition, but to one of global safety.</p> <p>In general, due to the way in which the analysis was conceived, the most relevant articles on the topic were left out, and which alone have much larger patient numbers than those of all those included in the present analysis, in addition to the definitions proposed mix cardiovascular and non-cardiovascular outcomes, leading to multiple errors in the analysis</p> <p>The RE-LY and Aristoteles studies are carried out in a very different population, in which the safety and effectiveness of anticoagulation is evaluated and not so much the effect of NSAIDS, so they should not carry out a joint analysis.</p> <p>Although it has a good methodology in its development. the shortcomings in the working definitions</p>	<p>NOTED</p>

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	and the selection of the studies mean that the results cannot be adequately interpreted and therefore have no validity for daily clinical practice.	
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PART 2:

	Reviewer's comment	Author's comment <i>(if agreed with reviewer, correct the manuscript and highlight that part in the manuscript. It is mandatory that authors should write his/her feedback here)</i>
Are there ethical issues in this manuscript?	<i>(If yes, Kindly please write down the ethical issues here in details)</i>	