Author’s response to reviews

Title: Dual anti-platelet therapy following percutaneous coronary intervention in a population of patients with thrombocytopenia at baseline: A meta-analysis

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POINT TO POINT RESPONSE TO REVIEWERS

Editor Comments:

Upon further checks, we felt the need for a further subject matter advice. We hence got a new reviewer to assess the manuscript. They have now requested further revisions that we feel with enhance the quality of the manuscript. We also ask the authors to copy-edit the manuscript using the help of a native English speaker.

AUTHORS RESPONSE: THANK YOU. AS REQUESTED, APPROPRIATE CORRECTIONS WERE MADE. THANK YOU.

Reviewer reports:

Peter Penson (Reviewer 2): Thank you for making the suggested changes
AUTHORS RESPONSE: THANK YOU VERY MUCH.

Matteo Bianco, M.D. (Reviewer 3):

Page 4 line 15-16 i suggest to replace the word thyenopiridine with P2Y12 inhibitors in order to include also ticagrelor which is not a thyenopiridine.
AUTHORS RESPONSE: THE REQUIRED CHANGE WAS MADE. THANK YOU.
Matteo Bianco, M.D. (Reviewer 3):

Page 5: can the authors specify the selection process of the papers? They started from abstract evaluation and then went deeply inside the paper? How they solved disagreement between selectors? Moreover i would simplify the inclusion/exclusion criteria this way: ex: We included studies reporting: 1. … 2 … 3 … etc and we excluded: 1. Systematic review and metaanalysis etc etc.

AUTHORS RESPONSE: FURTHER DETAILS WERE PROVIDED IN THE REVISED PAPER. THE INCLUSION AND EXCLUSION CRITERIA WERE SIMPLIFIED AS SUGGESTED.

Matteo Bianco, M.D. (Reviewer 3):

Page 5 line 45: "similar studies" or duplicated studies?

AUTHORS RESPONSE: DUPLICATED STUDIES. THIS HAS BEEN CORRECTED IN THE REVISED PAPER.

Matteo Bianco, M.D. (Reviewer 3):

Page 5-6 In my opinion the definition of thrombocitopenia used to select studies should be included not only in table but also in the methods. Moreover including studies with different cut-off could cause bias in the interpretation of results.

AUTHORS RESPONSE: WE HAVE INCLUDED THE DEFINITION OF THROMBOCYTOPENIA IN THE METHOD SECTION ALSO. INCLUSION OF STUDIES WITH DIFFERENT CUT OFF COULD CAUSE BIAS AND THIS WAS MENTIONED IN THE LIMITATION SECTION OF THE REVISED MANUSCRIPT. HOWEVER, ONLY TWO STUDIES HAD A CUT OFF VALUE OUTSIDE THE RANGE AND THIS SHOULD NOT AFFECT THE RESULTS.

Matteo Bianco, M.D. (Reviewer 3):

Page 5-6: the bleeding definition used in the studies included should be specified in the methods.

AUTHORS RESPONSE: BLEEDING DEFINITION WAS MENTIONED IN THE METHOD SECTION.

Matteo Bianco, M.D. (Reviewer 3):

Page 7: how was assessed the small studies bias in the present meta-analysis? Did the authors excluded patients requiring long term oral anticoagulation for atrial fibrillation or mechanical heart valve? Please provide information in the methods.

AUTHORS RESPONSE: BIAS ABOUT THE METHODOLOGY WAS ASSESSED BY THE CRITERIA OF THE NEWCASTLE OTTAWA SCALE OR THE CRITERIA OF THE
Cochrane Collaboration. We have provided references about the criteria. Thank you.

Matteo Bianco, M.D. (Reviewer 3):

Table 4: in my opinion the P2Y12 used should be specified for each single study included in order to clarify if a previous thrombocytopenia lead to a less intense P2Y12 inhibition after PCI. Authors response: The P2Y12 used was specified.

Matteo Bianco, M.D. (Reviewer 3):

Page 9 line 42: in order to understand the clinical relevance of access site bleeding the authors should specify the access site used in the study included. A bleeding avoidance strategy in patients with thrombocytopenia require the preferential use of radial access. Can the author give more information about this result?
Authors response: The access site was provided in the revised paper in Table 4 if access site was provided in the original study. However, to compensate for this, we have mentioned this point in the limitation section.

Matteo Bianco, M.D. (Reviewer 3):

Page 9 line 50-51: the authors should describe the BARC bleeding on the basis of the numbers included in the classification and not dividing them in minor or major in order to make the results more readable.
Authors response: Appropriate revisions were made. BARC Bleeding was properly defined in the methods section. However, since in the original papers, bleeding was classified as BARC minor and major bleeding respectively, we had to follow the same reporting outcome in our analysis. Thank you.

Matteo Bianco, M.D. (Reviewer 3):

In my opinion discussion and limitations are not publishable in the present form and require and extensive revision:
1. The discussion should complete the results observed in the meta analysis and not report anecdotally on other paper considering the same topic. Discussion should help the readers to understand the results and to comment the unsolved issue of the topic. In this case it would be very useful comment the use of bleeding scores as PARIS and PRECISE DAPT score focusing on why they did not used thrombocytopenia as a variable. In particular the authors can consider to include in the bibliography this paper: https://doi.org/10.1016/j.ijcard.2019.11.132. Comparative external validation of the PRECISE-DAPT and PARIS risk scores in 4424 acute coronary syndrome patients treated with prasugrel or ticagrelor.
2. The recent development of drug eluting stent with a safety interruption of DAPT after a short course of therapy could be a topic of interest to include in the discussion.

3. In my opinion the causes of thrombocytopenia are a very important determinant on prognosis and events. The authors should clearly specify in the limitations that was not possible to analyze prognosis on the basis of mechanism causing platelet deficit and for this reason the results on mortality are not generalizable and require more dedicated study.

AUTHORS RESPONSE: ALL THE SUGGESTED CHANGES WERE MADE. HOWEVER, WE COULD NOT SHORTEN THE DISCUSSION OR AVOID REPORTING WHAT WAS OBSERVED IN OTHER STUDIES SINCE THIS ADVICE TO REPORT CERTAIN STUDIES IN THE DISCUSSION WAS GIVEN BY THE PREVIOUS REVIEWER TO IMPROVE THE PAPER. THEREFORE, WE HAVE ADDED DISCUSSION ABOUT THE PARIS AND PRECISE DAPT AND STATED ABOUT SHORT COURSE OF DAPT, AS WELL AS MENTIONED ABOUT THE FACT THAT PROGNOSIS COULD NOT BE ANALYZED IN THE LIMITATION SECTION. THANK YOU.

Matteo Bianco, M.D. (Reviewer 3):

Conclusion: due to the large number of limitations the authors should soften the conclusion.

AUTHORS RESPONSE: THE CONCLUSION WAS SOFTENED. THANK YOU.

Matteo Bianco, M.D. (Reviewer 3):

Minor revision:

English revision from a mother tongue reviewer could be useful.

AUTHORS RESPONSE: THANK YOU. THE LANGUAGE WAS REVISED APPROPRIATELY.