## PEER REVIEW HISTORY



## ARTICLE DETAILS

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| **TITLE (PROVISIONAL)** | Safety and efficacy of dual vs. triple antithrombotic therapy (DAT vs. TAT) in patients with atrial fibrillation following a PCI: a systematic review and network meta-analysis |
| **AUTHORS** | Altoukhi, Renad; Alshouimi, Reema; Al Rammah, Shahad; Alzahrani, Mohammed; Almutairi, Abdulaali; Alshehri, Abdulmajeed; Alfayez, Osamah; Al Yami, Majed; Almohammed, Omar |

## VERSION 1 – REVIEW

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| **REVIEWER** | Isabel Elaine Allen<br>University of California San Francisco, USA |
| **REVIEW RETURNED** | 23-Dec-2019 |

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| **GENERAL COMMENTS** | There is no registration of the protocol on Prospero so it is difficult to understand the specific inclusion and exclusion criteria and the clear outcomes being examined. While it is too late to register the meta-analysis, the authors could include a table of inclusion/exclusion criteria and outcomes as a supplementary table. The Prisma diagram needs to give reasons for excluding studies specifically for the full article screening (n=40) and why they did not meet the inclusion criteria. I would like to compliment the authors on their clear description of the results in Figures 2, 3, & 4. This is an excellent way to present their results. |

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| **REVIEWER** | Philip Aylward<br>South Australian Health and Medical Research Institute, Flinders University<br>Adelaide<br>Australia |
| **REVIEW RETURNED** | 11-Jun-2020 |

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| **GENERAL COMMENTS** | This paper is a Bayesian network meta analysis of 4 trials comparing dual anti thrombotic regimens (DAT )with triple antithrombotic regimens (TAT). There have been previous standard meta analysis which are described.<br>The new methodology of Bayesian network analysis is unusual and difficult for me to fully interpret.I would recommend a statistical review.<br>The finding is the preference for individual DAT regimens on different outcomes ,MI, death ,stroke and bleeding ,stent thrombosis and recommending the use of different DOACs depending on patient risk.<br>These results should be interpreted with even more caution than presented in the paper about the advantages of one regimen over another for the different outcomes. |

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| | The overall numbers of patients and events are relatively small. The probabilities are relatively low around 50% at best.<br>I would suggest a clearer explanation of the methodology for the practising clinician so they understand what has been done. This would include how you interpret probability and the limitations of the technique in greater detail.<br>The conclusions should indicate even more strongly that they are suggestive only. |

**VERSION 1 – AUTHOR RESPONSE**

Reviewers comments and the responses to their valuable comments
Reviewer #1 (Dr. Isabel Elaine Allen) comments:
There is no registration of the protocol on Prospero so it is difficult to understand the specific inclusion and exclusion criteria and the clear outcomes being examined. While it is too late to register the meta-analysis, the authors could include a table of inclusion/exclusion criteria and outcomes as a supplementary table. The Prisma diagram needs to give reasons for excluding studies specifically for the full article screening (n=40) and why they did not meet the inclusion criteria. I would like to compliment the authors on their clear description of the results in Figures 2, 3, & 4. This is an excellent way to present their results.

Authors' response: Thank you for your valuable comments. A supplementary table of inclusion/exclusion criteria and outcomes was created, please see Supplementary Table 1. The Prisma diagram was updated with reasons for excluding studies. Please see the revised version of Figure 1.

Reviewer #2 (Dr. Philip Aylward) comments:
This paper is a Bayesian network meta-analysis of 4 trials comparing dual anti thrombotic regimens (DAT) with triple antithrombotic regimens (TAT). There have been previous standard meta-analyses which are described. The new methodology of Bayesian network analysis is unusual and difficult for me to fully interpret. I would recommend a statistical review. The finding is the preference for individual DAT regimens on different outcomes, MI, death, stroke and bleeding, stent thrombosis and recommending the use of different DOACs depending on patient risk.
These results should be interpreted with even more caution than presented in the paper about the advantages of one regimen over another for the different outcomes. The overall numbers of patients and events are relatively small. The probabilities are relatively low around 50% at best.
I would suggest a clearer explanation of the methodology for the practicing clinician so they understand what has been done. This would include how you interpret probability and the limitations of the technique in greater detail.

Authors' response: Thank you for your valuable comment. We agree with the reviewer that Bayesian network meta-analysis and ranking of different interventions from network meta-analysis might be challenging for some clinicians. However, the idea of the network meta-analysis is using a statistical model that indirectly compare different intervention that were not tested in head to head from a clinical trial using a common comparator and this model enable researchers to estimate the likelihood of ranking of competing treatments for certain outcome from best option to the least option. So, the ranking of competing treatments should be interpreted based on the data included in the analysis and for the specified outcome only. We have added clarification sentences in the method section to briefly describe the network meta-analysis and the ranking treatments. Please see page 5, line 18-19.

The conclusions should indicate even more strongly that they are suggestive only.

Authors' response: Thank you for the nice comment. We have updated the conclusion section in the abstract and the main document to be clear. Please see page 2, lines 29-30, and page 11, lines 23-25.

**VERSION 2 – REVIEW**

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| **REVIEWER** | Isabel Allen<br>University of California San Francisco |
| **REVIEW RETURNED** | 30-Jul-2020 |

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| **GENERAL COMMENTS** | nice revision and well documented network analysis |

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| **REVIEWER** | Philip Aylward<br>South Australian Health and Medical Research Institute, Flinders University and Medical Centre, Adelaide ,Australia |
| **REVIEW RETURNED** | 21-Jul-2020 |

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| **GENERAL COMMENTS** | Much Improved .No need for further changes |