

PEER REVIEW HISTORY

BMJ Open publishes all reviews undertaken for accepted manuscripts. Reviewers are asked to complete a checklist review form and are provided with free text boxes to elaborate on their assessment. These free text comments are reproduced below.

ARTICLE DETAILS

Title (Provisional)

Assessing the relative efficacy of components of opioid-free anaesthesia in adult surgical patients: protocol for a systematic review and component network meta-analysis

Authors

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VERSION 1 - REVIEW

Reviewer	1
Name	Ramsay, Michael
Affiliation	Baylor University
Date	01-Sep-2024
COI	Zero

This is a very welcome study with complicated statistical analysis for which I am not the best reviewer but I do have a strong clinical background. The opening sentence in the abstract OFA aims to reduce opioid-related side effects during surgery - this is really a primary post-operative pain score comparison then a side effect comparison. In the methods you include the "Grey Literature" - this is not peer-reviewed and will reduce the value of your results. NMA is used first in the abstract without a definition. In the methods the major comparator is intraoperative administration of opioids but then you don't include a single dose of opioid given for intubation - why not? This could cause significant complications peri-operatively. If data is missing from a publication the authors will be contacted directly - this is concerning as this is not peer-reviewed and may not be reliable. Study review and and selection will be carried out in Rayann - this is a commercial product that requires a little explanation or reference. Overall this will be a a useful study for the clinician.

Reviewer	2
Name	Bhalerao, Pradnya

Affiliation **BJ Government Medical College and Sasoon General Hospitals, Anaesthesia**

Date **24-Sep-2024**

COI **Nil**

Can the influencing factors be reduced & protocol include surgeries of similar duration and the same incision site?

Rest appears good

VERSION 1 - AUTHOR RESPONSE

Reviewer: 1

1. This is a very welcome study with complicated statistical analysis for which I am not the best reviewer, but I do have a strong clinical background. The opening sentence in the abstract OFA aims to reduce opioid-related side effects during surgery - this is really a primary post-operative pain score comparison then a side effect comparison.

We apologise for the lack of clarity. We modified the sentence in the abstract that now reads as follows:

“The rise of opioid-free anaesthesia (OFA) aims to reduce postoperative pain while reducing opioid-related side effects during surgery.” (Page 3; Line 2)

2. In the methods you include the "Grey Literature" - this is not peer-reviewed and will reduce the value of your results.

The PRISMA guidelines encourage an exhaustive search of all the potentially available information. In the published companion paper to the PRISMA 2009 guidelines (PLoS Med, 2009 6(7): e1000100. doi:10.1371/journal.pmed.1000100; for the PRISMA 2009 statement: Journal of Clinical Epidemiology 62 (2009) 1006e1012) the recommendation for ITEM 7–Information sources states: “In addition to searching databases, authors should report the use of supplementary approaches to identify studies, such as handsearching of journals, checking reference lists, searching trials registries or regulatory agency Web sites [67], contacting manufacturers, or contacting authors.” The PRISMA extension for Network Meta-analyses (Ann Intern Med. 2015; 162:777-784. doi:10.7326/M14-2385) recommend the guidance of this original statement. The updated version of PRISMA 2020 only expand this Item recommending the exact search to be reported for all databases (not just one as in the previous statement) without any other changes. We therefore consider that our protocol follows these guidelines and would like to maintain the literature search as reported.

3. NMA is used first in the abstract without a definition.

Thank you for spotting this mistake. Please see our reply to comment 3 by the Editor. The sentence containing the abbreviation has been removed from the updated version of the manuscript

4. In the methods the major comparator is intraoperative administration of opioids but then you don't include a single dose of opioid given for intubation - why not? This could cause significant complications peri-operatively.

Thank you for this comment. The rationale behind this choice is that some studies allow the OFA strategy to include a single opioid intubating dose. We modified the planned sensitivity analysis of moderators to include this factor. The paragraph in the methods section now reads:

“(v) to examine potential effect moderators we will fit the model with the following covariable: mean age of participants, the duration and the type of surgery, use of a single dose of opioids at intubation time.” (Page: 13; Line: 1)

5. If data is missing from a publication the authors will be contacted directly - this is concerning as this is not peer-reviewed and may not be reliable.

Please see our reply to your previous comment 2. Contacting authors is recommended by the PRISMA guidelines.

6. Study review and selection will be carried out in Rayann - this is a commercial product that requires a little explanation or reference.

We agree. We added an explanation in the updated version of the manuscript that reads as follows:

“Study review and selection will be carried out in Rayann, which is a free software tool for literature screening that provides similar features to those offered by pay software alternatives. [20]” (Page: 10; Line 3)

7. Overall, this will be a useful study for the clinician.

Thank you for this comment, we agree with the reviewer.

Reviewer: 2

1. Can the influencing factors be reduced & protocol include surgeries of similar duration and the same incision site?

Please see also our reply to comment 4 by reviewer 1. The reason to carry out this analysis is to expand on previous analysis that already assessed OFA as a whole (J Clin Anesth 2023 Nov;90:111215. doi: 10.1016/j.jclinane.2023.111215) therefore we would like to preserve as much granularity in this analysis. Of note we consider the type and duration of surgery in a prespecified sensitivity analysis as reported in the previous reply.

2. Rest appears good

Thank you.