

PEER REVIEW HISTORY

BMJ Open publishes all reviews undertaken for accepted manuscripts. Reviewers are asked to complete a checklist review form (<http://bmjopen.bmj.com/site/about/resources/checklist.pdf>) and are provided with free text boxes to elaborate on their assessment. These free text comments are reproduced below.

ARTICLE DETAILS

TITLE (PROVISIONAL)	Awareness and bispectral index (BIS) monitoring in mechanically ventilated patients in the emergency department and intensive care unit: a systematic review protocol
AUTHORS	Pappal, Ryan; Roberts, Brian; Winkler, Winston; Yaegar, Lauren; Stephens, Robert; Fuller, Brian

VERSION 1 - REVIEW

REVIEWER	John Andrzejowski Sheffield Teaching Hospitals NHS Trust United Kingdom
REVIEW RETURNED	11-Nov-2019

GENERAL COMMENTS	You mention throughout the protocol that BIS is used to prevent or decrease awareness. In fact it decreases the chances of recall following an awareness. I think you need to look at the language surrounding this very carefully prior to publication. In particular BIS does not prevent awareness in individuals but decreases overall incidence of AAGA in populations. Several studies have shown that patients can be aware with a response to isolated forearm with a BIS of less than 60, particularly in the induction phase of anaesthesia (Anesthesiology. 2017 Feb;126(2):214-222. doi: 10.1097/ALN.0000000000001479) and (Br J Anaesth. 2014 May;112(5):871-8. doi: 10.1093/bja/aet483. Epub 2014 Feb 13)
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REVIEWER	Richard L. Applegate II MD University of California Davis USA Masimo - research grants, advisory board
REVIEW RETURNED	28-Jan-2020

GENERAL COMMENTS	This is a good study design Minor issues: Abstract Page 3 line 31 should be "Ovid" in place of "Ovide" Page 3 line 45 should be "Ethics" Summary page 4
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	<p>first bullet point suggest "... of awareness in mechanically ventilated, sedated critically ill patients..."</p> <p>The data collection appears to be completed based on the timeline included; however the authors may wish to broaden the scope to include other types of processed EEG monitoring that have been used in studies (in addition to BIS). While inclusion is not mandatory, and BIS appears to be more widely reported than the others, exclusion of other processed EEG monitoring would be a relevant limitation.</p>
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REVIEWER	<p>Yohannes Woubishet Woldeamanuel Stanford University School of Medicine Propria Health Solutions USA Advanced Clinical & Research Center Ethiopia</p>
REVIEW RETURNED	07-Feb-2020

GENERAL COMMENTS	<p>Well written protocol that fulfills all necessary methodological and statistical requirements for conducting a systematic review and meta-analysis. I look forward to their research.</p>
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VERSION 1 – AUTHOR RESPONSE

Reviewer #1 comments

1. You mention throughout the protocol that BIS is used to prevent or decrease awareness. In fact it decreases the chances of recall following an awareness. I think you need to look at the language surrounding this very carefully prior to publication. In particular BIS does not prevent awareness in individuals but decreases overall incidence of AAGA in populations. Several studies have shown that patients can be aware with a response to isolated forearm with a BIS of less than 60, particularly in the induction phase of anaesthesia (Anesthesiology. 2017 Feb;126(2):214-222. doi: 10.1097/ALN.0000000000001479) and (Br J Anaesth. 2014 May;112(5):871-8. doi: 10.1093/bja/aet483. Epub 2014 Feb 13)

Response: We agree and thank you for pointing out this phrasing. In areas where we discuss BIS and awareness, we have modified our phrasing to state "awareness with recall" or "AWR". In the sections of the manuscript where we discuss awareness in the ICU or ED domains, with now specifically state "awareness with paralysis" throughout the manuscript.

Reviewer #2 comments

1. This is a good study design

Response: We thank you for taking the time to provide peer review to our manuscript.

2. Minor issues:

Abstract

Page 3 line 31 should be "Ovid" in place of "Ovide"

Page 3 line 45 should be "Ethics"

Response: Thank you for catching this. These changes have been made.

3. Summary page 4

first bullet point suggest "... of awareness in mechanically ventilated, sedated critically ill patients..."

Response: This has been done.

4. The data collection appears to be completed based on the timeline included; however the authors may wish to broaden the scope to include other types of processed EEG monitoring that have been used in studies (in addition to BIS). While inclusion is not mandatory, and BIS appears to be more widely reported than the others, exclusion of other processed EEG monitoring would be a relevant limitation.

Response: This is an excellent point. Given the fact that BIS is the most frequently reported processed EEG monitor, we have restricted our work to BIS only. However, you bring up a great point, so at the end of the next to last paragraph, we now state:

This systematic review will also focus only on BIS monitoring and not include other processed EEG monitors, limiting any conclusions regarding other processed EEG strategies that have been used to reduce the incidence of awareness with paralysis.

Reviewer #3 comments

1. Well written protocol that fulfills all necessary methodological and statistical requirements for conducting a systematic review and meta-analysis. I look forward to their research.

Response: We thank you for providing peer review to our manuscript.