

## 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

<b>TITLE (PROVISIONAL)</b>	Protocol for an observational study of delirium in the Post-Anesthesia Care Unit (PACU) as a potential predictor of subsequent postoperative delirium
<b>AUTHORS</b>	Cui, Victoria; Tedeschi, Catherine; Kronzer, Vanessa; McKinnon, Sherry; Avidan, Michael

### VERSION 1 - REVIEW

<b>REVIEWER</b>	George Djaiani Toronto General Hospital, Toronto, Canada
<b>REVIEW RETURNED</b>	10-Apr-2017

<b>GENERAL COMMENTS</b>	<p>This is a retrospective review designed to determine an association between 'emergence delirium' and postoperative delirium. I am not clear why the authors suggest to use structured chart review for detection of delirium if the data is coming from a prospective randomized trial using CAM-ICU tool. My concern is the sample size of only 100 patients to reach any meaningful conclusions.</p>
-------------------------	---

<b>REVIEWER</b>	Tobias Gauss East Anglian Air Ambulance, Norwich, United Kingdom Department of Anaesthesia and Critical Care Beaujon University Hospital Clichy, France
<b>REVIEW RETURNED</b>	13-Apr-2017

<b>GENERAL COMMENTS</b>	<p>Thank for the opportunity to assess this protocol. The objective of the protocol is to study the association between immediate post-extubation delirium and delayed delirium.</p> <p>Postoperative clinical delirium is a public health issue, so from a general point a view a clinically relevant topic.</p> <p>The objective and hypothesis are clearly stated. The protocol is well structured and responds to STROBE requirements for observational studies. The study is a convenience sub-sample of a larger study. Methods and sample size calculation appear appropriate. The authors assess very adequately the limitations of the protocol, in particular the single center nature that may generate a selection bias.</p> <p>Please allow me to suggest a few amendments or clarifications to consider for the authors:</p> <p>1) What would be the clinical impact of earlier identification of</p>
-------------------------	---

	<p>patients at risk, before the PACU and given known risk factors? How could the results change clinical management? Should e.g. patient stay longer in PACU or HDU or subjected to targeted delirium prevention bundle?</p> <p>2) The sample size calculation appears appropriate, the authors should however consider to increase it for two reasons: - the single center character, increasing the sample size may probably control for selection bias and transposition to other settings, however improve identification of other confounders - only three confounders have been pre-determined, although recent evidence indicates supplementary factors that the authors may take into consideration (doi:10.1111/ans.13874, doi: 10.1093/bja/aeu442). Other confounders may require consideration: immediate postextubation care (opioids...) or care in PACU and ward, and clinical events, immediate and delayed (complications, ...); all these may effect the dependant variable delayed delirium. More factors would require more patients to be able to perform the logistic regression.</p> <p>3) It would be interesting to learn more about care requirements of patients that presented with immediate and/or delayed delirium.</p> <p>I would be delighted to reassess the protocol, if the editorial board considers this to be necessary.</p>
--	--

### VERSION 1 – AUTHOR RESPONSE

Reviewer 1 –

The use of structured chart review for detection of delirium in the postoperative period being studied (postoperative days 1-5) has been clarified as providing data for comparison with delirium assessed in the PACU (in the "Data" section, pages 10-11). The structured chart review procedure is part of the larger ENGAGES study, of which this protocol describes the implementation of a sub-study.

The sample size of 100 patients has been identified as a limitation of this study (under the "Strengths and Limitations" section, pages 12-13). The sample size is likely to be adequate in identifying a possible association between "emergence delirium" and postoperative delirium at the effect size stated.

Reviewer 2 -

A brief discussion of the clinical impact of earlier identification of patients at risk for developing postoperative delirium, known risk factors, care requirements for patients with postoperative delirium, and possible changes to clinical management has been added to the "Introduction" section of the protocol (pages 5-7).

The single-center nature of this study as well as the sample size have been identified as limitations of this study (under the "Strengths and Limitations", pages 12-13). The sample size chosen for this study was determined by planned analysis with three confounders (Short Blessed Test, age, and Charlson Comorbidity index). Other possible confounders which may be evaluated in post-hoc analyses have been listed in the "Statistical considerations" section (pages 11-12).

Please let us know if additional revisions are needed. We appreciate the time taken by the peer reviewers and the editorial team in evaluating this protocol.

## VERSION 2 – REVIEW

<b>REVIEWER</b>	George Djaiani Toronto General Hospital, Toronto, Canada
<b>REVIEW RETURNED</b>	06-May-2017

<b>GENERAL COMMENTS</b>	I am satisfied with the manuscript in the current form
-------------------------	--

<b>REVIEWER</b>	Tobias Gauss Beaujon University Hospital APHP Clichy, France
<b>REVIEW RETURNED</b>	10-May-2017

<b>GENERAL COMMENTS</b>	The comments on the initial version have been well addressed. The only remaining issue from my humble point of view is the relatively small sample size and event incidence. It may allow to control and adjust to the three chosen explicative variables, but probably not for other confounders/events that may trigger delayed delirium in the care process up to day five, which is the association the authors decided to study.
-------------------------	---