

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.

This paper was submitted to a another journal from BMJ but declined for publication following peer review. The authors addressed the reviewers' comments and submitted the revised paper to BMJ Open. The paper was subsequently accepted for publication at BMJ Open.

(This paper received three reviews from its previous journal but only two reviewers agreed to published their review.)

ARTICLE DETAILS

TITLE (PROVISIONAL)	Automated oxygen administration vs. conventional oxygen therapy after major abdominal or thoracic surgery: study protocol for an international multicenter randomized controlled study
AUTHORS	I'her, erwan; Jaber, S.; VERZILLI, Daniel; JACOB, Christophe; HUIBAN, Brigitte; Futier, Emmanuel; KERFORNE, Thomas; PATEAU, Victoire; Bouchard, Pierre-Alexandre; GOUILLOU, Maellen; NOWAK, Emmanuel; Lellouche, Francois

VERSION 1 – REVIEW

REVIEWER	Siv Fonnes Herlev Hospital, Denmark
REVIEW RETURNED	20-May-2018

GENERAL COMMENTS	<p>To the authors</p> <p>This is a protocol for a randomised controlled trial that investigates if automated oxygen administrated by a FreeO2 system versus conventional oxygen can reduce postoperative hypoxemia.</p> <p>Comments:</p> <ol style="list-style-type: none">1. General: I am pleased to see that you have reported your protocol according to the SPIRIT guidelines. Please consider mentioning this with a reference in your e.g. in your "Ethics and Dissemination" section. You could also upload the SPIRIT checklist for your protocol as a supplementary file.2. Ethics and Dissemination: please correct "submitted to peer-reviewed journals" to "publish in a peer-reviewed journal"3. Ethics and Dissemination: please consider adding that you will report your results according to the CONSORT guidelines.4. Introduction, page 5, line 23: Please add manufacturer details the first time you write "The FreeO2 system" in parentheses.5. Introduction, page 5, line 50: Please correct "...etc..."6. Introduction, page 6, line 6-13: Please delete "...".7. Introduction, Objectives, page 6: You state that your objective is "The FreeO2 Post-Op trial aims to evaluate the clinical impact of automated O2 administration vs conventional O2 therapy in terms of oxygenation and hypoxemia prevention after major abdominal or thoracic surgeries". However, in your registration at clinicaltrials.gov your aim is different: "The aim of the study is to assess the use feasibility of the FreeO2 system so as to deliver automatically oxygen in the post anaesthesia care unit in a patient population
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	<p>admitted for major abdominal and thoracic surgery.” Why have you changed the phrasing of the aim?</p> <p>8. Methods, page 7-8: Please add your last exclusion criteria from clinicaltrial.gov: “perturbed or non-cooperative patient”.</p> <p>9. Methods, page 10, line 10: Please correct that figure 1 shows the participant timeline.</p> <p>10. Methods, page 10, line 16: Please add references to your statement: “Based on previous studies and data from the literature (..)”.</p> <p>11. Methods, page 11, line 32: Please elaborate why you have used reference 23 for the statement “All the analyses will be performed by the study statistician”.</p> <p>12. Reference list: Please correct reference 25 (capitalise journal name), 43 (capitalise “one”), and 48 (add journal name, year, issue, and page).</p> <p>13. Methods, page 14, Dissemination Policy: Please correct “Findings will be published in peer-reviewed journals” to “Findings will be published in a peer-reviewed journal” and consider adding that you will report your results according to the CONSORT guidelines.</p> <p>14. Reference list: Please correct reference 25, 43, and 48 (capitalise journal names and add information on journal, year, issue, and page).</p>
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REVIEWER	Ary Serpa Neto Hospital Israelita Albert Einstein, São Paulo, Brazil
REVIEW RETURNED	24-May-2018

GENERAL COMMENTS	This is a well written protocol for an ongoing RCT. The group of authors is well know in the field and have a lot of expertise in this type of study. The protocol is clear and I have nothing to add or suggest.
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REVIEWER	Dr. Hisham ElMoaqet German Jordanian University, JORDAN
REVIEW RETURNED	09-Jul-2018

GENERAL COMMENTS	<p>In this paper, FreeO2 Post-Op study is proposed to evaluate the clinical impact of automated oxygen administration vs conventional oxygen therapy after major abdominal or thoracic surgery. The study is promising to demonstrate the benefits of automated oxygen titration for post-op patients. Yet, I have the following suggestions:</p> <p>1. A very common way to characterize desaturations in thne post-op period is the Oxygen Desaturation Index of 4% (ODI4). A secondary outcome of this study could be to evaluate the automated oxygen therapy effect on the ODI4 for the patients in the study and compare this with manual oxygen administration.</p> <p>2 What is the basis for selecting these two particular surgeries (thoracic and abdominal). Is it too hard to include other categories of surgeries?</p> <p>3. Accurate oxygen adjustment will need high sensitivity to oxygenation condition variations. It might be interesting to analyze the effectiveness of short term predictions of oxygen levels which will be the basis for automatic oxygen adjustments in order to get a deeper insight to the performance/efficacy of this device in these patient populations.</p>
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VERSION 1 – AUTHOR RESPONSE

Reviewer #1

Thanks a lot for this careful revision of our protocol. All your comments/queries have been taken into account (see modifications within manuscript). We do hope that such modification will fulfill your requirements.

1. All recommended references have been added (SPIRIT and CONSORT) ;
2. The objective has been modified to the one that appears within Clinicaltrials ;
3. The last exclusion criteria within Clinicaltrials have been added. We are sorry for this omission ;
4. Sorry for the mistake about reference #23 during manuscript preparation ; it has been moved to the « Study setting » paragraph ;
5. References have been modified accordingly ;
6. All other minor comments have been taken into account.

Reviewer #2

Thanks a lot for this very kind appreciation of the protocol !

Reviewer #3

Thanks a lot for this very interesting reviewing. This is much appreciated, especially taking into account the fact that your comments will also enable us to improve and standardize the writing of the final report when all data will be available !

- 1- In fact, even if the ODI is not cited within the protocol and in the Clinicaltrials presentation of the methodology all data were already to be presented according to the level of desaturation below range with a 2 and 4% difference (ie. an ODI 2-4%) in the study analysis plan, even if not written using the same terms ;
- 2- The reasons why we chose to include only these types of surgeries were a- an attempt to homogenize as much as possible the population to be included ; b- a consideration that these patients were deemed to experience much more hypoxemia events than the other ones (see at least ref#40-42). Such statement is already present within the Discussion section ;
- 3- The device that adjusts oxygen flow to patients' requirements (FreeO2) is based on a proportional controller that modifies flow each second in response to oximetry variations; the last version of the algorithm that runs of the devices that are currently in use during the study has been validated in our previous studies (response time: 1 sec; precision 0.1 L/min). The accuracy of the device can also be assessed while taking into account the real output flow (measured by an independent electronic flowmeter), as compared to the goal, calculated by the controller.

VERSION 2 – REVIEW

REVIEWER	Siv Fonnes Department of Surgery, Herlev Hospital, Denmark
REVIEW RETURNED	12-Aug-2018
GENERAL COMMENTS	The authors have thoroughly revised and improved the manuscript. I have no further comments.
REVIEWER	Dr. Hisham ElMoaqet German Jordanian University, JORDAN
REVIEW RETURNED	30-Aug-2018
GENERAL COMMENTS	This is a much improved version.