Reviewer's report

Title: The use of a machine-learning algorithm that predicts hypotension during surgery in combination with personalized treatment guidance: study protocol for a randomized controlled clinical trial

Version: 0 Date: 02 Jul 2019

Reviewer: Paul Mouncey

Reviewer's report:

The protocol is comprehensive with no clear areas missing. I do though have some comments below, which I believe would aid clarity for the reader.

- The number of patients to be recruited for Phase A is not clear. As it states that overall 100 patients are to be recruited and the sample size calculation show that 30 patients are needed for each arm, I am assuming 40 patients are recruited to study any potential Hawthorne effect.

- Will this design actually be able to successfully study the Hawthorne effect? My understanding from reading the manuscript is that these patients and the clinical team, even though they don't know the purpose, will still know the patient is on a research study. This means that the patient may well receive additional observations etc, which may contribute to improved outcomes. Also will the sample size be enough to study this with any degree of certainty? There is a lack of information generally about this phase of the study.

- How are the authors adjusting for important baseline covariates that may be associated with the primary outcome (e.g. baseline blood pressure)? Is the randomisation stratified by any baseline variables?

- When reporting the sample size calculation, it is useful for context to report the expected control group TWA.

- The secondary outcomes seem to be missing incidence and time spent in hypotension when compared to clinicaltrials.gov.

- Can AE/SAEs be defined? Is this all adverse events irrespective of causality? There is the potential risk of over-treatment using a predictive algorithm, so it will be important to obtain safety data in relation to the treatment given to treat potential hypotension.

- I don't find figure 2 (algorithm) straightforward to understand. For example following the arrows start to HPI 50-85% 'Diagnose Cause' then to HPI>85% or MAP<65 'Start treatment'. I don't understand how HPI 50-85% flows into HPI>85%?

- There seems to be a typographical error on the acceptance for registration to clinicaltrials.gov. The trial was submitted in November 2017 and accepted in December 2018.
clinicaltrials.gov record states that it was last updated in December 2017, so I assume there is an error in the acceptance date.

**Level of interest**
Please indicate how interesting you found the manuscript:

An article whose findings are important to those with closely related research interests

**Quality of written English**
Please indicate the quality of language in the manuscript:

Acceptable

**Quality of figures**

All images and figures within the manuscript should be genuine i.e. without evidence of manipulation. No specific feature within an image may be enhanced, obscured, moved, removed, or introduced. If you have concerns about the veracity of the figures you should choose the first option below.

**Statistical review**

Is it essential that this manuscript is seen by an expert statistician? If so, please give your reasons in your report.
Declaration of competing interests
Please complete a declaration of competing interests, considering the following questions:

1. Have you in the past five years received reimbursements, fees, funding, or salary from an organisation that may in any way gain or lose financially from the publication of this manuscript, either now or in the future?

2. Do you hold any stocks or shares in an organisation that may in any way gain or lose financially from the publication of this manuscript, either now or in the future?

3. Do you hold or are you currently applying for any patents relating to the content of the manuscript?

4. Have you received reimbursements, fees, funding, or salary from an organization that holds or has applied for patents relating to the content of the manuscript?

5. Do you have any other financial competing interests?

6. Do you have any non-financial competing interests in relation to this paper?

If you can answer no to all of the above, write 'I declare that I have no competing interests' below. If your reply is yes to any, please give details below.

I declare that I have no competing interests

I agree to the open peer review policy of the journal. I understand that my name will be included on my report to the authors and, if the manuscript is accepted for publication, my named report including any attachments I upload will be posted on the website along with the authors' responses. I agree for my report to be made available under an Open Access Creative Commons CC-BY license (http://creativecommons.org/licenses/by/4.0/). I understand that any comments which I do not wish to be included in my named report can be included as confidential comments to the editors, which will not be published.

I agree to the open peer review policy of the journal

Were you mentored through this peer review?

No