PEER REVIEW HISTORY

ARTICLE DETAILS

TITLE (PROVISIONAL)	Protocol and statistical analysis plan for the PREventing cardiovascular collaPse with Administration of fluid REsuscitation during Induction and Intubation (PREPARE II) randomized clinical trial
AUTHORS	Russell, Derek; Casey, Jonathan; Gibbs, Kevin; Dargin, James; Vonderhaar, Derek; Joffe, AM; Ghamande, Shekhar; Khan, Akram; Dutta, Simanta; Landsperger, Janna; Robison, Sarah; Bentov, Itay; Wozniak, Joanne; Stempek, Susan; White, Heath; Krol, Olivia; Prekker, Matthew; Driver, Brian; Brewer, Joseph; Wang, Li; Lindsell, Christopher; Self, Wesley; Rice, Todd; Semler, Matthew; Janz, David

VERSION 1 – REVIEW

REVIEWER	Daniel Fein Albert Einstein College of Medicine, USA
REVIEW RETURNED	20-Mar-2020

GENERAL COMMENTS	The authors have presented a very thorough and well thought out plan to answer a question that they themselves have exposed from their prior, well regarded work in this field. Their question is concise and their plan of analysis is extensive. It would benefit other researchers to be able to review the methods of the authors to learn more about how this logistically challenging and very clinically relevant research can be feasibly conducted and so I applaud the publication of this submission.

REVIEWER	Reignier Median Intensive Reanimation Nantes University Hospital France
REVIEW RETURNED	05-Apr-2020

GENERAL COMMENTS	This is an important study. Just one major concern: inclusion and non inclusion criteria should be more detailed. Moreover the sentence "...feel that fluid bolus administration is either required or contraindicated" is unclear. On which medical or scientific knowledge does this "feeling" rely?

VERSION 1 – AUTHOR RESPONSE

Reviewer: 1
Reviewer Name: Daniel Fein

Institution and Country: Albert Einstein College of Medicine, USA Please state any competing interests or state ‘None declared’: None

The authors have presented a very thorough and well thought out plan to answer a question that they themselves have exposed from their prior, well regarded work in this field. Their question is concise and their plan of analysis is extensive. It would benefit other researchers to be able to review the methods of the authors to learn more about how this logistically challenging and very clinically relevant research can be feasibly conducted and so I applaud the publication of this submission.

Thank you for your encouraging remarks. We look forward to learning the eventual results of this study.

Reviewer: 2
Reviewer Name: J Reignier
Institution and Country: Median Intensive Reanimation, Nantes University Hospital, France Please state any competing interests or state ‘None declared’: None declared

This is an important study.
Just one major concern: inclusion and non inclusion criteria should be more detailed. Moreover the sentence "...feel that fluid bolus administration is either required or contraindicated" is unclear. On which medical or scientific knowledge does this "feeling" rely?

Thank you for your encouraging comments and helpful feedback. The inclusion and exclusion criteria are designed to allow us to study, to the extent possible, the broadest possible population in order to understand the real-world effectiveness of giving or not giving a 500 mL crystalloid bolus to prevent post-intubation cardiovascular collapse, and thus maximize the trial’s generalisability. For this reason the inclusion criteria are meant to be relatively broad, and the exclusion criteria are meant to exclude only those patients in whom an operator would not have equipoise on this clinical question. In other words, the exclusion criteria were designed so that treating clinicians would not be asked to provide an intervention that they judge to be wrong for this patient (from their synthesis of available clinical data at the time). This essentially allows providers to enroll subjects for whom there is clinical equipoise on this question, which is precisely the population this trial is intended to study. To better explain and clarify this, we have added a brief discussion of clinical equipoise into the “Population” section (pages 10, 11).

VERSION 2 – REVIEW

REVIEWER	Reignier J Medecine Intensive Reanimation, University Hospital, Nantes, France
REVIEW RETURNED	01-Jun-2020

GENERAL COMMENTS	Than you for this revised manuscript. Authors have addressed my concerns. To my opinion, the manuscript is suitable for publication in BMJ Open.