Patient and public involvement in contemporary large intensive care trials

Protocol for a meta-epidemiological study

Barot, Emily; Kjaer, Maj-Brit Nørregaard; Collet, Marie; Crescioli, Elena; Rasmussen, Bodil Steen; Estrup, Stine; Mortensen, Camilla Bekker; Vesterlund, Gitte Kingo; Sivapalan, Praleene; Anthon, Carl Thomas; Bruun, Camilla Rahbek Lysholm; Poulsen, Lone Musaeus; Møller, Morten Hylander; Perner, Anders; Granholm, Anders

Published in:
Acta Anaesthesiologica Scandinavica

DOI (link to publication from Publisher):
10.1111/aas.13953

Publication date:
2021

Document Version
Accepted author manuscript, peer reviewed version

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Article type : Review

Patient and public involvement in contemporary large intensive care trials: protocol for a meta-epidemiological study.

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Short title: Patient involvement in ICU RCTs

Word count main text: 1969

Word count abstract: 181

Abstract

Background*:* Patient and public involvement (PPI) in randomised clinical trials (RCTs) has increased in recent years but remains the exception rather than the rule. We aim to assess the frequency and extent of PPI in large, contemporary RCTs conducted in an intensive care setting.

Methods and design: We will conduct a meta-epidemiological study of RCTs conducted in intensive care settings published since 2019 and assess their use of PPI. We will extract trial characteristics and verify the use of PPI with trial authors unless specifically stated in the published paper. The primary outcome will be the proportion of trials that use PPI. Secondary outcomes will explore which groups are consulted, at what stage of the trial process this occurs, and by which means these opinions are collected and implemented.

Discussion: This meta-epidemiological study will provide an important insight into the use of PPI in large, contemporary intensive care trials. We wish to reveal ways in which patient involvement could be incorporated more broadly and purposefully here and help to empower clinicians, researchers, and patients to collaborate further on future research processes and goals.

Introduction

Patient and public involvement (PPI) in healthcare has greatly increased in recent years.[1] However, the inclusion of patients' preferences and opinions in clinical research appears to be the exception rather than the rule,[2] and the research agenda continues to be set by academia, industry, and other non-patient and public stakeholders.[3] To level this discrepancy, numerous policy directives and organisations have been initiated to better facilitate PPI at all stages of health research, including Involve in the United Kingdom (www.involve.org.uk) and the Patient-Centered Outcomes Research Institute (PCORI) in the United States (www.pcori.org)[4].

Involving patients, caregivers, communities, and patient organisations in the research process is warranted for a variety of reasons. Principally, PPIs' agenda is to bring the perspectives of patients and their relatives into the design, recruitment, analysis, and implementation of the results of the research project to insure relevance and quality of future research.[4]

It is possible to include PPI at many different stages within the research process; Pii and colleagues[4] defined 6 stages of possible patient involvement: 1) development of research focus, 2) development of research design, 3) recruitment, 4) data generation, 5) data processing and 6) research dissemination. PPI encompasses a wide range of methods and approaches, including traditional qualitative and quantitative methods (e.g., interviews, focus groups, questionnaires), as well as more comprehensive techniques such as Delphi processes[4]. One prominent PPI approach brings patients, caregivers, and clinicians together into *Priority Setting Partnerships*. This approach was developed in the James Lind Alliance and works to identify potential research questions before putting these through rounds of prioritization.[5]

Due to the nature of care provided in the intensive care unit (ICU), the extent to which an individual patient can be involved in research is highly dependent on their health condition.[6] Therefore, PPI in ICU research is more likely to include the input of relatives, survivors, and patient organisations. Despite the potential challenges, the heterogeneity of patients treated in

ICUs and high disease burden make PPI very relevant to ICU research, as a means of aligning the needs and priorities of all these different groups.

The aim of the outlined meta-epidemiological study is to investigate the inclusion of PPI in contemporary, large randomised clinical trials (RCTs) conducted in the ICU setting. A comprehensive overview of PPI in large ICU RCTs, will help to inform when and how patients are involved in research, and identify opportunities for increased PPI in future research.

Methods

Objectives

We aim to assess how frequently and to what extent contemporary, large ICU-based RCTs use PPI. More specifically, we will explore how frequently PPI happens, which groups are consulted, how this involvement is carried out and at what stage in the trial process this occurs. Our primary research question is therefore, "to what extent do contemporary, large ICU RCTs use patient and public involvement?"

Study Design

This is a meta-epidemiological study of contemporary RCTs conducted in an ICU setting. This study was not eligible for registration at The Prospective Register of Systematic Reviews (PROSPERO), as it will not assess health related outcomes. Our protocol was prepared according to the Preferred Reporting Items for Systematic Review and Meta-Analysis Protocols (PRISMA-P) guidelines.[8] The manuscript will be prepared in accordance with the guidelines for reporting meta-epidemiological research produced by Murad and Wang,[9] which built upon the Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) statement.[10] This protocol was submitted and accepted prior to the conduct of the study.

Criteria for Considering Studies for Inclusion

This study will include data from large, contemporary RCTs conducted in an ICU setting from 2019 and onwards. We define 'large' RCTs as those with a sample size greater than 224 participants, which Anthon and colleagues[7] identified as the upper quartile of sample size in 604 ICU RCTs conducted between 1977 and 2018. These larger trials have the potential to change clinical practice and are therefore more likely to consider incorporating the needs and priorities of patients and their representatives as a research imperative. We have chosen to focus on RCTs published in recent years in order to to get an overview of the role PPI plays in current ICU research.

The RCTs will be identified using the search strategy outlined below. Abstracts and titles will be screened independently and in duplicate; potentially eligible trials will be assessed independently and in duplicate in full-text and assessed for inclusion. Any disagreements will be resolved through discussion or involvement of a third author. We will use Covidence (https://www.covidence.org) to manage search records and document reasons for exclusion. The inclusion criteria must all be fulfilled for a trial to be included in this study and are as follows: 1) Intervention given to adults (as defined by the trial authors) in an ICU setting, 2) Published online after 1st January 2019 and 3) Inclusion of at least 225 participants. If trials are not restricted to adults only or if this is not specified, we will include trials if the majority of participants appear to be over 18 years of age or above, based on presented population characteristics. We will assume an ICU setting if more than half of the patients received typical ICU interventions such as vasopressors/inotropes, mechanical ventilation, or invasive monitoring. RCTs studying interventions primarily outside the ICU, but with subsequent ICU admission or follow-up (e.g., peri-operative trials with subsequent ICU admission, where the intervention primarily happens before ICU admission) will not be included.

Types of Outcome Measures

Primary outcomes

The primary outcome will be the proportion of the included RCTs that incorporate PPI.

Secondary outcomes

Secondary outcomes will include which participant groups were consulted (patients, families, clinicians, patient organisations), how many people were consulted in total, at what stage of the trial process was this involvement was implemented (according to the six stages defined above by Pii et al[4]) and how/by what means the views and opinions of patients and their representatives were collected and used (individual interview, group interview, survey, focus group, workshop, Delphi, discussion, Priority Setting Partnerships/James Lind Alliance method - as in Pia et al[4]).

Search methods

Two members of the study group will search the PubMed database using a search string focused on keywords and filters to identifying ICU trials. The search string will include keywords: 'intensive care unit', 'critical care', 'critical illness', 'critically ill', 'intensive care', 'icu' and 'randomised controlled trial', 'controlled clinical trial', 'randomized', 'randomly', 'trial', 'clinical trial'. The full search strategy is included as a supplement. The search will be limited to title, abstract, and keywords and filtered to include papers published from 1st January 2019 onwards. An updated search will be performed before submission of the final manuscript to an international peer-reviewed journal.

Data extraction and management

Data from eligible trials will be extracted in duplicate by two independent members of the research group, using a pre-defined electronic extraction form (supplied as a supplement), which will be pilot tested by at least two authors on the first 10 trials and revised if necessary. Any discrepancies or disagreements will be settled with a third member of the group.

We will extract characteristics of each trial (author, year of publication, countries, number of centers, trial size, funding source and funding type (industry, philanthropic, other, or not specified), as well as information on the intervention under investigation (intervention type (drug, device, management or combinations[7]), name of intervention(s) and disease area) and whether the manuscript mentions the use of patient involvement. For trials that mention patient involvement, information about this will also be extracted (how involvement was collected, who was asked, at which stage of the trial was involvement included, how many patients were consulted). If the inclusion of PPI is unclear or not thoroughly reported, we will first consult the trial protocol (when available) and then contact the trial authors to confirm this information.

Dealing with missing data

Unless thoroughly described in the paper or protocol, we will contact trial authors to verify their inclusion of PPI in their trial, more specifically, which participant groups were consulted, how many people were consulted in total, at what stage of the trial process was the involvement incorporated and how/by what means the views and opinions of patients and their

representatives were collected and implemented. A second email will be sent if we have not received a reply after 14 days, but due to time restrictions and the potentially large number of trials, we will assume that trials did not include PPI if no response is obtained after the second reminder email is sent.

Statistical analysis

Outcomes will be analysed using simple descriptive statistics, i.e., numbers and percentages for categorical data and medians with interquartile ranges for numeric data. The primary analyses will be conducted on all included trials. Additionally, we will present descriptive statistics in separate groups according to intervention type, number of centres (one or more), and type of funding (as specified above).

Ethics and dissemination

This study does not require ethical approval as we will extract and evaluate data that is already available in the public domain. This study was not eligible for registration at The Prospective Register of Systematic Reviews (PROSPERO), as it will not assess health related outcomes. The results of this study will be published in accordance the protocol with any deviations described along with reasonings, and the final paper will be submitted to a peer-reviewed journal.

Discussion

The proposed meta-epidemiological study will provide an important insight into PPI in contemporary, large ICU RCTs in adult patients. By drawing attention to this issue, we hope to reveal ways in which patient, relative and public involvement could be incorporated more broadly and purposefully within ICU trials and help to empower clinicians, researchers, patients and the public to collaborate further on future research goals.

The outlined study comes with important strengths. By having a relatively broad search strategy we intend to include a wide range in intervention types, published in a variety of journals. Further, by contacting the trial authors directly about their use of PPI, even when its inclusion is not mentioned in the published paper, we will be able to assess the use of PPI more accurately in all aspects of large-scale, contemporary ICU research.

There are some important limitations to this study, as well. First, by solely focusing on contemporary, larger trials we will not be able to assess trends in patient involvement over time. Additionally, it is reasonable to assume that larger trials will be more likely to include PPI, meaning our sample of trials may not be representative of all ICU RCTs. However, larger trials are more likely to change ICU practice, meaning the inclusion of PPI is arguably more vital and meaningful, and a restriction to recent years is necessary to get an overview of the current status, as a means to inform change. Another limitation is the relatively small number of trial characteristics that are to be extracted, particularly the absence of any data on quality indicators such as appropriate randomisation or blinding. These indicators are usually captured through a risk of bias assessment, which is not considered appropriate here as risk of bias assessments rely not only on trial characteristics, but also on other factors e.g., type of outcome and how likely trial characteristics are to affect the outcomes of interest[11]. However, as these quality indicators are usually assessed in relation to a particular intervention or clinical outcome, this is not within scope of this project.

In conclusion, the proposed study will provide a necessary overview of the extent to which large, contemporary ICU RCTs use PPI. The results of this study will help to inform and effect how ICU research incorporates and uses the views of patients and their representatives, and may ultimately pave the way for more PPI, leading to more patient-important research.

Funding

This study was conducted as part of the Intensive Care Platform Trial (INCEPT) research program (www.incept.dk), which has received funding by Sygeforsikringen "danmark" and Ehrenreich's Foundation. The funders have no influence on any aspects of this study.

Author contributions

Study design: EB, MBNK, MOC, MHM, AP, AG. Drafting of the protocol: EB. Critically revising the protocol for important intellectual content and approving final version: all authors. AG is the guarantor of the study.

Conflicts of interest

The Department of Intensive Care at Rigshospitalet has received funding for other projects from The Novo Nordisk Foundation, Pfizer, Ferring and Fresenius Kabi.

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