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Effectiveness of participant recruitment strategies for critical care trials: a systematic review and narrative synthesis

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Abstract

Background: Critical care trials are limited by problems with participant recruitment, and little is known about the most effective ways to enhance trial participation. Despite clinical research improving in the past decades within intensive care, participant recruitment remains a challenge. Not all eligible patients are identified, and opportunities for enrolment into clinical trials are often missed. Interventions to facilitate recruitment need to be identified to improve trial conduct in the critical care environment. Therefore, we aimed to establish the effectiveness of recruitment strategies in critical care trials in order to inform future research practice.

Methods: Databases including Medline, Embase, CINAHL and PsychInfo were searched for English language papers from inception to February 2020. The objectives were to: (a) establish the effectiveness of recruitment strategies; and (b) recommend how effective recruitment strategies can inform research practice. Two reviewers independently assessed papers for inclusion and critically appraised the quality of the studies. Discrepancies were discussed within the research team. Relevant data were extracted and thematically coded into five overarching themes using a narrative synthesis approach. The review was prospectively registered on PROSPERO (CRD42019160519).

Results: The search resulted in 2509 initially identified articles, with 15 that met the inclusion criteria. Articles reported a combination of quantitative, mixed methods, and qualitative studies and a range of low, moderate, and high-quality studies. Although, in-keeping with narrative synthesis approaches, none were excluded based on methodological quality. Five themes were identified relating to: patient eligibility identification; who provides information and seeks consent; resource limitations; research culture or environment; and the consent model used. The relative success of recruitment strategies was dependent upon the experience and availability of the staff involved in the approach, trial design, the application of the strategy to the specific intensive care environment, the acceptability of the recruitment and consent models used, and the efficiency of the recruitment procedures. Opportunities for consent were missed in a proportion of eligible patients in most studies, suggesting that clinicians may avoid recruiting more complex patients or in more complex situations and that further development of strategies is needed.

Conclusions: More effective recruitment strategies are required to enhance recruitment and the representativeness of the patient sample obtained in critical care trials, in order to expand the evidence-base for treatments in this field. Greater focus is needed on assessing the performance of different recruitment strategies within different types of studies and critical care research environments. Future research should explore key stakeholders' experiences of, and attitudes towards, recruitment and establish the most important and feasible modifiable barriers to recruitment.

Keywords

critical care, ICU, ITU, intensive care, recruitment method, recruitment strategy, systematic review

Introduction

Intensive care (or critical care) is a highly technical and specialised healthcare setting that provides treatment and support for critically ill patients with life-threatening conditions.¹ There are 291,836 critical care cases in the UK per year, and it accounts for a total proportion of 1% of NHS expenditure.² However, despite intensive medical and nursing care, and provision of complex ventilatory and other organ support, in-hospital mortality rates are 23.9%.³ Whilst this is likely due to the critical condition of the patients admitted, treatment in critical care is lacking a robust evidence base. Despite considerable international research, many unanswered questions remain regarding the care of critically ill patients.⁴ One of the major limitations in conducting trials in this field is the difficulty of patient recruitment, however little is known about the most effective ways to enhance research participation.⁵

Barriers to patient recruitment in critical care trials are heavily centred around the challenges of obtaining informed consent.⁶ Unlike other settings, researchers are limited in their interactions with patients due to illness severity, delirium, presence of sedatives and life-sustaining treatments. Additionally, patients in critical care often lack decisional capacity. Burns et. al found that approximately 90% of critical care patients are unable to make decisions regarding their inclusion in research, and most decisions will be made by representatives such as family members.⁶ Additionally, it can be difficult to identify family members to act as the patient's surrogate decision-maker (SDM), and many will not know the patient's preferences and views about participation, increasing the difficulty in making a decision.⁷⁻⁹

Not all critical care patients will have family members present, and the unavailability of a surrogate to provide consent by proxy may be as high as 40%.^{5, 6, 10} This is problematic for trials with narrow recruitment windows. Some studies have used deferred consent (research without prior consent) to achieve adequate recruitment in emergency situations, however some families have expressed concerns regarding the use of a deferred consent model.¹¹

Previous studies show that patient recruitment strategies in the wider context of clinical research are poorly defined.¹¹ A Cochrane review exploring interventions to improve recruitment in randomised trials,¹² outlined the need for the research community to prioritise research into recruitment interventions.^{12, 13} Although the review authors identified useful methods, they only included recruitment interventions rather than recruitment strategies more broadly, and did not include other models of consent, therefore findings from the research are less applicable to critical care settings. For example, the optimisation of participant information leaflets is beneficial for recruitment, but may be of less benefit in a critical care context, due to the complexity of studies and a greater need for verbal explanation.¹¹ Clinician involvement is variable in clinical research, and may contribute to patient refusal rates being as high as 20%,^{5, 6, 10} occurring more frequently in complex cases of care or cases involving elderly patients,^{6, 11} both of which are more likely in a critical care setting. Despite prior research evaluating recruitment interventions in non-critical care settings¹² and anecdotal and ad hoc reporting from critical care studies, there is limited evidence around the most effective strategies of participant recruitment in critical care. We conducted a systematic review and narrative synthesis to explore different recruitment strategies. The aim of this review was to systematically collate and synthesise published studies on recruitment strategies for critical care research. The objectives were to: (a) establish the effectiveness of recruitment strategies in critical care research; and (b) recommend how effective recruitment strategies can inform research practice. Based on a preliminary review of the literature, a narrative synthesis approach was chosen because there was expected to be wide heterogeneity between studies. Unlike

reviews of solely qualitative or quantitative findings, for which other approaches to synthesis such as meta-ethnography or meta-analysis are appropriate, this approach can be used to textually summarise the data, enabling data to “tell a story.”¹⁴

Methods

A systematic search methodology was used.¹⁵ The protocol was prospectively registered in the PROSPERO database (CRD42019160519). A narrative synthesis was performed in accordance with the Cochrane Collaboration guidance.¹⁶

Eligibility criteria

English language studies were included with no date restriction on the year of publication. Qualitative, quantitative and mixed-methods papers which reported the evaluation of a recruitment strategy within a critical care setting were eligible for inclusion. Papers exploring clinicians’ or patients’ attitudes to a specific recruitment strategy were also included. Critical care was defined according to the NHS Core Standards,¹⁷ as an area of medicine where patients receive more intensive monitoring and treatment for life threatening conditions. This includes high dependency units and intensive care units (ICUs) which are sometimes collectively known as critical care units.¹⁷ Papers concerning patients in a critical care condition but not treated within a critical care setting were excluded. Papers reporting other aspects of research (such as retention of participants), describing disease criteria for selecting patients for inclusion into a trial and those which did not describe a specific strategy, were also excluded.

Systematic search

Four electronic databases (Medline, Embase, CINAHL and PsychInfo) were searched from inception to February 2020. Grey literature sources were also searched, and additional resources such as the ORRCA database (Online Resource for Recruitment Research in Clinical Trials).¹⁸ Additional papers were also found by searching the reference lists of key relevant papers (the pearl-growing technique). A search strategy (Figure 1) was developed with the support of a Subject Librarian and refined with key word search terms identified in titles and abstracts or using medical subject headings. Boolean terms “OR” and “AND” were used to search for key concepts in combination with each other. The search strategy comprised of strings for critical care, recruitment strategy and study design. The recruitment search string was adapted from Treweek *et. al.* Cochrane Collaboration systematic review.¹² Papers from database searches were imported to EndNote X8. Titles and abstracts were then screened for relevance by one of the authors. Of these papers, 10%, were double screened by another author independently. Following de-duplication, those papers that met the inclusion criteria (n=98) were independently assessed for eligibility by two authors with reasons for exclusion recorded, in accordance with PRISMA guidance.¹⁵ Disagreements over eligibility of papers were resolved through discussion with a third author.

[inset Figure 1]

Figure 1. Example search strategy from Ovid MEDLINE.

Critical appraisal

The quality of included studies was assessed using tools relevant to study design (Mixed Methods Appraisal Tool 2018 version,¹⁹ appraisal tool for cross-sectional studies (AXIS)²⁰ and Specialist Unit for Review Evidence²¹ checklists) by one author. A 10% sample of studies was independently critically appraised by a second researcher. No papers were excluded based on methodological

quality, in-keeping with narrative synthesis guidance.¹⁴ Any identified methodological issues arising within the studies was noted and considered during the data synthesis stage.

Data extraction

A data extraction tool was developed and piloted for this review. Extracted data included study aims, design, population, and setting. Information regarding the recruitment strategy used was also recorded, and the numbers of patients screened and/or recruited where reported. All data extraction was performed by one author, with data extraction for one study of each design (approximately 10%) independently performed by a second researcher. Data were entered into NVivo12 software to assist with coding and information retrieval.

Data synthesis

A narrative synthesis was performed following the approach proposed by Popay et. al.¹⁴ This is based on an iterative process with distinct stages. The first stage involved preliminary synthesis of findings, coding extracted data and organising it according to the research question. Inductive thematic analysis was performed, involving the extraction, coding, and organisation of data into appropriate overarching themes which were refined. Studies were reviewed again after this process to ensure that themes represented appropriate extracted data from all studies.

Results

Systematic search

The database searches yielded 2,509 papers. An additional 17 papers were identified through other sources, resulting in a total of 2,526 records screened using title and abstract. After de-duplication, 98 records were eligible for full-text assessment against the inclusion criteria and 15 papers^{6, 10, 22-34} were subsequently included in the analysis (Figure 2). Study settings included the US (n=6), Canada (n=5), Australia (n=2), Europe (n=1) and North America (n=1). All except 4 papers were published between 2008 and 2019. The papers reported a combination of quantitative (n=13), mixed methods (n=1), and qualitative studies (n=1). Specific population characteristics included research staff,²³ patients receiving mechanical ventilation,²² stress ulcer prophylaxis,²⁵ blood transfusions,²⁵ fungal infection prevention,²⁴ thromboprophylaxis,¹⁰ patients with sepsis,^{24-27, 30} acute respiratory distress syndrome,²⁵ arterial or central venous lines,³³ or traumatic brain injury,³⁴ those eligible for various trials,³² and surrogate decision-makers (SDMs).^{28, 29, 31} Study characteristics are reported in Table 1.

[insert Figure 2]

Figure 2. PRISMA flow diagram.¹⁵

Quality appraisal

Studies were appraised based on whether they reported a clear statement of aims, justification of research methodology and clear explanation of the research design and recruitment strategy. Studies were of mixed quality and included some high-quality studies,^{6, 25, 27-31} although some were considered to be of medium to low quality due to a lack of methodological detail, non-reporting of recruitment processes or potential for non-response bias. These could be meaningful factors, as there may be an association between those who decline participation in critical care research, and those who are not approached for recruitment.

[Insert Table 1]

Table 1. Included study characteristics.

Synthesis of findings

Extracted data reported a wide range of recruitment strategies and were grouped according to the objectives of the review. Codes were grouped into five overarching themes, organised according to stages in the recruitment process which are outlined below: patient eligibility identification, nature of approach, resource limitations, research culture of environment, and consent model. Table 2 provides examples of data coded at each theme. A conceptual map of the interactions and relationships between the strategies, recruitment barriers, and contextual factors was iteratively developed following discussion between the review team and is depicted in Figure 3.

[Insert Table 2]

Table 2. Overarching themes and examples.

[Insert Figure 3]

Figure 3. Conceptual map of the interrelation between key themes identified.

Interventions to enhance eligibility identification

Methods to identify trial eligibility ranged from in-person screening to the development and testing of electronic systems.^{24, 27, 29} The use of technology was found to reduce the time to identify eligible patients from 3 to 1 hour, and, in addition, identified more patients in a study comparing a sepsis alert tool vs manual screening.³⁰ In one study, which used a 'sepsis sniffer' to screen routine medical data for eligible patients, the number of patients enrolled was doubled.²⁷ However, electronic systems had high specificity, but compromised sensitivity and high false positives had to be filtered out by study coordinators, suggesting that tools required double-checking.²⁷ Eligibility data could be reviewed remotely, reducing workload and reliance on paper-based charts.^{24, 30} However, the applicability of software to other electronic systems was limited by the available data, requiring specific search terms and relevant diagnostic criteria to capture eligible patients.^{24, 27}

In-person screening rounds allowed for reassessment of patients who might become eligible following initial screening and identification.³² In one study, manually screening the unit twice a day for 7-days, resulted in surrogate contact in a third of eligible patients. Recruitment was more likely on day one with availability decreasing each day.²⁹ This approach was limited by the 2-hour screening window used daily, as patients with short stays or whose families visited briefly were excluded.²⁹

The use of screening logs to monitor recruitment was also found to be beneficial.³³ In units that didn't use screening logs, recruitment rates were often lower and reasons for excluding patients were unclear in 10% of cases.³³ Although monitoring was used as a solution to drive recruitment, screening logs required considerable investment of staff time.^{22, 25} However, their use was important for monitoring site performance, identifying obstacles to recruitment and evaluating co-enrolment where patients were enrolled in more than one concurrently operating trial.²⁵

Who provides information and seeks consent

Six studies included information about who provided information about studies. The consent approach was most often undertaken by research coordinators, meaning clinicians were infrequently involved in the process.^{6, 29, 33} In the Consent Study, consent was declined less often when sought by experienced researchers.⁶

Additionally, the Approach Trial found that the duration of time between identifying an eligible patient, surrogate contact and consent being provided was similar regardless of whether the approach was made by a researcher or clinician.³¹ Most surrogates were satisfied with being approached for consent by research co-ordinators, and while SDMs perceived benefits to physician involvement, they thought their time was better allocated to attending to clinical duties.³¹ Although this dichotomisation between research and clinical roles may not be reflective of the increasing integration of clinical practice and research and was not explored in the study. The important role of nurses in the consent approach was also evident.³² Approaching potential participants with a dual approach involving the staff nurse giving basic information first and then more detailed trial information provided later by a researcher, was found to be useful in enhancing recruitment in Chlan et al's multi-site clinical trial.²²

Resource limitations and related recruitment barriers

Unavailability of research staff limited recruitment, including for studies that used eligibility-identification tools,^{6, 27, 34} and where clinical staff were involved in the consent encounter.¹⁰ The Consent Study, which evaluated consent rates between different research scenarios, showed that 57.3% of opportunities for consent from patients themselves or surrogates were either missed (28.8%) or not feasible due to operational reasons (28.5%).⁶ In a minority of cases, missed patient recruitment was attributed to researcher workload, and this was more evident in patients with multiple clinical conditions.⁶

Narrow recruitment windows contributed to a fifth of missed research opportunities,²⁵ suggesting that recruitment benefits from trial designs which provide researchers with more time for identification and families with more decision-making time.⁶ In some cases, assessment of eligible patients did not occur until after 24 hours from initial identification. Such delays could occur when researchers assessed several patients in batches rather than immediately after identification.²⁷ In one study, it was estimated that a quarter of extra eligible patients could have been enrolled if there was a more timely evaluation.²⁷

Additional "recruitment hours", including during evenings, was associated with patient enrolment.^{6, 27, 29} Expanded recruitment hours increased the number of proxies approached by one and a half times as much as daytime shifts alone,^{23, 29, 33} despite the fact that family members being equally likely to be present on weekdays, evenings and weekends.²⁹ The positive impact of additional hours was likely synergised by the regular presence of researchers.^{22, 29}

Lack of surrogate availability hindered recruitment,^{6, 28, 32, 33} with one study reporting the majority of patients having no visitors whatsoever.²⁹ Surrogate availability was related to socioeconomic factors. Availability increased in patients of high median income, as well as in patients with a longer hospital stay.²⁹ Surrogates were not always approached due to issues regarding family dynamics, confusion over who the surrogate is and their absence,^{6, 10, 29} and only a small proportion of patients had the legally authorised surrogate documented in the medical notes.^{6, 25, 29}

Research culture and environment

Co-enrolment (where patients are simultaneously enrolled into more than one trial) was an identified strategy to maximise recruitment but was generally not used due to protocol prohibition and, as a method, was not widely supported by researchers.^{25, 32} Co-enrolment benefits include greater opportunity for research questions to be answered quickly, additional support for families, contributing positively to research participation.⁶ However, co-enrolment is complicated by the lack of guidance assisting selection when patients are eligible for multiple studies, with some researchers

recruiting patients into the study with the lowest recruitment number.²⁵ The Consent Study reported that some ICUs allowed co-enrolment as long as surrogate burden appeared low.⁶ Surrogates were often approached for a single study, however consent for multiple studies decreased as the number of studies that consent was requested for, increased. This demonstrated apprehension regarding multiple surrogate approaches.⁶

Communication was essential to building confidence and trust with families which further increased likelihood of consenting.³² This included being known to the family, and staff who were professional, empathetic, positive, and took time to thoroughly explain the need for research and enrolment.^{10, 23} Consent was also more likely if surrogates had adequate time to read and reflect on the patient information sheets.^{10, 25} Higher enrolment rates correlated with patients' or family members' awareness of the health issue being researched.³³ Language barriers prohibited enrolment in some studies, with most units utilising translators but only a minority provided research documentation in another language.^{6, 25}

Promotion of research culture within the critical care environment and team cohesion was key to successful recruitment.^{10, 32} This could be promoted through weekly meeting updates, educational sessions and research coordinators providing feedback to staff addressing recruitment challenges.^{10, 22, 25} The use of unit liaison staff aided in tailoring strategies to specific research priorities, balancing the needs of both patients and staff.²² Lack of awareness of research amongst junior staff in particular, made recruitment more difficult.^{6, 22}

Researcher experience was a predictor of fewer declined consents, providing a confounding explanation for increased enrolment in some studies.^{6, 27} Specific strategies that correlated with experience involved the assistance of a nurse counsellor during consenting encounters.^{22, 32} Staff training increased confidence in obtaining consent, which subsequently increased recruitment.^{10, 22}

Consent model used

Different models of consent (from patients, surrogates, or deferred or waived consent) were described in a number of studies. First-person consent is considered to be the most ethically preferred model of informed consent for research in critical care, with critical care patients reporting that they provided consent due to a desire to help others.⁶ However, it is often problematic in critical care as most patients lack capacity to consent for themselves.^{6, 26, 32}

Surrogate-decision maker (SDM) consent, used in circumstances where patients lacked capacity to consent, was the most widely adopted approach. Surrogate consent prior to enrolment was more acceptable compared to consent sought following enrolment into the trial.^{6, 28, 35} Most surrogates consented as they believed their loved one could benefit, whilst those that declined had a desire to keep current treatment.^{6, 32} However, relying solely upon SDMs may bias the recruitment sample and is often time-consuming, making it unsuitable for trials with narrow recruitment windows.^{26, 28}

Deferred consent was used much less often than surrogate consent models.⁶ Few patients deemed it unacceptable, despite recognising surrogate absence as an important factor to impact the consent decision.²⁸ Deferred consent requires consent to be sought retrospectively following the emergency from either the surrogate or the patient once recovered. However, is difficult to obtain deferred consent from the patient themselves, especially in studies characterised by high mortality or prolonged incapacity.²⁸ However, a deferred consent approach may offer a timely alternative for trials where rapid initiation of an intervention is needed, providing specific ethical requirements are met.

Waived consent, where no formal consent is obtained, was found to be effective in maximising recruitment.^{23, 26} Whilst a minority of patients considered deferred consent by surrogates as acceptable, few agreed to no consent whatsoever.^{6, 26, 28} Waived consent was considered by studies as a future avenue to maximise recruitment, but there are several notable issues surrounding its use.^{22, 26, 28} Waiving the need for a consenting signature specifically, was found to be useful in patients with peripheral muscle weakness.²²

There was an identified lack of formal evaluation of pre-emptive consent, (prior consent given before being identified as eligible for a study), with many just acknowledging the potential for its use in future situations.^{6, 28} In a hypothetical scenario of lost capacity, pre-emptive consent from patients or proxies was considered by patients to be more acceptable than deferred consent.²⁸

The Consent Study reported that the chosen consent model had an impact on the time interval between eligibility recognition and consent decision.⁶ Patient, family and clinician attitudes and preferences towards different approaches to obtaining consent, also governed the chosen method adopted by the primary research coordinator even if less efficient.^{6, 23, 25, 29}

Discussion

Understanding the effectiveness of strategies to optimise research practice around recruitment in a critical care environment can help to expand the evidence-base for treatments for the most critically ill patients. In this review, identified studies were diverse in terms of research design and findings, but narrative synthesis has allowed the identification of a number of themes.

Despite differences between study consent rates, our review has identified several modifiable factors which could affect the consenting process. Strategies to address the challenges around consent and who makes the initial approach showed that the most widely adopted approach was to seek consent by surrogates.^{6, 32, 35-38} The timeliest approach was deferred consent, however the use of this differed between studies and researchers report discomfort in using this model.^{26, 39-41} Whether the approach was by a researcher or clinician had no significant difference on consent rates, but characteristics of the approach such as rapport was found to affect participation.^{10, 23, 32} This is supported by previous research which suggests that rather than the professional role or level of seniority of the person seeking consent, it is whether the person delivering the trial information is approachable, trustworthy, participant-centred and knowledgeable.⁴²

This review found that high staff workload and poor availability hindered the recruitment process, whilst researcher experience, increased recruitment hours, research team cohesion and familiarity of staff to research processes enhanced it.^{10, 22, 23, 32} Factors inherent to the study itself, such as recruitment windows and study protocol regulations, exacerbated existing recruitment issues.²⁵ These findings reflect previous research on strategies maximising recruitment in clinical research,^{12, 43} however, application of these findings to critical care is limited by the inherent challenges of the environment and the need to rapidly administer life-saving treatments and interventions.⁵

Despite the introduction of a range of identification and screening strategies to improve recruitment, reasons for non-enrolment in the included studies were often unidentified.^{25, 34} This highlights that research sites may benefit from better enrolment monitoring, and thus reduce potential bias.³⁴ This is supported by the literature, stating that clinicians may subconsciously focus on specific patients and act favourably toward some study designs.²⁴ They may also see their role as that of the patient's protector, including from the perceived burdens of research, but in doing so

they create barriers to the inclusion of potential research participants.²² This role of ‘gatekeeping’ in research, particularly where vulnerable populations are involved, is widely acknowledged in the previous literature.⁴⁴

The strengths of this review are that it includes quantitative, qualitative and mixed-methods research, allowing for a more thorough overview of current evidence. The review was conducted according to systematic review standards.^{15, 16} By including data regarding critical care recruitment strategies, the review attempts to narrate the different strategies and their surrounding factors.¹⁴ The findings may also be relevant to other clinical settings and populations where there are particular recruitment challenges around obtaining consent from acutely unwell patients and trials involving time critical treatments such as emergency medicine research.

Quality of evidence

This review included some studies with poorer methodological quality (see Table 1. Included study characteristics). Study environments were diverse, with some considering specific sub-groups of ICU patients, although it was not possible to statistically assess heterogeneity due to the mixed-methods studies included in the review. However, themes were relatively consistent amongst studies considering the same type of recruitment strategy, with more rigorous studies contributing substantially to overall findings. Studies that evaluated recruitment approach or eligibility screening were prone to sampling bias, as participants were excluded due to surrogate unavailability or communication barriers.^{28, 32, 33} This limits the generalisability of the study findings. This is important because those from a higher socioeconomic group are more likely to have an available surrogate.²⁹ None of the included studies involved a randomised trial to evaluate the effectiveness of a recruitment strategy.

A proportion of studies only included surrogate attitudes to consent models and approaches. This was problematic because proxies’ views towards acceptability of recruitment strategies are characteristically different to patients’ attitudes to consent.³⁸ Several studies focused on surrogate-consent, despite being time-consuming, whilst evidence was limited on the use of other consent models^{6, 32, 35-38} despite them being widely used.^{34, 36-38} Patient/participant views were underrepresented, due to the large proportion lacking capacity, meaning that direct participant views could not be ascertained unless through hypothetical scenarios. Variability between recruitment strategies in this review, limits generalisability to all critical care patients and populations. There may also be contextual factors relating to the differences in culture, legal frameworks, research personnel, healthcare systems and research infrastructure between countries, although this could not be meaningfully explored due to the relatively low numbers of studies from each region or country. Resource limitations meant that only English language articles were included in the synthesis.

Conclusions

Exploring different recruitment strategies is important for the effective conduct of trials in critical care. Adopted recruitment strategies differed between ICUs, dependent upon the characteristics of patients, proxies, the environment, and resources available. The most effective strategies for recruitment capacity, like deferred consent, may be problematic when considering participant satisfaction and attitudes. However, ensuring that patients who are unable to consent are included in trials is essential in order to develop evidence-based treatments for those who require critical care.

Practical implications

Recruitment strategies should be tailored to the specific ICU environment with a focus on embedding research in routine clinical practice and promoting a research culture in critical care units. Methodological implications include designing studies to avoid a narrow recruitment window where possible and ensuring careful consideration when selecting information provision and consent models and which personnel who will be making the approach. Future strategies to reduce decision-maker burden include hybrid or dual consent models with staged information provision and consent, whereby research is introduced to the patient or surrogate and recruitment completed at a later time.^{31, 45} In critical care populations where there are complex barriers to informed consent, patient decision aids may be appropriate to enhance understanding,⁴⁶ and support surrogate-decision makers.⁴⁷ Adopting strategies to build trust and develop rapport with gatekeepers,⁴⁴ and understanding clinician reluctance to enrol patients into trials,²⁵ may improve recruitment. Opposition to co-enrolment requires further evaluation, to determine impact on trial validity.²⁵ Recommendations to enhance enrolment include monitoring decision making capacity, using consent processes that parallel study-risk and designing scalable multi-site strategies.⁴⁸

Areas for future research

Greater consideration should be given to exploring specific contextual factors surrounding recruitment strategies and evaluate which modifiable barriers impact recruitment the most. Further qualitative studies within non-research active ICUs or those with lower levels of research activity may identify additional barriers to recruitment. Additionally, further research is required regarding surrogate, patient, and clinician-related factors that may introduce recruitment bias, and stakeholder attitudes towards approaching patients for consent to remain in the study once capacity is regained. Future studies should also seek to provide higher quality evidence about the effectiveness of recruitment strategies, such as through the use of multi-site randomised trials, improved reporting of recruitment processes, and exploration of potential response bias.

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Declaration of conflicting interests

The author(s) declare that there is no conflict of interest.

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Figure 1. Example search strategy from Ovid MEDLINE

1. exp Intensive Care/
2. (intensive care or critical care or itu or icu).mp.
3. exp Patient Recruitment/
4. Research Subjects/
5. (recruit* strategy or (recruit* adj2 strategy) or (recruit* adj3 strategy)).mp. or (recruit* adj4 strategy).ti,ab,kw. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]
6. (recruit* method or (recruit* adj2 method) or (recruit* adj3 method)).mp. or (recruit* adj4 method).ti,ab,kw. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]
7. exp Clinical Trial/
8. exp Surveys/ and Questionnaires/
9. (("semi-structured" or semistructured or unstructured or informal or "in-depth" or indepth or "face-to-face" or structured or guide) adj3 (interview* or discussion* or questionnaire*)).ti,ab.
10. (trial? or study or studies or research).mp.
11. 7 or 8 or 9 or 10
12. 1 or 2
13. 3 or 4 or 5 or 6
14. 11 and 12 and 13

Figure 2. PRISMA flow diagram.

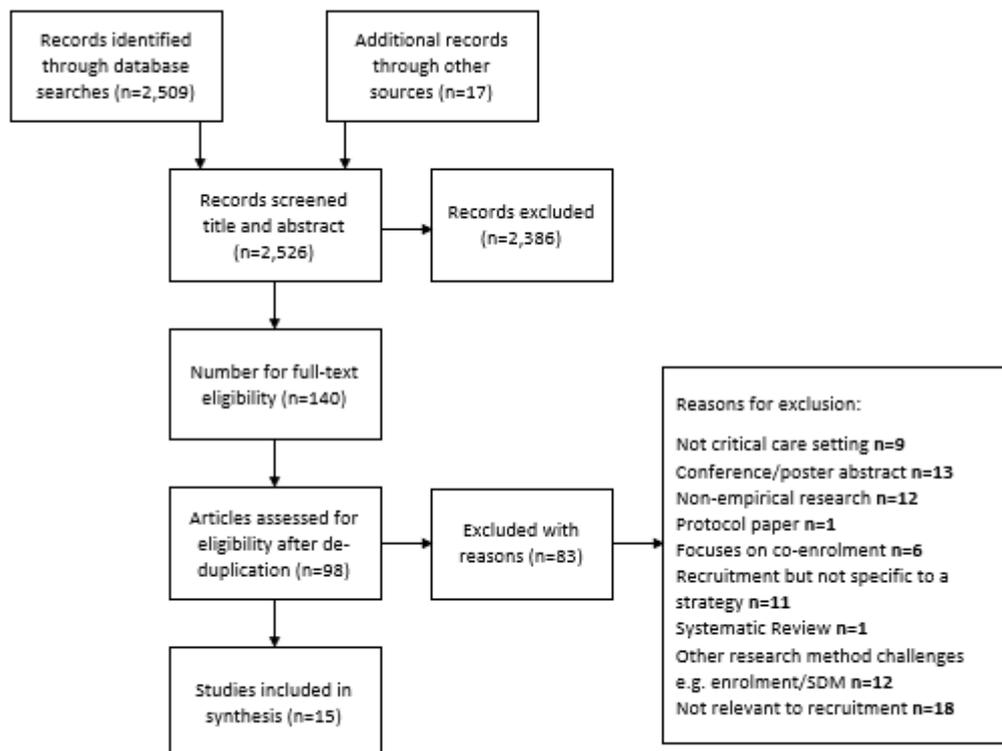


Table 1: Included study characteristics

Study: Author and country	Study aims	Design	Participant characteristics	Setting	Trial characteristics	Definition of recruitment strategy	Quality appraisal
Annane et. al ²⁶ France	To illustrate the difficulties in approaching critically ill patients for informed consent and consider the impact of a waiver of consent	Quantitative: descriptive study	First-person consent: N=10/300 Next-of-kin consent: N=70/300 Deferred consent: N=220/300	19 intensive care centres	Septic shock patients in a placebo-controlled randomised study on the efficacy and safety of a 7-day treatment with 50mg hydrocortisone every 6h IV and 50µg fludrocortisone every 24h.	Deferred or waived consent	Moderate
Burns et. al ⁶ Canada	To explore the reasons for missed consent in eligible study participants and the rationale behind declined consent (Consent Study).	Quantitative: cross-sectional study	Eligible patients included: N=452	23 community and tertiary adult intensive care units	Critically ill adults who were eligible to participate in any critical care research study in various types of ICU*	In-person approach for consent by research staff	High
Burns et. al ³¹ Canada	To assess the feasibility of conducting a randomised trial comparing 2 strategies (physician vs. non physician involvement) for approaching	Mixed-methods randomised controlled trial with nested qualitative study	Physician approach: N=67 Non-physician approach: N=70	3 ICU*s (medical surgical, neurotrauma, multi-disciplinary)	Any (actual) critical care research study for which in-person or telephone surrogate consent was required	In-person SDM ^o approach for consent by research staff vs. doctor	High

	substitute decision makers for research and to evaluate SDMs ^o experiences in being approached for consent (Approach Trial)						
Chlan et. al ²² United States	To describe the challenges faced in a multisite clinical trial and strategies that addressed those challenges	Quantitative: descriptive study	Not specified	ICU* units in 7 sites	Mechanically ventilated patients with anxiety who were eligible for self-management using music therapy	In-person approach for consent by a research nurse	Low
Cook et. al ²³ Canada, Australia and New Zealand	To understand the experiences, beliefs and practices of the critical care clinical trials groups regarding enrolment of critically ill adults and children into studies	Quantitative: descriptive study	Total: N=279 Physicians: N=159 Research coordinators: N=90 Others: N=8	2 critical care clinical trials in Canada and Australia and New Zealand	Researchers such as principal investigators, co-investigator, research coordinators, participants and substitute decision makers completing a survey	Not applicable	Moderate
Diesch et. al ²⁴ Germany	To compare the recruitment efficiency of two IT tools (an experimental Arden Syntax version and an existing commercial	Quantitative: descriptive study	Eligible cases identified: Anaesthesiology: N=131 Nephrology: N=77	Three intensive care units (anaesthesiology, gastro-enterology and nephrology)	As part of the REDUCE-AM study to reduce excessive administration of antimycotics	Routine medical data (electronic records)	Low

	business intelligence (BI) application)		Gastroenterology: N=123				
Foster et. al ²⁵ Canada	To develop and evaluate a screen log for monitoring enrolment in multiple randomised clinical trials conducted in a single centre.	Quantitative: descriptive study	Eligible patients screened: N=157/1292	20 bed tertiary care medical-surgical intensive care unit	As part of recruitment for 4 research studies	Screening log to assess patient eligibility	High
Herasevich et. al ²⁷ United States	To evaluate the impact of the sepsis sniffer on enrolment into a time sensitive clinical study of echocardiography in severe sepsis and septic shock.	Quantitative: pre-test post-test design	Eligible patients identified before: N=4149 Eligible patients identified after: N=4460	3 medical, mixed, and surgical ICU*s with 62 beds across 2 hospitals	As part of a clinical study evaluating right and left ventricular performance by transthoracic ECHO in critically ill patients with severe sepsis	Routine medical data (electronic records)	High
Larkin et. al ³³ United States	To determine whether differences in proportions consenting to trial enrolment existed among patients eligible to consent directly versus those requiring SDM ^o s in a minimal-risk study to	Quantitative: descriptive study	Patients identified: n=410 Neuro ICU* n=295 Medical ICU* n=277 Surgical ICU*	900-bed academic medical centre	As part of a minimal-risk glucose monitoring study in the ICU*	In-person approach for consent comparing SDM ^o approach and patient approach	Moderate

	evaluate the accuracy of continuous glucose monitoring in the ICU* setting.		Total approached: N=119 First person consent: N=57 Surrogate consent: N=62				
Pinder et. al ³² South Africa	To establish a protocol within international and local ethical guidelines to obtain informed consent for critical care research, overcoming constraints previously described and to evaluate eventual recruitment using this protocol.	Quantitative: descriptive study	Patients screened: N=249 Patients eligible: N=100 Patients enrolled: N=30	1 multidisciplinary intensive care-unit	3 antibiotic pharmacokinetics trials and a study evaluating the use of a haemoglobin substitute in acute anaemia in the critically ill.	In-person approach for consent	Low
Scales et. al ²⁸ Canada	To determine patients' preferences for different consent frameworks for enrolling incapable patients into critical-care trials.	Quantitative: descriptive study	Eligible patients enrolled: N=240	5 hospitals	Multicentre study to examine preferences to consenting scenarios	In-person approach by doctor vs. researcher	High

Slieker et. al ³⁴ Multiple countries	To investigate the benefits of collecting screening logs in two randomized clinical trials conducted in traumatic brain injury.	Quantitative: descriptive study	Atherosclerosis trial: N=4166 enrolled Dexabinol trial: N=7052 enrolled Screening logs submitted: Atherosclerosis trial N=924 Dexabinol trial N=861	SAPHIR was conducted in 54 centres across Europe and the dexanabinol trial was conducted in Europe, Israel, Australia, and the US.	Subjects involved in two trials – the SAPHIR study looking at patients with traumatic brain injury. Pharms-dexanabinol trial looking at patients with severe traumatic brain injury.	Screening logs to record patient enrolment	Moderate
Smith et. al ¹⁰ , North America	To present strategies that may optimise the process of obtaining informed consent from substitute decision-makers for participation of critically ill patients in trials using examples from a randomised trial of heparin thromboprophylaxis	Unspecified	North American research coordinators of all experiences	Meetings by collaborators	Research coordinators involved in the PROTECT trial (heparin thromboprophylaxis in critically ill patients)	Strategies that enhanced the informed consent process	Low
Thompson et. al ³⁰	To evaluate the reliability of a sepsis alert tool and used a	Quantitative:	Manually screened: MICU = 82	Surgical ICU* and Medical ICU*	Theoretical study to identify patients with	Routine medical data (SADS tool vs	High

United States	time-motion diary to assess the effect of the system on study coordinator resource consumption	Cohort-controlled study	Electronically screened: SICU = 121		sepsis according to a screening criterion	manual screening) (paper and electronic records)	
Turnbull et. al ²⁹ United States	To evaluate a strategy for recruiting families of patients currently being treated in an ICU* using limited human resources and time-varying daily screening over 7 consecutive days	Quantitative: descriptive study	Eligible patients identified: N=284 Eligible family members enrolled: N= 108/117	Medical ICU*	As part of an ongoing pilot study to evaluate the acceptability of a brief educational intervention to prepare families to act as SDM ^o s in the medical ICU*	In-person approach with increased recruitment hours	High

Table 2: Overarching themes and examples

Overarching themes and their definition	Example
<p><i>Interventions to enhance eligibility identification</i></p> <p>Identifying eligible participants is the first stage in the recruitment process and requires some form of screening. This can be in the form of technology using criterion-based systems, or by screening in-person to find potential study candidates.</p>	<p><i>“Technology use in the surgical ICU* led to time savings of more than 2 hours during this 2-week study. The total time consumed to screen eligible patients in the surgical ICU* fell from 207 minutes to 70 minutes. Annualised, this conservatively represents 52 hours saved for a single coordinator in a single 15-bed ICU*.”²⁹</i></p>
<p><i>Research culture and environment</i></p> <p>Factors inherent to the unit environment enhance the performance of recruitment actions such as the awareness and promotion of research, good communication between staff and with patients, and researcher experience and confidence.</p>	<p><i>“A number of themes were identified when exploring family and surrogate-decision maker attitudes. These included personal responsibility, personal and patient values toward research, trust in the team and knowledge of the voluntary nature of participation.”³⁰</i></p>
<p><i>Consent model used</i></p> <p>Different ways of obtaining informed consent used within research have differing impacts on the success of recruitment, due to their suitability, acceptability, and practicality for use within a critical care environment.</p>	<p><i>“76% of ICU* patients preferred consent by an SDM^o prior to enrolment, with 24% preferring a deferred consent model. Increasing the risk of harm of the study had no significant impact on patients’ preferred consent framework. p value=0.12 where p<0.05 was statistically significant.”²⁷</i></p>
<p><i>Who provides information and seeks consent</i></p> <p>Approaching participants for informed consent may be performed by different members of staff, such as researchers, clinicians or nurses which has a subsequent impact on the willingness to participate.</p>	<p><i>“There was no difference in consent rates based on the person who was approached for consent. 92% were approached by a research coordinator, of which 21% declined consent. 8% were approached by a clinician, of which 33% declined. p value=0.32 where p<0.05 was statistically significant.”⁶</i></p>
<p><i>Resource limitations and related recruitment barriers</i></p> <p>The ability to identify and approach patients for research is restricted by recruitment barriers such staff availability, recruitment hours and recruitment windows, in addition to external factors like surrogate availability.</p>	<p><i>“Adding study staff to cover evening shifts increased the number of participants approached. 16% of eligible participants were approached with the addition of evening hours, compared to 10% approached during day-shift hours alone.”³²</i></p>

Figure 3. Conceptual map of the interrelation between key themes identified

