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A qualitative synthesis regarding the factors surrounding UK critical care trial infrastructure

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Complete List of Authors:	Pattison, Natalie; University of Hertfordshire and East & North Hertfordshire NHS Trust, School of Health and Social Work; University of Hertfordshire Arulkumaran, Nishkantha; UCL, Critical Care O'Gara, Geraldine; Royal Marsden Hospital NHS Trust Connolly, Bronwen; King's College London, Lane Fox Respiratory Unit Humphreys, Sally; West Suffolk Hospitals NHS Trust, Critical Care Walsh, Tim; University of Edinburgh Royal Infirmary Edinburgh, Critical Care Hopkins, Philip; Kings College Hospital, Critical Care Dark, Paul; University of Manchester, Intensive Care Unit
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Title : A qualitative synthesis regarding the factors surrounding UK critical care trial infrastructure

Corresponding author: Professor Natalie Pattison*, Florence Nightingale Foundation Clinical Professor of Nursing, University of Hertfordshire/East & North Herts NHS Trust Natalie.pattison@nhs.net

Co-authors: Dr Nishkantha Arulkumaran*, University College London, UK; Geraldine O'Gara, Royal Marsden Foundation NHS Trust, London, UK; Dr Bronwen Connolly*, Guys and St Thomas' NHS Foundation Trust/Intensive Care National Audit and Research Centre (ICNARC), London, UK; Sally Humphreys, West Suffolk NHS Trust, Suffolk, UK; Professor Tim Walsh*, University of Edinburgh, Edinburgh, UK; Dr Phillip Hopkins*, Kings College Hospital, London, UK; Professor Paul Dark*, University of Manchester, Manchester, UK.
*Former/current members of the NIHR CRN Specialty Group for Critical Care

Abstract:

Conducting clinical trials in critical care is integral to improving patient care. Unique practical and ethical considerations exist in this patient population that make patient recruitment challenging, including narrow recruitment timeframes and obtaining patient consent often in time-critical situations. Units currently vary significantly in their ability to recruit according to infrastructure and level of research activity.

Aim

To identify potential barriers and facilitators to study delivery in order to inform strategies to enhance future critical care trial activity and identify how research staff could be supported. A secondary aim was to identify variability in the research infrastructure of UK intensive care units (ICUs) and their ability to recruit patients into clinical trials.

Design

We evaluated factors related to intensive care patient enrolment into clinical trials in the UK. This consisted of a qualitative synthesis carried out with two datasets of in-depth

interviews. Primary and secondary analysis of two datasets was undertaken in the thematic analysis.

Participants/Setting

Interviews were conducted with intensive care consultants, research nurses and trial coordinators (n=27) from across the UK (from each of the clinical research networks).

Findings

The synthesis yielded the following six themes: Organisational, Human, Study, Practical resources, Clinician, and Patient/family factors. The overarching core theme of Normalising Research was characterised by motivations for promoting research and fostering research-active cultures within resource constraints. There was a strong sense of integrating research in routine clinical practice, and recommendations are outlined.

Conclusions

The central and transferable tenet of Normalising Research advocates the importance of developing a culture where research is inclusive alongside clinical practice in routine patient care and is requisite for all healthcare individuals from organisational to direct patient contact level.

Keywords: Qualitative synthesis; critical care trials; access to research; barriers; facilitators; normalising research

Article Summary

Strengths and limitations of this study:

1. There are significant challenges to conducting trials in critical care in the UK due to time-limited opportunities for recruitment. Patients are almost always unable to provide informed consent, adding a layer of complexity.
2. Few in-depth studies have been conducted exploring this in the UK, and do not focus on less-research active units, so we do not know what the potential issues are for these units.

3. This study is the first to present new data on less-research active critical care units, and to present a synthesis of findings that focus on these issues for the UK
4. Drawing together two datasets presents a rich picture of barriers/facilitators to conducting critical care trials in the UK
5. Gaining perspectives across the multi-disciplinary team is important for understanding the complex issues associated with delivering trials, and provide context for the organisational settings.

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Introduction

Clinical trials in critical care are integral to improving patient care, presenting unique practical and ethical challenges including the time-sensitive treatment and enrolling patients who lack capacity.[1] Data exploring barriers to conducting clinical trials in this setting are scarce, but include managing changing clinical courses, communication breakdowns, and requests for more time for consent [2]. Our recent pilot study,[3] demonstrated enhanced patient recruitment in centres valuing research with equal importance to clinical care, with the most commonly cited barriers insufficient human and financial resource, inadequate personnel funding, and limited career opportunities impeding staff retention.[3] Several additional factors may also preclude recruitment, such as lack of clinician equipoise and competing clinical commitments.

The UK National Institute for Health and Research (NIHR) is the government-funded research arm of the National Health Service (NHS), responsible for driving bench-to-bedside research with tangible patient benefit [4]. Unique infrastructure, including Clinical Research Networks (CRN) and specialty groups (SG) overseeing clinical areas such as critical care (CC), enhance the UK's national and international position to deliver high quality clinical trials. Research teams invest significantly in recruitment to critical care trials with emphasis on mitigating modifiable factors. In particular, understanding barriers and facilitators in less research-active institutions, such as non-university-affiliated hospitals, is crucial to enhance trial infrastructure across the UK. Our aim was to identify potential barriers and facilitators, and understand variability, to critical care trial delivery in order to inform strategies to enhance future trial recruitment, and identify how research staff could be supported.

Methods

Design

A qualitative synthesis was conducted [5], involving two datasets comprising in-depth interviews with critical care consultants, research nurses, and trial coordinators (n=27) across England and Wales. Dataset 1 included 10 participants and is reported in detail elsewhere [3]. Dataset 2, a follow-on study, included a further 17 participants from different backgrounds/units specifically to explore issues in less research-active critical care units. Service evaluation and quality improvement methods underpinned the projects.[6] Therefore, this synthesis involved both primary and secondary data analysis. Qualitative synthesis is a well-established method that draws together findings to reach over-arching themes.[5], ensuring similar research can be reliably compared.[7,8] Patient/public were not involved in the design of this study since the focus is on research infrastructure.

Data collection

Individual telephone, digitally audio-recorded, interviews were conducted with participants, using a pre-determined interview schedule agreed by team consensus. Written and verbal project information was provided and confidentiality was assured. Transcripts were anonymised prior to analysis. Team review of the interview structure was refined as interviews progressed in both datasets and also informed refinement of the framework analysis [10]. This enhanced dependability and qualitative rigour through developing credibility and transferability.[11] NP was unknown to all but one participant.

Ethical considerations

The study was supported and facilitated by the NIHR Critical Care Specialty Group (NIHR CCSG). No ethical approval or written consent, as per the UK Health Research Authority, was required since only anonymised data with staff were used. No local institutional Research & Development (R&D) approval was deemed necessary, since this was a project to represent views on behalf of the NIHR CCSG and recruitment did not take place via institutions. Demographic data about each critical care unit's research activity were also

collected. Participation was voluntary; verbal consent was obtained both before and after the interview, to allow interviewees the opportunity to withdraw/withhold any data discussed.

Patient and public involvement

This study was focused on delivery and mechanistic issues behind research, therefore no patient/public involvement (PPI) was sought and patients/public were not involved in the design/conduct. However, priorities related to PPI in the NIHR Specialty Group, which several of the authors represent, informed this research, namely how can we support participation in research, a high-level NIHR objective.

Settings/sample

Two purposive samples were recruited, with the aim of representing different regions and professional grades (critical care nurses, trainees, trial co-ordinators and consultants) across the UK. The purposive sampling technique involved maximum variation sampling,[12] using UK trial accrual and activity data from the NIHR. The aim was to include clinicians representing critical care units across the 16 CRNs (15 in England, one in Wales). Specifically, the second dataset focused on units with limited trial recruitment, or engaged in few trials. Invites were circulated via the NIHR network using established mailing lists, and targeted recruitment to ensure unbiased representation. Using the principles of Grounded Theory,[13,14] a sample size of 20-30 interviews was deemed sufficient to build an emergent theory.

Analysis

Themes were explored at an overall and ICU-specific level. Potential barriers/facilitators within individual critical care units, hospitals, locally and nationally were identified. In both datasets, analysis was conducted using thematic analysis, a technique congruent with Grounded Theory [13] aided by principles of framework analysis,[10] where categories were

refined as analysis progressed. Data from verbatim transcripts were coded at a line level, with sub-themes derived from those codes applied to a framework, with constant comparison. Datasets were compared and contrasted, and a new framework was devised, and all data were re-analysed according to this. An independent researcher verified the analysis on anonymised data to enhance dependability. The framework provided a further degree of dependability in regards to analysis,[11] and allowed for contextual differences to emerge. The matrix provided detail of within case and cross-case analysis,[14] which was developed into themes.

Findings

In Dataset 1 (collected in 2015), 10 interviews were conducted across nine CRN regions across England (n=8) and Wales (n=1). Dataset 2 (collected 2016/17) included 17 interviews conducted across 12 English CRNs. Interviews ranged from 27-79 minutes. The framework analysis for each studies yielded six main themes. Demographics are supplied in Table 1, supplementary file 1.

Overarching findings from synthesis

There was an overarching theme of *Normalising Research*, describing the notion that critical care research should be entrenched in routine practice. Six sub-themes existed around this central tenet: *Organisational, Human, Study, Practical resources, Clinician,* and *Patient/family factors.* Resource issues permeated each theme and were evident throughout the organisational, unit, study, or trial level, and at a human, individual level. In centres, units, and teams where research activity was regarded with equal importance as clinical activity, research was considered routine practice. Teams and individuals with a strong sense of integrating research in routine practice acted as the motivating driving force fostering a research culture, whether in primary, translational biomedical, or applied health services streams. A broader cultural influence from organisations was also evident, where research was seen as critical to organisational values, up to executive level, in turn

contributing to enhanced research activity. Barriers and enablers to trial activity and conduct are outlined in each theme below.

Organisational factors

This theme related to organisational systems in which units were situated. Research-active and less research-active institutions contrasted with regards prioritisation of research by senior management, with the latter placing lower profile on supporting and conducting research. This was particularly marked at challenging times e.g. during care failure reports, or financial or bed crises, even though these could be opportune periods for potential trial enrolment.

> "Research and development is not high profile. At an organisational level it is service driven, research is seen as an aside and there is no support for it." (Res nurse 2 Study 2)

Despite income-generating research activity, such as involvement in commercial studies, increased demand on resources posed limitations to engagement. Some critical care research leads had to seek executive and/or R&D approval prior to confirming participation, while others could decide unilaterally. Centre factors also determined how trials were embedded through initiatives that increased engagement such as simulated trial runs. Embedding research into routine, or what was perceived as 'normal', care required a conceptual shift.

> "No, research is not a priority. New [intensive care unit] ICU consultants very keen, as are research [specialist registrars] SpRs. The resistance mainly comes from nurses. It is about perceived additional work or disagreement with the protocol. . .it's not part of routine care" (Research nurse 4 study 1)

> "Research should be part of everyone's job. If prescribed it should be given, regardless of it is [part of] research or not." (Research nurse 3, study 2)

The nature of funding for research nurses, primarily funded via CRNs and dependent on trial activity levels, created significant challenges to research conduct, given the lack of continuity. Some units ensured varied funding sources beyond the NIHR, to include commercial and higher education, and internally managed their own research budgets. This

successfully allowed flexibility in deciding which trials to undertake, and managing staffing and out-of-hours support. Planning for future trials was evidently problematic on occasion. During periods with fewer critical care trials, many research teams broadened activity to cover Emergency Department (ED) and anaesthetic trials. Whilst this maintained research activity overall, it also resulted in research teams having to cover many studies. Thus, it was hard to focus on critical care trials when activity in this area resumed. For university-affiliated hospitals, additional support for research overall could be obtained through links with academia.

Human and Unit resources

Staffing was a factor impacting on research delivery. Varied models existed for staffing research teams, from rotational and secondments out of critical care, cross-hospital site and cross-specialty working, to research staffing being managed via the CRN. Most research staff had a clinical critical care background, which facilitated fluid working arrangements and carryover of research skills to non-research staff. Many participants commented that while critical care research staff could cover other specialties, reciprocal cover for critical care was less successful given the unique patient population and time-limited nature of recruitment. This was often poorly appreciated by hospital R&D and regional CRN level. Research staff with a clinical background in critical care found communication easier and could support clinical staff, thus developing a mutually beneficial working relationships and helping with the normalisation of research. Grading of research nurse positions and lack of career development was identified as problematic; line management sometime lay with the regional CRN offices, rather than local critical care units. Some research-active centres created attractive positions that afforded career progression and mitigated against job insecurity, a common feature of research nurse roles that are primarily funded on a yearly contract basis via the CRNs.

> "The career ladder is limited for them and so they move to management or work in R&D roles, and the use of temporary contracts is demoralising and a disincentive." (Consultant intensivist 1, study 1)

Few consultants received programmed activity (PA) sessions specifically for research, especially within non-university affiliated hospitals. Many clinicians relied upon financial support and time from their organisations to undertake research activity.

> "They do it effectively out of interest, there is nothing in their job plan apart from a reference to research, but no time to actually do it. . .it is voluntary and many don't do it" (Research nurse 4, study 2)

This lack of support overlaps with the organisational theme; allocated time and finances to support research activity was rare, occurring only in centres where research was viewed as core activity. Few medical trainees had opportunities for research involvement, and again primarily only in research-active centres with novel initiatives designed to engage those interested in research e.g. year-long fellowships with research contributing to their training programme. However, short clinical placements precluded meaningful trainee participation in primary research. Designated trial coordinators were rare in smaller non-university-affiliated hospitals with less opportunity to enrol patients. Unit, staffing and centre factors were closely associated in the two datasets. Unit factors pertained to strategies to enhance engagement, provision, recruitment and delivery of critical care research. These varied from simulated runs of screening, recruitment and intervention, to teaching programmes and incentive schemes. Having a physical presence on the unit was seen as a crucial element for ensuring clinical credibility. Driven individuals were critical to success in recruitment and study conduct, with both research nurses and consultants assuming principal investigator roles.

Study/trial factors

Trial complexity appeared a considerable factor contributing to trial success, in terms of acceptance by local staff and potential ability to achieve recruitment targets. Feasibility and capacity assessment moderated concerns about delivering to time and target, a national metric captured by NIHR. Studies requiring significant pharmacy support (e.g. Clinical Trials of Investigational Medicinal Products [CTIMP]) had variable success with implementation and recruitment. Some units reported pressure from the regional CRN and local R&D departments to undertake high-recruiting studies, generating maximum income. In contrast,

complex studies perceived as interesting but with low recruitment targets would yield less or even insufficient income to cover costs. Demonstrating quick, tangible 'wins' for organisations and staff, through health service research, helped engagement. Complex studies were considered problematic for balancing effort against outcomes achieved, in particular the staff training requirements to implement detailed interventions, and strict eligibility criteria with narrow recruitment windows leading to few, if any, patients enrolled. Studies requiring significant preparation, including co-enrolment agreements, time-scheduling, competing population assessment, and importantly, ensuring unit staff were committed and had clinical equipoise, could be particularly challenging:

> "they say they have equipoise, but when it comes down to it, they don't, you get surreptitious opposition and stark persuasion is used in those situations."
> (Consultant intensivist 1, study 1)

Time associated with daily screening was also a factor influencing success of complex trials; often this could not be performed remotely and required extensive clinical data review. In keeping with study set-up, funding was rarely allocated for this activity, or for follow-up. In units where research was considered part of routine practice, clinical staff also helped with identification of potential participants.

> "There needs to be appropriate costing of studies including NHS support costs, for drugs for example. . .long-term follow-up needs to be considered as well."
> (Consultant intensivist 6, study 2)

Strategies to facilitate complex trials included engagement with local clinical staff to integrate the trial procedures with standard care, thereby enabling all staff to contribute to patient screening and enrolment, including out-of-hours. Units could achieve this through training and cross-team working.

Clinician factors

This theme focused on how unit clinicians, nurses, trainees and intensivists, were perceived as engaged in research; this did not appear linked to how research-active an organisation was. Where research staff originated from the unit this was a facilitator, often resulting in

good team working from both clinical and research team perspectives. Where research was viewed as additional activity, rather than integral to patient care, research staff reported cases of open hostility, particularly early on in their roles, until unit staff developed an appreciation for research.

> "I've tried working on the unit and taking patients and doing shifts to build relationships" (Research nurse 7, study 2)

Research resources were factored by unit staff where there was good inter-boundary working. For instance, research staff attended senior nurse meetings to identify local issues that might adversely affect recruitment. Equally, unit staff could help identify barriers to recruitment to certain studies. Creating link roles supported nurse-level engagement and enhanced out-of-hours opportunities for recruitment when research nurses were not present. Very limited funding for out-of-hours cover enforced the need for research nurse flexibility.

Equipoise featured again in this theme; clinicians could undermine research activity by appearing supportive in meetings, but not in practice. Permission to recruit patients had to be negotiated at an individual clinician level, which could compromise unit objectivity toward the study.

> "The consultants are all GCP [Good Clinical Practice] trained but there is mixed interest and support, ranging from active obstruction. . ., to more neutral through to full support." (Consultant intensivist 9, study 2).

> "People believe they have equipoise but on the day people change what they do." (Research nurse 5, study 2).

Investment for trainee engagement arose as an important issue, particularly in those less research-active organisations. Ensuring the next generation of critical care consultants prioritised research activity with clinical practice was recognised as imperative. Many trainees were taught to obtain patient consent. At the time of the study, regional trainee research networks were emerging across the UK. However, according to these participants, in larger portfolio NIHR trials trainee engagement was noted to be minimal, and unit pressures contributed to lack of engagement. Trainee fellowship roles successfully

addressed this in two units, with staff continuing research in their careers as consultants, with an emphasis on personal motivation.

> "we actively encourage fellows not to go onto the [unit] rota so that their role is protected for research." (Consultant intensivist 11, study 2)

Personal commitment was a key factor; research activity often required working beyond allocated hours or sessions, or flexible working out-of-hours. This demonstrated how research teams worked to emphasise how research should be considered the norm, with efforts devoted to successful implementation comparable to efforts in clinical practice. Skills of research nurses was a factor common to both datasets, with ability (and R&D permission) to consent improving recruitment. Extended skills also meant that some research nursing staff were supported to undertake further study, including at doctoral level, fostering motivation, willingness to work flexibly and promoting emergence of independent researchers. Portfolio studies requiring a nurse Principal Investigator particularly motivated nurses. For consultants, feelings were mixed: studies with no personal interest fostered less engagement, unless it was likely to be income-generating.

Patient/family factors

Difficulties communicating information about trial procedures to patients and their families was reported by participants. A positive but realistic attitude was deemed essential. The volume of paperwork was identified as problematic. Ensuring that patients or families fully understood complex research interventions, without overburdening them at a sensitive time, was seen as central.

> "We've got savvier about taking consent and have learnt lessons; you don't gain it by giving more paper." (Consultant intensivist 1, study 1)

Managing clinical uncertainty in the context of clinical trials was difficult. Whilst it did not seem to hinder recruitment, managing the process was challenging for research staff. Many families agreed to assent for patients for altruistic reasons, understanding there may be no benefit to the patient. An important issue emerged in relation to addressing cultural perspectives. Different attitudes were perceived towards research, centring on trust in

healthcare. Immediate dismissal by family members, on behalf of patients, was not uncommon. Conversely, some reported a paternalistic medical attitude still prevailing. Despite efforts to address this, provide more information and demonstrate equipoise, families and patients were reluctant and preferred to defer to doctors' opinions regarding enrolment.

> "I work in a deprived area with a lower level of education compared to the UK average, because of that the cultural norms mean they tend to trust what the doctors say: 'whatever you think doctor'" (Research nurse 11, study 2).

Neither of these opposing views about consent were regarded by participants as hindering recruitment. Units serving a disproportionately elderly or rural population reported difficulties gaining access to relatives for assent, particularly where time-sensitive consent was required. Research teams estimated a third of families were likely to decline participation when calculating recruitment targets and reasons for non-participation appeared to be complex and poorly understood. Where approaches to families were prefaced by an explanation that research was part of normal clinical practice in that particular unit, there was increased receptivity to recruitment. Reported preference for treatment arms was rare, and usually managed through explanation. Facilitating understanding was viewed as crucial when approaching families and patients for consent, with issues related to ongoing assessment of mental capacity also highlighted as difficult.

A summary of all of these factors is outlined in Table 2 and represented in Figure 1.

Table 2. Summary and recommendations

Recommendations for normalising research in critical care

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• 1. Training:
○ Offer Good Clinical Practice (GCP)/research training for all staff on induction; Research staff running GCP sessions for critical care staff ○ Offer research training by research staff for critical care nurses/AHPs to recruit/learn about research processes
• 2. Staffing
○ Offer trainee fellowships to support medical trainees wanting a career in research ○ Create rotational nursing posts in critical care, overseen by senior research nurses ○ Facilitate reciprocal working between ICU staff and research teams; research staff working in ICU to enhance links and recruitment opportunities ○ Create more career structures for doctors, AHPs and nurses working in critical care research ○ Incentivise clinical staff with training opportunities
• 3. Communication and interdisciplinary working
○ Attend senior nurse meetings in critical care ○ Create link nurse positions (to be extended to link trainee positions) ○ Engage with and attend unit staff meetings to identify study barriers ○ Create tools/training/peer review to aid conveying complex information to families and patients ○ Work on engagement and links with ED and other research departments in the same NIHR divisions to support teams ○ Ensure early scoping of capacity/equipoise concerns by research team
• 4. Funding/Trial Design
○ Negotiation of leveraged funding to ensuring staffing and trial continuity; maintain a broad study portfolio ○ Consider trial amendments in studies that are difficult to recruit to

Discussion

This synthesis outlines six inter-related themes under a new over-arching theme of *Normalising Research*. Research activity was regarded as equally important as clinical work by these participants, albeit this was acknowledged as not a representative view across all organisations or units. Where research was embedded into routine care and considered as

the norm, undertaking screening and recruitment were easier. Emphasising the need for normalcy of research, at unit and organisational level, means cohesive units evolve with the unified aim of leading improvements in patient care. However, there are prerequisites for normalcy, including communication towards a shared understanding [15] in this case, that research is an integral part of everyday patient care. Furthermore, this communication needs to take place at a systems level.[15] Specific issues in the synthesis related to variation in funded time and resources, clinician engagement, individual roles, and perceived gains from research, which proved noteworthy, acting as barriers or facilitators to clinical trial recruitment. Bruce et al,[1] outlined how navigating rapidly changing clinical courses and communication breakdown adversely affected recruitment.[1] That these factors did not emerge in this synthesis may reflect different healthcare systems, funding, and larger number of hospitals. Similarities emerged related to challenges of recruitment within narrow timeframes. Good communication between clinical and research teams was important for successful trial implementation.

Inclusion of data from less research-active organisations strengthens this study providing richer data, more transferable across the NHS and to healthcare systems in other jurisdictions. Our findings will resonate with other international settings where, despite variability in national infrastructure, similar challenges are faced by researchers. The tenet of normalising research transcends unit, institutional and country boundaries. Approaches to improve recruitment included simple incentive schemes to reward clinical staff, broadening the range of clinicians who could take consent. The latter is particularly pertinent to CTIMPs where time-limited recruitment was more relevant.[1,2] Previous work has suggested lack of equipoise as a barrier to enrolment;[16,17]. An area for further exploration relates to consent waivers, already explored in some recent research [1,16,19], albeit with less known of patient and family perspectives. 'Overburdening' has been described previously [20] as has concern regarding making initial approaches to families during particularly sensitive times [19-23] but again the patient/family voice in these studies is absent.[18- 20] This would be an important area for future practice and research.

In keeping with existing literature, competition between trials requiring similar patient cohorts and the number of eligible patients were further barriers to trial recruitment [1,23].

Another factor related to lack of clear professional development opportunities and structured career paths. Recent strategy published by the NIHR offers novel career options for research staff [25,26] such as consultant research nurse models [24]. Emerging trainee networks across the UK have also helped create a case for formalised processes.[27, 28] NIHR initiatives to engender a culture of research in healthcare, with every patient being offered the opportunity to participate in research aimed at improving care [29] are also reflected in these individual participants' motivations to improve care through research. Systematic review and large-scale survey evidence highlight key areas to improve trial recruitment as training site staff, communication with patients, and incentives, albeit some suggestions are not applicable to an ICU setting, such as telephone calls to non-respondents and opt-out procedures.[30,31] There have been significant advances over the past five years in critical care research recruitment.[32] In a current climate of significant fiscal pressures in the UK healthcare system with £22 billion of NHS efficiency savings to be achieved by 2020,[33] there was still a universal desire to undertake critical care research. This was driven by key motivated individuals who viewed research as integral to best practice and normal care provision, as well as deriving evidence to drive and support best use of resources.

This qualitative synthesis draws together two sets of original research findings. A limitiation is that data were not collected simultaneously, however, both studies complemented each other. The second study built on the first by focusing specifically on a target participant cohort not initially represented in order to generate novel data to further understand the question at hand. Furthermore, the timeframe between acquisition of each dataset was short (twelve months) with minimal, if any, change in practice likely occurring. Potential sampling bias from recruiting primarily research-active units in the first dataset, was mitigated by employing purposive recruitment in the second dataset from less research-active units, to build theory. Research-active and less research-active units were defined both on subjective reports from individuals, and standardised objective metrics. Qualitative research is often criticised for lack of generalisability, due to sample size limitations, but notions of transferability can be considered [8,11] and what Payne and Williams term 'moderatum generalisations'.[34] Figure 1. outlines a summary of the main points and four key areas for learning. The core concept of Normalising Research can feasibly be applied

beyond critical care trials recruitment, across the full spectrum of clinical specialties represented within the NIHR, as well as internationally.

Conclusion

This qualitative synthesis integrating two original datasets has yielded recommendations for improving trials recruitment in the unique clinical specialty of critical care. Several suggestions are made from the six themes that emerged: Organisational, Human, Study, Practical resources, Clinician, and Patient/family factors, under the overarching theme of Normalising Research, that relate to enhanced staffing, training, trial design and communication. Fostering a culture where research is considered part of routine patient care must be the ultimate goal, from organisational strategy to bedside care.

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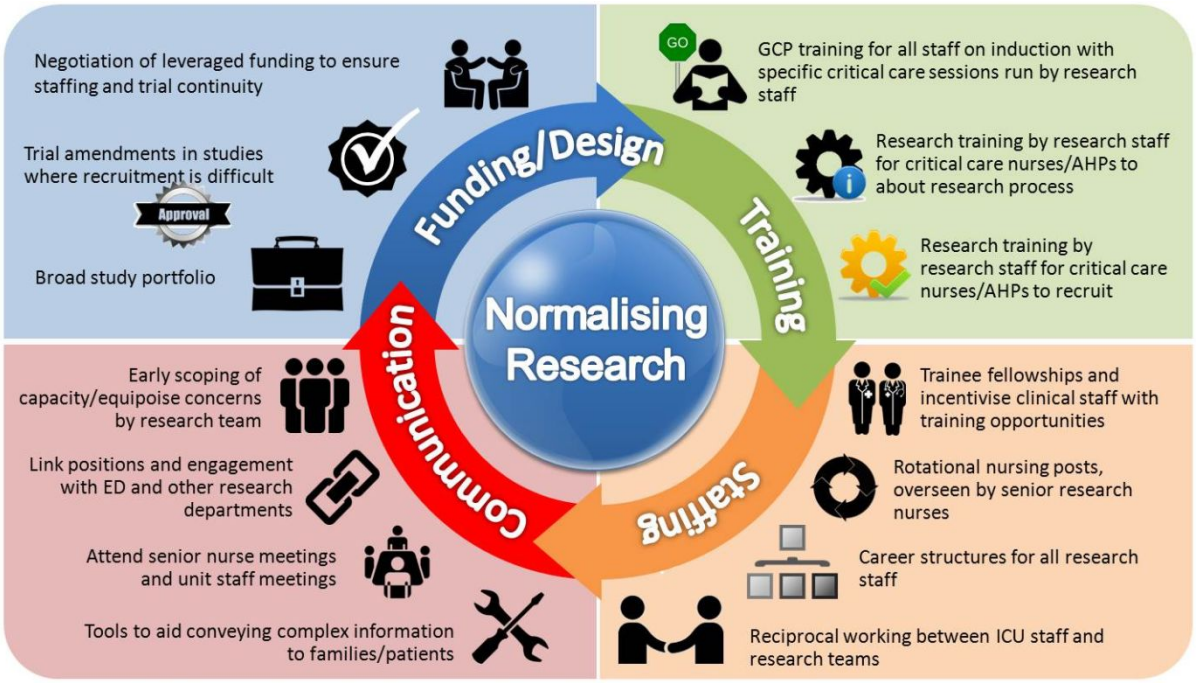
Data access: All data pertaining to this project are reported here. Please contact the authors regarding accessing aggregated data analysis. Raw data is not available to be shared since this could lead to identification.

A qualitative synthesis regarding the factors surrounding UK critical care trial infrastructure

Figure 1. Normalising Research



A qualitative synthesis regarding the factors surrounding UK critical care trial infrastructure

Supplemental file

Table 1. Demographics and setting

Profession/Area	1. Level 3/2 beds	2. Annual admissions	3. General /Specialist unit	4. Research staff numbers	5. Research staff working*	6. Research team working patterns	7. Consultant numbers and working patterns	8. Details of consultant time for research	9. Number (total) of ongoing clinical trials (both NIHR and non- NIHR/in set-up)	10. Underway/active
Nurse CRN Eastern	14	1000	General	1 (work with Emergency Department [ED])	1 WTE	5 days/week 8-4pm (flexible)	7	1 PA†	6	5
Nurse CRN Yorkshire and Humber	24	1600	General	2	2 WTE	5 days (flexible – 9 hour cover)	13	0.5 PA (shared)	5	5
Nurse CRN West Midlands	25	1600	General	1 (was 4)	1 WTE	5 days/week; 8-4pm	*Data not provided/unknown*	1 PA	6	4
Consultant CRN Wessex	12	900	General	2 (across all Div 6, not just ICU)	1 WTE	5 days/week; 8-4pm	*Data not provided/unknown*	2 PAs	6	4
Trial co-ordinator CRN London South	63	3100	General/trauma	6 across ED/ICU	*Data not provided/unknown*	5 days/week (and on-call)	>50	0 PA	5	3
Consultant CRN North West London	44	2600	General/ Trauma/ Neuro	2 fellows + 5 RNs	2 fellows at 2 WTE; 5 RNs at 4.5 WTE. 1 WTE research assistant	7 days/week	21	1 PA	*Data not provided/unknown*	4
Nurse CRN Greater Manchester	40	2000	General	4 (across ED)	4 WTE	8-8pm 5 days/week + on	22	1 PA	8 + 2 in set-up + 1 ED	8

A qualitative synthesis regarding the factors surrounding UK critical care trial infrastructure

						call				
Nurse CRN TV and South Midlands	9	500	General	0.5	0.5 WTE	p/time (early/late shift pattern; weekdays	10	0.5 PA	2	1
Consultant CRN Wessex	11	750	General	4 + 0.5 trainee	2.5 WTE + 0.5 WTE trainee	7 days/week (plus trainee shifts)	6	0 PA	4	2
Consultant CRN West Midlands	102	4000	Cardiac/ Trauma/ Burns/ Neuro/ General	7 (across ED/Trauma and ICU)	6 WTE (inc Trial Coordinator and administrators)	7 days/week	34	1 PA	7 + 2 in set-up	7
Consultant CRN North West Coast	33	1550	General	3	3 WTE + 0.5 trainee	5 days/week (flexible)	17	1 PA	3 + 1 in set-up	3
Consultant A. CRN West of England	15	5-600	General	0	0	N/A	18	0.5 PA	1 + 2 in set-up	1
Consultant B. CRN West of England	15	5-600	General	0**	0	n/a	18	0.5 PA	1 + 2 in set-up	1
Nurse CRN South West Peninsula	28	1700	General/trauma/ Neuro/ Cardiac	1 (across dermatology/neuro)	1 WTE	8-4pm; 5 days/week	14	*Data not provided/unknown*	0 (1 in set-up)	0
Nurse CRN West of England	20	1300	General	9	5 WTE + 4 rotational posts	7-7pm; 7 days a week	*Data not provided/unknown*	2 PAs (shared)	10	10
Nurse CRN East Midlands	69	4000	General/trauma/neuro	6 (covering ED) – split site	4.2 WTE	7-7pm; 7 days/week	*Data not provided/unknown*	0 PA	13	13
Nurse CRN Norfolk	19	850	General	2 (covering div 6)	1.45 WTE	8-4pm 5 days/week (+ on call)	*Data not provided/unknown*	0 PA	4 + 1 in set-up	4

A qualitative synthesis regarding the factors surrounding UK critical care trial infrastructure

Nurse, Wales	33	1500	General/ neuro	5	4 WTE	8-4pm 5 days a week	14	1 PA	6	5
Nurse CRN North West Coast	35	1880	General	2	1 WTE band 7 shared 4 x band 6 (0.8)	7.30-3.30pm 5 days a week	13	0 PA	9	8
Nurse CRN South West Peninsula	26	1580	General/ Neuro	1	*Data not provided/unknown*	8-4pm 5 days a week	14	0 PA	7	5
Nurse CRN North East North Cumbria	18	1000	General	2	1 band 3 res asst; 1 band 6	9-5pm 5 days a week	9	0 PA	8	6
Nurse CRN East Midlands	19	1200	General	3	2.8 WTE	8-7pm	*Data not provided/unknown*	2 Pas	11	9
Nurse CRN Eastern	20	1890	General	4	*Data not provided/unknown*	8-8pm	*Data not provided/unknown*	1 PA	7	7
Nurse CRN Greater Manchester	19	1700	General	0.8	0.8 WTE	8-4pm	12	0 PA	4	4
Consultant CRN Wessex	24	1200	General	3	1.6 WTE + 2 WTE for 3 month rotations	7 days a week 8am-12pm	14	2 PAs	5	5
Consultant CRN London South	63	3500	General/ Neuro	9	2 band 7; 7 band 6*	8-8pm	*Data not provided/unknown*	1 PA	10	9
Nurse CRN West of England	21	2000	General	5	4 WTE (1 band 7; rest band 6)	7-7pm	12	*Data not provided/unknown*	8	8

†PAs=Professional Activities *Working across all Division 6 studies, not limited to critical care; **Able to access other Division 6 nurses when studies are active

A qualitative synthesis regarding the factors surrounding UK critical care trial infrastructure

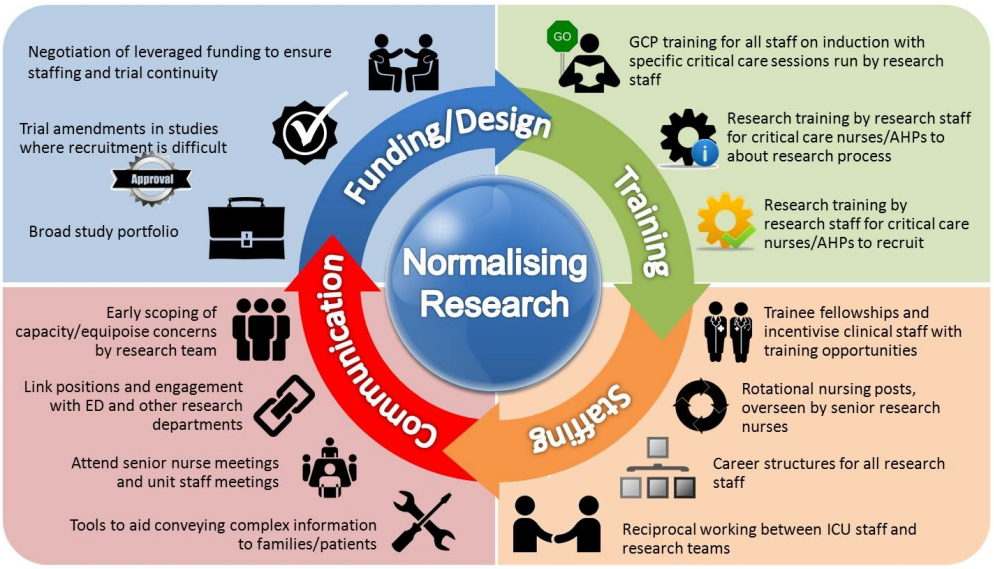


Figure 1. Normalising Research

242x137mm (150 x 150 DPI)

Supplemental file

Table 1. Demographics and setting

Profession/Area	1. Level 3/2 beds	2. Annual admissions	3. General /Specialist unit	4. Research staff numbers	5. Research staff working*	6. Research team working patterns	7. Consultant numbers and working patterns	8. Details of consultant time for research	9. Number (total) of ongoing clinical trials (both NIHR and non-NIHR/in set-up)	10. Underway /active
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Consultant A. CRN West of England	15	5-600	General	0	0	N/A	18	0.5 PA	1 + 2 in set-up	1
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Reporting checklist for qualitative study.

Based on the SRQR guidelines.

Instructions to authors

Complete this checklist by entering the page numbers from your manuscript where readers will find each of the items listed below.

Your article may not currently address all the items on the checklist. Please modify your text to include the missing information. If you are certain that an item does not apply, please write "n/a" and provide a short explanation.

Upload your completed checklist as an extra file when you submit to a journal.

In your methods section, say that you used the SRQR reporting guidelines, and cite them as:

O'Brien BC, Harris IB, Beckman TJ, Reed DA, Cook DA. Standards for reporting qualitative research: a synthesis of recommendations. Acad Med. 2014;89(9):1245-1251.

		Reporting Item	Page Number
	#1	Concise description of the nature and topic of the study identifying the study as qualitative or indicating the approach (e.g. ethnography, grounded theory) or data collection methods (e.g. interview, focus group) is recommended	1
	#2	Summary of the key elements of the study using the abstract format of the intended publication; typically includes background, purpose, methods, results and conclusions	1
Problem formulation	#3	Description and signifcance of the problem / phenomenon studied: review of relevant theory and empirical work; problem statement	3
Purpose or research question	#4	Purpose of the study and specific objectives or questions	3
Qualitative approach and research paradigm	#5	Qualitative approach (e.g. ethnography, grounded theory, case study, phenomenolgy, narrative research)	4

		and guiding theory if appropriate; identifying the research paradigm (e.g. postpositivist, constructivist / interpretivist) is also recommended; rationale. The rationale should briefly discuss the justification for choosing that theory, approach, method or technique rather than other options available; the assumptions and limitations implicit in those choices and how those choices influence study conclusions and transferability. As appropriate the rationale for several items might be discussed together.	
Researcher characteristics and reflexivity	#6	Researchers' characteristics that may influence the research, including personal attributes, qualifications / experience, relationship with participants, assumptions and / or presuppositions; potential or actual interaction between researchers' characteristics and the research questions, approach, methods, results and / or transferability	4
Context	#7	Setting / site and salient contextual factors; rationale	4
Sampling strategy	#8	How and why research participants, documents, or events were selected; criteria for deciding when no further sampling was necessary (e.g. sampling saturation); rationale	4
Ethical issues pertaining to human subjects	#9	Documentation of approval by an appropriate ethics review board and participant consent, or explanation for lack thereof; other confidentiality and data security issues	4
Data collection methods	#10	Types of data collected; details of data collection procedures including (as appropriate) start and stop dates of data collection and analysis, iterative process, triangulation of sources / methods, and modification of procedures in response to evolving study findings; rationale	4
Data collection instruments and technologies	#11	Description of instruments (e.g. interview guides, questionnaires) and devices (e.g. audio recorders) used for data collection; if / how the instruments(s) changed over the course of the study	4

Units of study	#12	Number and relevant characteristics of participants, documents, or events included in the study; level of participation (could be reported in results)	5
Data processing	#13	Methods for processing data prior to and during analysis, including transcription, data entry, data management and security, verification of data integrity, data coding, and anonymisation / deidentification of excerpts	4
Data analysis	#14	Process by which inferences, themes, etc. were identified and developed, including the researchers involved in data analysis; usually references a specific paradigm or approach; rationale	4
Techniques to enhance trustworthiness	#15	Techniques to enhance trustworthiness and credibility of data analysis (e.g. member checking, audit trail, triangulation); rationale	4
Syntheses and interpretation	#16	Main findings (e.g. interpretations, inferences, and themes); might include development of a theory or model, or integration with prior research or theory	5
Links to empirical data	#17	Evidence (e.g. quotes, field notes, text excerpts, photographs) to substantiate analytic findings	6
Intergration with prior work, implications, transferability and contribution(s) to the field	#18	Short summary of main findings; explanation of how findings and conclusions connect to, support, elaborate on, or challenge conclusions of earlier scholarship; discussion of scope of application / generalizability; identification of unique contributions(s) to scholarship in a discipline or field	10
Limitations	#19	Trustworthiness and limitations of findings	11
Conflicts of interest	#20	Potential sources of influence of perceived influence on study conduct and conclusions; how these were managed	2
Funding	#21	Sources of funding and other support; role of funders in data collection, interpretation and reporting	2

https://www.goodreports.org/, a tool made by the EQUATOR Network in collaboration with Penelope.ai

BMJ Open

A qualitative synthesis regarding the factors surrounding UK critical care trial infrastructure

Journal:	*BMJ Open*
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Date Submitted by the Author:	07-Aug-2019
Complete List of Authors:	Pattison, Natalie; University of Hertfordshire and East & North Hertfordshire NHS Trust, School of Health and Social Work; University of Hertfordshire Arulkumaran, Nishkantha; UCL, Critical Care O'Gara, Geraldine; Royal Marsden Hospital NHS Trust Connolly, Bronwen; King's College London, Lane Fox Respiratory Unit Humphreys, Sally; West Suffolk Hospitals NHS Trust, Critical Care Walsh, Tim; University of Edinburgh Royal Infirmary Edinburgh, Critical Care Hopkins, Philip; Kings College Hospital, Critical Care Dark, Paul; University of Manchester, Intensive Care Unit
Primary Subject Heading:	Intensive care
Secondary Subject Heading:	Qualitative research
Keywords:	Qualitative synthesis, Critical care trials, Barriers, Facilitators, Normalising Research, Access to Research

Title: A qualitative synthesis regarding the factors surrounding UK critical care trial infrastructure

Corresponding author: Professor Natalie Pattison, Florence Nightingale Foundation Clinical Professor of Nursing, University of Hertfordshire/East & North Herts NHS Trust
Natalie.pattison@nhs.net

Co-authors: Dr Nishkantha Arulkumaran*, University College London, UK; Geraldine O'Gara, Royal Marsden Foundation NHS Trust, London, UK; Dr Bronwen Connolly*, Guys and St Thomas' NHS Foundation Trust/Intensive Care National Audit and Research Centre (ICNARC), London, UK; Sally Humphreys, West Suffolk NHS Trust, Suffolk, UK; Professor Tim Walsh*, University of Edinburgh, Edinburgh, UK; Dr Phillip Hopkins*, Kings College Hospital, London, UK; Professor Paul Dark*, University of Manchester, Manchester, UK.
*Former/current members of the NIHR CRN Specialty Group for Critical Care

Abstract:

Conducting clinical trials in critical care is integral to improving patient care. Unique practical and ethical considerations exist in this patient population that make patient recruitment challenging, including narrow recruitment timeframes and obtaining patient consent often in time-critical situations. Units currently vary significantly in their ability to recruit according to infrastructure and level of research activity.

Aim

To identify variability in the research infrastructure of UK intensive care units (ICUs) and their ability to conduct research and recruit patients into clinical trials.

Design

We evaluated factors related to intensive care patient enrolment into clinical trials in the UK. This consisted of a qualitative synthesis carried out with two datasets of in-depth interviews (distinct participants across the two datasets) conducted with 27 intensive care consultants (n=9), research nurses (n=17) and trial coordinators (n=1) from 27 units across the UK. Primary and secondary analysis of two datasets was undertaken in the thematic analysis.

Findings

The synthesis yielded an overarching core theme of Normalising Research, characterised by motivations for promoting research and fostering research-active cultures within resource constraints, with six themes under this to explain the factors influencing critical care research capacity: Organisational, Human, Study, Practical resources, Clinician, and Patient/family factors. There was a strong sense of integrating research in routine clinical practice, and recommendations are outlined.

Conclusions

The central and transferable tenet of Normalising Research advocates the importance of developing a culture where research is inclusive alongside clinical practice in routine patient care and is requisite for all healthcare individuals from organisational to direct patient contact level.

Keywords: Qualitative synthesis; critical care trials; access to research; barriers; facilitators; normalising research

Revised word count: 4688

Article Summary

Strengths and limitations of this study:

1. There are significant challenges to conducting trials in critical care in the UK due to time-limited opportunities for recruitment. Patients are almost always unable to provide informed consent, adding a layer of complexity.
2. Few in-depth studies have been conducted exploring this in the UK, and do not focus on less-research active units, so we do not know what the potential issues are for these units.
3. This study is the first to present new data on less-research active critical care units, and to present a synthesis of findings that focus on these issues for the UK
4. Drawing together two datasets presents a rich picture of barriers/facilitators to conducting critical care trials in the UK
5. Gaining perspectives across the multi-disciplinary team is important for understanding the complex issues associated with delivering trials, however these need to be contextualised within the organisational settings.

Funding: This project was supported with infrastructure from the National Institute for Health Research Comprehensive Research Network in Critical Care (NIHR Theme Hub C King's College London).

Competing interests: The authors have none to declare.

Background

Clinical trials in critical care are integral to improving patient care, albeit unique practical and ethical challenges exist including the time-sensitive nature of treatment and enrolling patients who lack capacity.[1] Data exploring barriers to conducting clinical trials in this setting are scarce, but include managing changing clinical courses, communication breakdowns, and requests for more time for consent [2]. Our previous study, focussing on research active centres,[3] described enhanced patient recruitment in centres valuing research with equal importance to clinical care, with the most commonly cited barriers insufficient human and financial resource, inadequate personnel funding, and limited career opportunities impeding staff retention.[3] Several additional factors may also preclude recruitment, such as lack of clinician equipoise and competing clinical commitments.

Implications for the NIHR

The UK National Institute for Health and Research (NIHR) is the government-funded research arm of the National Health Service (NHS), responsible for driving bench-to-bedside research with tangible patient benefit [4]. Unique infrastructure, including the national coordinated Clinical Research Network (CRN) and specialty groups (SG) with oversight for specific clinical areas such as critical care (CC), enhance the UK's national and international position to deliver high quality clinical trials. Research teams invest significantly in recruitment to critical care trials with emphasis on mitigating modifiable factors. In particular understanding barriers and facilitators in institutions which are less research-active, such as non-university-affiliated hospitals, is crucial to enhance trial recruitment across the NIHR CRN.

Our objective was therefore to identify examples of these potential barriers and facilitators to patient enrolment in order to inform strategies to enhance future critical care trial recruitment, and identify how research staff could be supported in these organisations.

Methods

Design

A qualitative synthesis was conducted [5], involving two datasets comprising in-depth interviews (n=27) with critical care consultants (n=9), research nurses (n=17), and trial coordinators (n=1) across England and Wales (26 hospitals; 27 units). Dataset 1 included 10 participants and is reported in detail elsewhere [3]. For that dataset a sampling frame across the CRNs was used to represent a mix of smaller and larger ICUs, from teaching hospitals and district general type hospital ICUs, including one person within each CRN to ensure region-wide representation. Dataset 2, a follow-on study, included a further 17 participants from different backgrounds/units, with the aim of specifically exploring issues in less research-active critical care units. Service evaluation and quality improvement methods underpinned the projects.[6] Therefore, this synthesis involved both primary and secondary data analysis. Qualitative synthesis is a well-established method that draws together findings to reach over-arching themes.[5], ensuring similar research can be reliably compared.[7,8,9]

Patient public involvement

Patient/public were not involved in the design of this study since the focus is on research infrastructure.

Data collection

Individual telephone, digitally audio-recorded, interviews were conducted with participants, using a pre-determined semi-structured interview schedule agreed by team consensus. The aim of the second set of interviews was to understand how to engage and promote research activity and increase trial recruitment in critical care units that find it challenging to recruit to trials. Interview questions included: *What can you tell me about how the unit decides whether to participate in a research project? Tell me about the infrastructure in your critical care unit to support research. What is your experience of recruiting to time-limited critical care trials?* Written and verbal information about the project was provided and confidentiality was assured. Transcripts were anonymised prior to analysis. Team review of both the interview structure, which was refined as interviews progressed in both datasets (including more targeted questions to elicit nuances such as local capacity to conduct research) and also informed refinement of the framework analysis [10], enhanced

dependability in research findings and qualitative rigour through developing credibility and transferability.[11]

Ethical considerations

The study was supported and facilitated by the NIHR Critical Care Specialty Group (NIHR CCSG). No ethical approval or written consent, as per the UK Health Research Authority, was required since only anonymised data with staff were used. No local institutional Research & Development approval was deemed necessary, since this was a project to represent views on behalf of the NIHR CCSG and recruitment did not take place via institutions. Demographic data about each critical care unit's research activity and staffing were also collected. Participation was voluntary and verbal consent was obtained both before and after the interview, to allow interviewees the opportunity to withdraw/withhold any data discussed.

Settings

Two purposive samples were recruited, with the aim of representing different regions and professional grades (critical care nurses, trainees, trial co-ordinators and consultants) across the UK. The purposive sampling technique involved maximum variation sampling,[12] using UK trial accrual and activity data from the NIHR. The aim was to include clinicians representing critical care units across the 16 CRNs (15 in England, one in Wales). Specifically, the second dataset focused on units with limited trial recruitment, or engaged in few trials. We did not ascribe a set value to define 'less research active', but focused on unit-level activity in terms of participants recruited and active studies, according to NIHR yearly summary data. The NIHR centralises this information in a 'portfolio', and all sites are required to submit this information. Invites were circulated via the NIHR network using established mailing lists, and targeted recruitment to ensure unbiased representation. Using the principles of theoretical sampling (as used most commonly in Grounded Theory),[13,14] a sample size of 20-30 interviews was deemed sufficient to reach data saturation and build up a comprehensive picture of the UK landscape in relation to factors that influence critical care research provision.

Analysis

Themes were explored at an overall and ICU-specific level. Potential barriers/facilitators within individual critical care units, hospitals, locally and nationally were identified. In both datasets, analysis was conducted using thematic analysis, a technique congruent with different types of qualitative research [15], aided by principles of framework analysis,[10] where categories were refined as analysis progressed. Data from verbatim transcripts were coded at a line level, with sub-themes derived from those codes applied to a framework, with constant comparison. Datasets were compared and contrasted, and a new framework was devised, and all data were re-analysed according to this. An independent researcher verified the analysis on anonymised data to enhance dependability. The framework provided a further degree of dependability in regards to analysis,[11] and allowed for contextual differences to emerge. The matrix provided detail of within case and cross-case analysis,[14] which was developed into themes.

Findings

In Dataset 1 (collected in 2015), 10 interviews were conducted across nine CRN regions across England (n=8) and Wales (n=1). Dataset 2 (collected 2016/17) included 17 interviews conducted across 12 English CRNs. Two CRNs were not represented due to lack of response. Interviews ranged from 29-81 minutes (mean length was 45.2 mins). The framework analysis for each studies yielded six main themes. Demographics are supplied in Table 1, supplementary file 1.

Overarching findings from synthesis

There was an overarching theme of *Normalising Research*, describing the notion that critical care research should be entrenched in routine practice. Six sub-themes existed around this central tenet: *Organisational, Human and Unit Resources, Study, Clinician,* and *Patient/family factors.* Resource issues permeated each theme to a different extent and were evident throughout the organisational, unit, study, or trial level, and at a human,

individual level. Resources could be managed and influenced at an individual level, for instance. In centres, units, and teams where research activity was regarded with equal importance as clinical activity, research was considered routine practice. In turn, teams and individuals with a strong sense of integrating research in routine practice acted as the motivating driving force fostering a research culture, whether in primary, translational biomedical, or applied health services streams. A broader cultural influence from organisations was also evident, where research was seen as critical to organisational values, up to executive level, which in turn contributed to enhanced research activity. Barriers and enablers to trial recruitment and conduct are outlined in each theme below. A summary of these factors is outlined in Table 2 (supplementary file 2) and represented in Figure 1.

Organisational factors

This theme related to the organisational system in which units were situated, and incorporated Trust or Board level factors; perceived priority of research; infrastructure; trial planning; funding and external links, such as academia. Research-active and less research-active institutions contrasted with regards prioritisation of research activity by senior management, with the latter placing lower profile on the support and conduct of research. This was particularly marked at challenging times e.g. during care failure reports, or financial or bed crises, even though these could be opportune periods for potential trial enrolment.

> "Research and development is not high profile. At an organisational level it is service driven, research is seen as an aside and there is no support for it." (Research nurse 2, study 2)

Despite income-generating research activity, such as involvement in commercial studies, increased demand on resources posed a limitation to engagement. Some critical care research leads had to seek executive and/or Research and Development Department (R&D) approval prior to confirming participation, while others could make these decisions unilaterally. Centre factors also determined how trials were embedded through initiatives that increased engagement such as simulated trial runs. Embedding research into routine, or what was perceived as 'normal', care required a conceptual shift.

> "No, research is not a priority. New [intensive care unit] ICU consultants very keen, as are research [specialist registrars] SpRs. The resistance mainly comes from

nurses. It is about perceived additional work or disagreement with the protocol. . .it's not part of routine care" (Research nurse 4, study 1)

"Research should be part of everyone's job. If prescribed it should be given, regardless of it is [part of] research or not." (Research nurse 3, study 2)

"The Trust don't adequately prioritise research; the management don't 'get it' and [the] financial position takes precedence." (Consultant intensivist 13, study 2)

The nature of funding for research nurses, primarily funded via the CRNs and dependent on trial activity levels, created significant challenges to research conduct, given the lack of continuity. Some units ensured varied funding sources beyond the NIHR, to include commercial and higher education, and internally managed their own research budgets. This successfully allowed flexibility in deciding which trials to undertake, and managing staffing and out-of-hours support. Planning for future trials was evidently problematic on occasion. During periods with fewer critical care trials, many research teams broadened activity to cover Emergency Department (ED) and anaesthetic trials. Whilst this maintained research activity overall, it also resulted in research teams being stretched across many studies and it was hard to focus on critical care trials when activity in this area resumed. For university or university-affiliated hospitals, additional support for research overall could be obtained through links with academia.

"We have a historical arrangement with the University that they will fund a unit-based research fellow for a year." (Consultant intensivist 11, study 2)

Human and Unit resources

These sub-themes are reported together since they were closely aligned, incorporated staffing; reciprocity within research and ICU teams; models of provision; management; research opportunities and career structures (nurses/trainees). Staffing was a factor affecting research delivery. Varied models existed for staffing research teams, from rotational and secondments out of critical care, cross-hospital site and cross-specialty working, to research staffing being managed via the CRN. Most research staff had a clinical critical care background, which facilitated fluid working arrangements and carryover of research skills to non-research staff.

> "We instigated rotation of three months from ICU into the research team for 3 months, introducing fresh people and it invigorated the team." (Research nurse 15, study 2).

Many participants commented that while critical care research staff could cover other specialties, reciprocal cover for critical care was less successful given the unique patient population and the time-limited nature of recruitment, and this was often poorly appreciated by hospital R&D and regional CRN level. Research staff with a clinical background in critical care found communication easier and were able to support clinical staff, thus developing a mutually beneficial working relationships and helping with the normalisation of research. Grading of research nurse positions and lack of career development was identified as problematic; line management (direct management of the individual) was at times with the regional CRN offices, rather than the local critical care unit. Some research-active centres created attractive positions that afforded career progression and mitigated against job insecurity, a common feature of research nurse roles that are primarily funded on a yearly contract basis via the CRNs.

> "The career ladder is limited for them and so they move to management or work in R&D roles, and the use of temporary contracts is demoralising and a disincentive." (Consultant intensivist 1, study 1)

Few consultants received programmed activity (PA) sessions specifically for research, especially within non-university affiliated hospitals. Many clinicians relied upon financial support and time from their organisations to undertake research activity.

> "They do it effectively out of interest, there is nothing in their job plan apart from a reference to research, but no time to actually do it. . .it is voluntary and many don't do it" (Research nurse 4, study 2)

This lack of support overlaps with the organisational theme; allocated time and finances to support research activity was rare, occurring only in centres where research was viewed as core activity. Few medical trainees had the opportunity for research involvement, and again primarily only in research-active centres with novel initiatives designed to engage those interested in research e.g. year-long fellowships where research activity contributed to their training programme. Limited time was also a factor: "we have had less [trainees] over the

years, enthusiasm fades and other things take over" (Consultant intensivist 9, study 2). However, short clinical placements precluded meaningful trainee participation in primary research.

"They mainly don't get involved and when [they do], they don't do their own research" (Research nurse 15, study 2)

Designated trial coordinators were rare in smaller non-university-affiliated hospitals with less opportunity to enrol patients. Unit, staffing and centre factors were closely associated in the two datasets. Unit factors pertained to strategies to enhance engagement, provision, recruitment and delivery of critical care research. These varied from simulated runs of screening, recruitment and intervention, to teaching programmes and incentive schemes. Having a physical presence on the unit was seen as a crucial element for ensuring clinical credibility.

" you need to be there, being present, going on ward rounds and to handovers…" (Research nurse 14, study 2).

Driven individuals were critical to success in recruitment and study conduct, with both research nurses and consultants assuming principal investigator roles.

Study/trial factors

This sub-theme was characterised by study practicalities and how studies could be actualised within internal and external constraints. There were process and infrastructure issues associated with studies that affected the team's ability to conduct the trial.

Trial complexity appeared a considerable factor contributing to trial success, in terms of acceptance by local staff and potential ability to achieve recruitment targets. Feasibility and capacity assessment moderated concerns about delivering to time and target, a national metric captured by the NIHR CRN. Studies requiring significant pharmacy support, such as Clinical Trials of Investigational Medicinal Products had variable success with implementation and recruitment. Some units reported pressure from the regional CRN and local R&D departments to undertake high-recruiting studies that yielded maximum income generation, rather than complex studies perceived as interesting but with low recruitment targets that might yield less or insufficient income to cover costs. Demonstrating quick,

tangible 'wins' for an organisation and staff, through health service research, helped engagement. Complex studies were considered problematic for balancing effort against outcomes achieved, in particular around training requirements for staff to implement detailed interventions, and strict eligibility criteria with narrow recruitment windows leading to few, if any, patients enrolled. Studies requiring significant preparation, including co-enrolment agreements, time-scheduling, competing population assessment, and importantly, ensuring unit staff were committed and had clinical equipoise, could be particularly challenging:

> "they say they have equipoise, but when it comes down to it, they don't, you get surreptitious opposition and stark persuasion is used in those situations."
> (Consultant intensivist 1, study 1)

Time associated with daily screening was also a factor influencing success of complex trials, as often this could not be performed remotely and required extensive clinical data review. In keeping with study set-up, funding was rarely allocated for this activity, or for follow-up. In units where research was considered part of routine practice, clinical staff also helped with identification of potential participants.

> "There needs to be appropriate costing of studies including NHS support costs, for drugs for example. . .long-term follow-up needs to be considered as well."
> (Consultant intensivist 6, study 2)

Strategies to facilitate complex trials included engagement with local clinical staff on the relevant unit to integrate the trial procedures with standard care, thereby enabling all staff to contribute to patient screening and enrolment, including out-of-hours. Units could achieve this through training and cross-team working.

Clinician factors

This theme focused on how unit clinicians, nurses, trainees and intensivists, were perceived as engaged in research; this did not appear linked to how research-active an organisation was. Where research staff originated from the unit this was a facilitator, often resulting in good team working from both clinical and research team perspectives. Where research was

viewed as additional activity, rather than integral to patient care, research staff reported cases of open hostility, particularly early on in their roles, until unit staff developed an appreciation for research.

> "I've tried working on the unit and taking patients and doing shifts to build relationships" (Research nurse 7, study 2)

Research resources were factored by unit staff where there was good inter-boundary working. For instance, research staff attended senior nurse meetings to identify local issues that might adversely affect recruitment. Equally, unit staff could help identify barriers to recruitment to certain studies. Creating link roles supported nurse-level engagement and enhanced out-of-hours opportunities for recruitment when research nurses were not present. Very limited funding for out-of-hours cover enforced the need for research nurse flexibility.

Equipoise featured again in this theme; clinicians could undermine research activity by appearing supportive in meetings, but not in practice. Permission to recruit patients had to be negotiated at an individual clinician level, which could compromise unit objectivity toward the study.

> "The consultants are all GCP [Good Clinical Practice] trained but there is mixed interest and support, ranging from active obstruction. . ., to more neutral through to full support." (Consultant intensivist 9, study 2).

> "People believe they have equipoise but on the day people change what they do." (Research nurse 5, study 2).

Investment for trainee engagement arose as an important issue, particularly in those less research-active organisations. Ensuring the next generation of critical care consultants prioritised research activity with clinical practice was recognised as imperative. Many trainees were taught to obtain patient consent. At the time of the study, regional trainee research networks were emerging across the UK. However, according to these participants, in larger portfolio NIHR trials trainee engagement was noted to be minimal, and unit pressures contributed to lack of engagement. Trainee fellowship roles successfully

addressed this in two units, with staff continuing research in their careers as consultants, with an emphasis on personal motivation.

> "we actively encourage fellows not to go onto the [unit] rota so that their role is protected for research." (Consultant intensivist 11, study 2)

Personal commitment was a key factor; research activity often required working beyond allocated hours or sessions, or flexible working out-of-hours. This demonstrated how research teams worked to emphasise the sense that research should be considered the norm, with efforts devoted to successful implementation comparable to efforts in clinical practice. Skills of research nurses was a factor common to both datasets, with the ability (and R&D permission) to consent improving recruitment. Extended skills also meant that a number of research nursing staff were supported to undertake further study, including at doctoral level, fostering motivation, willingness to work flexibly and promoting emergence of independent researchers. Portfolio studies requiring a nurse Principal Investigator particularly motivated nurses. For consultants, feelings were mixed: studies with no personal interest fostered less engagement, unless it was likely to be income-generating.

Patient/family factors

This sub-theme encompassed issues such as participant burden, support available, communication, and anticipating declines to participate. Difficulties communicating information about trial procedures to patients and their families was reported by participants. A positive but realistic attitude was deemed essential. The volume of paperwork was identified as problematic. Ensuring that patients or families fully understood complex research interventions, without overburdening them at a sensitive time, was seen as a central issue.

> "We've got savvier about taking consent and have learnt lessons; you don't gain it by giving more paper." (Consultant intensivist 1, study 1)

Managing clinical uncertainty in the context of clinical trials was difficult. Whilst it did not seem to hinder recruitment, managing the process was challenging for research staff. Many families agreed to assent for patients for altruistic reasons, understanding there may be no

benefit to the patient. An important issue emerged in relation to addressing cultural perspectives. Different attitudes were perceived towards research, centring on trust in healthcare. Immediate dismissal by family members, on behalf of patients, was not uncommon. However, sometimes families were keen, but patients weren't.

> "The patient, who was not intubated [breathing tube for mechanical ventilation], had capacity and her family were keen for her to take part, but she wasn't (Research Nurse 9, study 1).

Conversely, some reported a paternalistic medical attitude still prevailing. Despite efforts to address this, provide more information and demonstrate equipoise, families and patients were reluctant and preferred to defer to doctors' opinions regarding enrolment.

> "I work in a deprived area with a lower level of education compared to the UK average, because of that the cultural norms mean they tend to trust what the doctors say: 'whatever you think doctor'" (Research nurse 11, study 2).

Neither of these opposing views about consent were regarded by participants as hindering recruitment. Units serving a disproportionately elderly or rural population reported difficulties gaining access to relatives for assent, particularly where time-sensitive consent was required. Research teams estimated a third of families were likely to decline participation when calculating recruitment targets and reasons for non-participation appeared to be complex and poorly understood. Where approaches to families were prefaced by an explanation that research was part of normal clinical practice in that particular unit, there was increased receptivity to recruitment. Reported preference for treatment arms was rare, and usually managed through explanation. Facilitating understanding was viewed as crucial when approaching families and patients for consent, with issues related to ongoing assessment of mental capacity also highlighted as difficult.

Discussion

This synthesis outlines six inter-related themes under a new over-arching theme of *Normalising Research*. Research activity was regarded as equally important as clinical work by these participants, albeit this was acknowledged as not a representative view across all

organisations or units. Where research was embedded into routine care and considered as the norm, undertaking screening and recruitment were easier. Emphasising the need for normalcy of research at a unit, as well as organisational level, means cohesive units evolve with the unified aim of improvements in patient care as the driving force. However, there are prerequisites for normalcy, including communication towards a shared understanding [16] in this case, that research is an integral part of everyday patient care. Furthermore, this communication needs to take place at a systems level.[16] Specific issues in the synthesis related to variation in funded time and resources, clinician engagement, individual roles, and perceived gains from research, which proved noteworthy, acting as barriers or facilitators to clinical trial recruitment. Bruce et al,[1] outlined how navigating rapidly changing clinical courses and communication breakdown adversely affected recruitment.[1] That these factors did not emerge in this synthesis may reflect different healthcare systems, funding, and the larger number of hospitals. Similarities emerged related to the challenges of recruitment within a narrow timeframe. Good communication between clinical and research teams was important for successful trial implementation.

Inclusion of data from less research-active organisations strengthens this study providing richer data, more transferable across the NHS and to healthcare systems in other jurisdictions. Our findings will resonate with other international settings where, despite variability in national infrastructure, similar challenges are faced by researchers. The tenet of normalising research transcends unit, institutional and country boundaries. Approaches to improve recruitment included simple incentive schemes to reward clinical staff, broadening the range of clinicians who could take consent. The latter is particularly pertinent to CTIMPs where time-limited recruitment was more relevant.[1,2] Previous work has suggested lack of equipoise as a barrier to enrolment[17,18]. An area for further exploration relates to consent waivers, already explored in some recent research [1,17,19, 20], albeit with less known of patient and family perspectives. 'Overburdening' has been described previously [21] as has concern regarding making initial approaches to families during particularly sensitive times [19-23] but again the patient/family voice in these studies is largely absent.[19-21] This would be an important area for future practice and research.

In keeping with existing literature, competition between trials requiring similar patient cohorts and the number of eligible patients were further barriers to trial recruitment [1,24]. Another factor related to lack of clear professional development opportunities and structured career paths. Recent strategy published by the NIHR offers novel career options for research staff [25-27] such as consultant research nurse models [25]. The emergence of medical trainee networks across the UK have also helped create a case for formalised processes.[28, 29] NIHR initiatives to engender a culture of research in healthcare, with every patient being offered the opportunity to participate in research aimed at improving care [30] are also reflected in these individual participants' motivations to improve care through research. Systematic review and large-scale survey evidence highlight key areas to improve trial recruitment as training site staff, communication with patients, and incentives, albeit some suggestions are not applicable to an ICU setting, such as telephone calls to non-respondents and opt-out procedures.[31,32] There have been significant advances over the past five years in critical care research recruitment.[33] In a current climate of significant fiscal pressures in the UK healthcare system with £22 billion of NHS efficiency savings to be achieved by 2020,[34] there was still a universal desire to undertake critical care research. This was driven by key motivated individuals who viewed research as integral to best practice and normal care provision, as well as deriving evidence to drive and support best use of resources.

This qualitative synthesis draws together two sets of original research findings. Whilst data were not collected simultaneously, both studies complemented each other. The second study built on the first by focusing specifically on a target participant cohort not initially represented in order to generate novel data to further understand the question at hand. Furthermore, the timeframe between acquisition of each dataset was short (twelve months) with minimal, if any, change in practice likely occurring during the interim. Potential sampling bias from recruiting primarily research-active units in the first dataset, was mitigated by employing purposive recruitment in the second dataset from less research-active units. We also acknowledge the possible introduction of bias through refining the interview schedule as we proceeded through the interviews. Research-active and less research-active units were defined both on subjective reports from individuals, and standardised objective metrics. Qualitative research is often criticised for lack of

generalisability, due to sample size limitations, but notions of transferability can be considered [8,11] and what Payne and Williams term 'moderatum generalisations'.[35] Figure 1. outlines a summary of the main points and four key areas for learning. The core concept of Normalising Research can feasibly be applied beyond critical care trials recruitment, across the full spectrum of clinical specialties represented within the NIHR, as well as internationally.

Conclusion

This qualitative synthesis integrating two original datasets has yielded recommendations for improving trials recruitment in the unique clinical specialty of critical care. Several suggestions are made from the six themes that emerged: Organisational, Human, Study, Practical resources, Clinician, and Patient/family factors, under the overarching theme of Normalising Research, that relate to enhanced staffing, training, trial design and communication. Fostering a culture where research is considered part of routine patient care must be the ultimate goal for those working at all levels, from organisational to bedside.

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manuscript preparation. All authors have reviewed and contributed to the manuscript. NP is the custodian of the intellectual integrity and property arising from this project.

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Data access: All data pertaining to this project are reported here. Please contact the authors regarding accessing aggregated data analysis. Raw data is not available to be shared since this could lead to identification.

Figure 1. Normalising Research

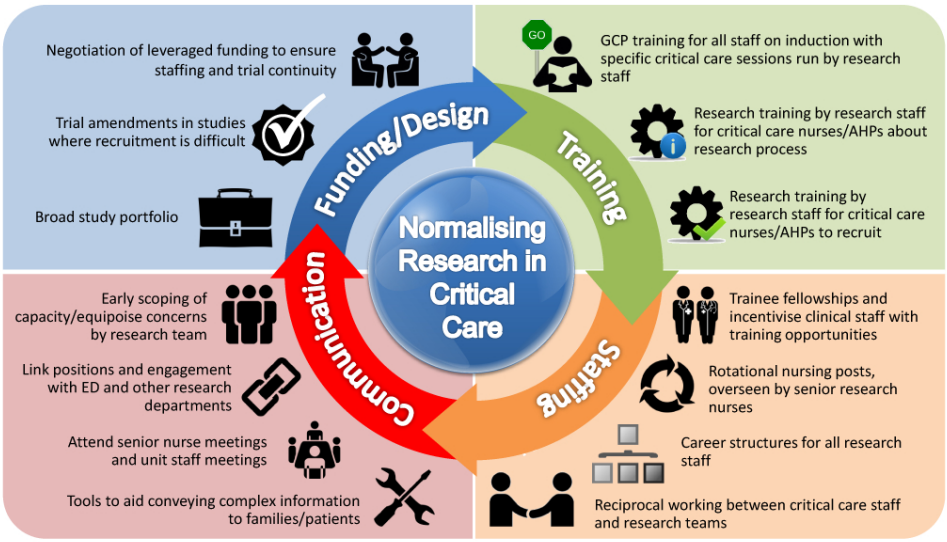

Figure 1. Normalising Research

Table 1 Participants/units (Supplemental File 1)

Profession and Area	Level 3/2 beds†	Annual admissions	General /Specialist unit	Research staff numbers including whole time equivalent (WTE)	Research team working patterns	Consultant numbers and funded consultant time (Professional Activity session [PA]) †† for research	Number (total) of ongoing clinical trials (both NIHR and non-NIHR/in set-up)
Nurse/ CRN Eastern	14	1000	General	**1** (work with Emergency Department [ED]); (1 WTE)	5 days/week 8-4pm (flexible)	**7** 1 PA	**6**
Nurse/CRN Yorkshire and Humber	24	1600	General	**2**; (2 WTE)	5 days (flexible – 9 hour cover)	**13** 0.5 PA (shared)	**5**
Nurse/ CRN West Midlands	25	1600	General	**1** (was 4); (1 WTE)	5 days/week; 8-4pm	*Data not provided/ unknown* 1 PA	**6**
Consultant/ CRN Wessex	12	900	General	**2** (across all Division 6*, not just ICU); 1 WTE)	5 days/week; 8-4pm	*Data not provided/ unknown* 2 PAs	**6**
Trial co-ordinator/ CRN London South	63	3100	General/trauma	**6** across ED/ICU; *(Data not provided/ unknown)*	5 days/week (and on-call at weekends/nights as required)	**>50** (exact number unknown) 0 PA	**5**
Consultant/ CRN North West London	44	2600	General/ Trauma/ Neuro	**2** fellows + **5** nurses; (2 fellows at 2 WTE; 5 nurses at 4.5 WTE. 1 WTE research assistant)	7 days/week	**21** 1 PA	**4**
Nurse/ CRN Greater Manchester	40	2000	General	**4** (across ED); (4 WTE)	8-8pm 5 days/week (and on-call at weekends/nights as required)	**22** 1 PA	**8**/ 2 in set-up
Nurse/ CRN TV and South Midlands	9	500	General	**0.5**; (0.5 WTE)	part/time (early/late shift pattern; weekdays)	**10** 0.5 PA	**2**
Consultant/ CRN Wessex	11	750	General	**4 + 0.5** trainee; (2.5 WTE + 0.5 WTE trainee)	7 days/week (plus trainee shifts)	**6** 0 PA	**4**
Consultant/ CRN West Midlands	102	4000	General/ Cardiac/ Trauma/ Burns/ Neuro	**7** (across ED/Trauma and ICU); (6 WTE including Trial Coordinator and administrators)	7 days/week	**34** 1 PA	**7**/ 2 in set-up
Consultant/ CRN North West Coast	33	1550	General	**3 + 0.5** trainee; (2.5 WTE + 0.5 WTE trainee)	5 days/week (flexible)	**17** 1 PA	**3**/ 1 in set-up
Consultant/ CRN West of England	15	5-600	General	**0**	n/a	**18** 0.5 PA	**1**/ 2 in set-up

Consultant/ CRN West of England	15	5-600	General	**0****	n/a	**18** 0.5 PA	**1/** 2 in set-up
Nurse/ CRN South West Peninsula	28	1700	General/trauma/ Neuro/ Cardiac	**1** (across dermatology/ neuro); (1 WTE)	8-4pm; 5 days/week	**14** *Data not provided /unknown*	**0**/ 1 in set-up
Nurse/ CRN West of England	20	1300	General	**9**; 5 WTE + 4 rotational posts	7-7pm; 7 days a week	***Data not provided /unknown*** 2 PAs (shared)	**10**
Nurse/ CRN East Midlands	69	4000	General/trauma/ Neuro	**6** (covering ED) – split site; (4.2 WTE)	7-7pm; 7 days/week	***Data not provided /unknown*** 0 PA	**13**
Nurse/ CRN Norfolk	19	850	General	**2** *; (1.45 WTE)	8-4pm 5 days/week (and on-call at weekends/nights as required)	***Data not provided /unknown*** 0 PA	**4**/ 1 in set-up
Nurse/ Wales	33	1500	General/ Neuro	**5**; (4 WTE)	8-4pm 5 days/week	**14** 1 PA	**6**
Nurse/ CRN North West Coast	35	1880	General	**2**; (1 WTE nurse at band[+] 7 shared and 4 x nurse at band 6 at 0.8 WTE)	7.30-3.30pm 5 days/week	**13** 0 PA	**9**
Nurse/ CRN South West Peninsula	26	1580	General/ Neuro	**1**; (*Data not provided /unknown)*	8-4pm 5 days/week	**14** 0 PA	**7**
Nurse/ CRN North East North Cumbria	18	1000	General	**2**; (1 nurse at band 3 research assistant; 1 nurse at band 6 WTE)	9-5pm 5 days/week	**9** 0 PA	8
Nurse/ CRN East Midlands	19	1200	General	**3**; (2.8 WTE)	8-7pm	***Data not provided /unknown*** 2 PAs	**11**
Nurse/ CRN Eastern	20	1890	General	**4**; *(Data not provided/unknown)*	8-8pm	***Data not provided /unknown*** 1 PA	**7**
Nurse/ CRN Greater Manchester	19	1700	General	**0.8**; (0.8 WTE)	8-4pm	**12** 0 PA	**4**
Consultant/ CRN Wessex	24	1200	General	**3**; (1.6 WTE + 2 WTE for 3 month rotations)	8am-12pm 7 days a week	**14** 2 PAs	**5**
Consultant/ CRN London South	63	3500	General/ Neuro	**9**; (2 nurse at band 7; 7 nurse at band 6* WTE)	8-8pm	***Data not provided /unknown*** *1 PA*	**10**
Nurse/ CRN West of England	21	2000	General	**5**; (4 WTE (1 nurse at band 7; remainder nurse at band 6)	7-7pm	**12** *Data not provided /unknown*	**8**

† Level 2 beds are where patients require more detailed observation or intervention including support for a single failing organ system or post-operative care and those 'stepping down' from higher levels of care Level 3 beds only. Level 3 care is defined as patients needing advanced respiratory support alone or support of at least two organ systems. Note basic respiratory and basic cardiovascular support occurring on one day count as one organ. This level includes beds for all complex patients requiring support for multi-organ failure. Flexible critical care beds where there is a mix of level 2 and level 3 beds (NHS data dictionary: https://www.datadictionary.nhs.uk/data_dictionary/attributes/u/unit_bed_configuration_de.asp?shownav=1) ††PAs=Professional Activities Sessions are four hour weekly sessions for consultants only *Working across all Division 6 studies, not limited to critical care; Division 6 is one of six NIHR overarching divisions that encompasses critical care, anaesthesia/peri-operative/pain, emergency care/injuries, surgery, respiratory,

gastroenterology, infectious diseases/microbiology, hepatology, ophthalmology, ENT and **Able to access other Division 6 nurses when studies are active. + Band refers to the grade of nurse/research assistant as per Agenda for Change https://www.nhsemployers.org/pay-pensions-and-reward/agenda-for-change/pay-scales/annual. Band 7 is considered a senior nurse.

Supplementary File 2. Table 2. Summary and recommendations

Recommendations for normalising research in critical care
Organisational factors:
○ Training: Offer Good Clinical Practice (GCP)/research training for all staff on induction; Research staff running GCP sessions for critical care staff ○ Offer research training by research staff for critical care nurses/AHPs to recruit/learn about research processes ○ Negotiation of leveraged funding to ensuring staffing and trial continuity; maintain a broad study portfolio ○ Work on engagement and links with ED and other research departments in the same NIHR divisions to support teams
Human and Unit resources
○ Offer trainee fellowships to support medical trainees wanting a career in research ○ Create rotational nursing posts in critical care, overseen by senior research nurses ○ Facilitate reciprocal working between ICU staff and research teams; research staff working in ICU to enhance links and recruitment opportunities ○ Create more career structures for doctors, AHPs and nurses working in critical care research (through each of the bands, so there is an identified progression ladder up to the most senior grade) ○ Incentivise clinical staff with training opportunities (e.g. create and offer free study opportunities in a clinical area associated with the relevant study)
Clinician factors
○ Communication and interdisciplinary working: Attend senior nurse/clinical meetings in critical care ○ Create link nurse positions (to be extended to link trainee positions) ○ Ensure early scoping of capacity/equipoise concerns by research team
Study/trial factors ○ Consider/request trial amendments in studies that are difficult to recruit to ○ Engage with and attend unit staff meetings early on in study planning to identify potential study barriers (such as out of hours pharmacy provision
Patient/family factors ○ Create tools/training/peer review to aid conveying complex information to families and patients

- Have visible evidence of research activity in the unit (e.g posters) so it is apparent that research is part of routine care

Reporting checklist for qualitative study.

Based on the SRQR guidelines.

Instructions to authors

Complete this checklist by entering the page numbers from your manuscript where readers will find each of the items listed below.

Your article may not currently address all the items on the checklist. Please modify your text to include the missing information. If you are certain that an item does not apply, please write "n/a" and provide a short explanation.

Upload your completed checklist as an extra file when you submit to a journal.

In your methods section, say that you used the SRQR reporting guidelines, and cite them as:

O'Brien BC, Harris IB, Beckman TJ, Reed DA, Cook DA. Standards for reporting qualitative research: a synthesis of recommendations. Acad Med. 2014;89(9):1245-1251.

		Reporting Item	Page Number
	#1	Concise description of the nature and topic of the study identifying the study as qualitative or indicating the approach (e.g. ethnography, grounded theory) or data collection methods (e.g. interview, focus group) is recommended	1
	#2	Summary of the key elements of the study using the abstract format of the intended publication; typically includes background, purpose, methods, results and conclusions	1
Problem formulation	#3	Description and signifcance of the problem / phenomenon studied: review of relevant theory and empirical work; problem statement	3
Purpose or research question	#4	Purpose of the study and specific objectives or questions	3
Qualitative approach and research paradigm	#5	Qualitative approach (e.g. ethnography, grounded theory, case study, phenomenolgy, narrative research)	4

		and guiding theory if appropriate; identifying the research paradigm (e.g. postpositivist, constructivist / interpretivist) is also recommended; rationale. The rationale should briefly discuss the justification for choosing that theory, approach, method or technique rather than other options available; the assumptions and limitations implicit in those choices and how those choices influence study conclusions and transferability. As appropriate the rationale for several items might be discussed together.	
Researcher characteristics and reflexivity	#6	Researchers' characteristics that may influence the research, including personal attributes, qualifications / experience, relationship with participants, assumptions and / or presuppositions; potential or actual interaction between researchers' characteristics and the research questions, approach, methods, results and / or transferability	4
Context	#7	Setting / site and salient contextual factors; rationale	4
Sampling strategy	#8	How and why research participants, documents, or events were selected; criteria for deciding when no further sampling was necessary (e.g. sampling saturation); rationale	4
Ethical issues pertaining to human subjects	#9	Documentation of approval by an appropriate ethics review board and participant consent, or explanation for lack thereof; other confidentiality and data security issues	4
Data collection methods	#10	Types of data collected; details of data collection procedures including (as appropriate) start and stop dates of data collection and analysis, iterative process, triangulation of sources / methods, and modification of procedures in response to evolving study findings; rationale	4
Data collection instruments and technologies	#11	Description of instruments (e.g. interview guides, questionnaires) and devices (e.g. audio recorders) used for data collection; if / how the instruments(s) changed over the course of the study	4

Units of study	#12	Number and relevant characteristics of participants, documents, or events included in the study; level of participation (could be reported in results)	5
Data processing	#13	Methods for processing data prior to and during analysis, including transcription, data entry, data management and security, verification of data integrity, data coding, and anonymisation / deidentification of excerpts	4
Data analysis	#14	Process by which inferences, themes, etc. were identified and developed, including the researchers involved in data analysis; usually references a specific paradigm or approach; rationale	4
Techniques to enhance trustworthiness	#15	Techniques to enhance trustworthiness and credibility of data analysis (e.g. member checking, audit trail, triangulation); rationale	4
Syntheses and interpretation	#16	Main findings (e.g. interpretations, inferences, and themes); might include development of a theory or model, or integration with prior research or theory	5
Links to empirical data	#17	Evidence (e.g. quotes, field notes, text excerpts, photographs) to substantiate analytic findings	6
Intergration with prior work, implications, transferability and contribution(s) to the field	#18	Short summary of main findings; explanation of how findings and conclusions connect to, support, elaborate on, or challenge conclusions of earlier scholarship; discussion of scope of application / generalizability; identification of unique contributions(s) to scholarship in a discipline or field	10
Limitations	#19	Trustworthiness and limitations of findings	11
Conflicts of interest	#20	Potential sources of influence of perceived influence on study conduct and conclusions; how these were managed	2
Funding	#21	Sources of funding and other support; role of funders in data collection, interpretation and reporting	2

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A synthesis of qualitative research studies regarding the factors surrounding UK critical care trial infrastructure

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Complete List of Authors:	Pattison, Natalie; University of Hertfordshire and East & North Hertfordshire NHS Trust, School of Health and Social Work; University of Hertfordshire Arulkumaran, Nishkantha; UCL, Critical Care O'Gara, Geraldine; Royal Marsden Hospital NHS Trust Connolly, Bronwen; King's College London, Lane Fox Respiratory Unit Humphreys, Sally; West Suffolk Hospitals NHS Trust, Critical Care Walsh, Tim; University of Edinburgh Royal Infirmary Edinburgh, Critical Care Hopkins, Philip; Kings College Hospital, Critical Care Dark, Paul; University of Manchester, Intensive Care Unit
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Title: A synthesis of qualitative research studies regarding the factors surrounding UK critical care trial infrastructure

Corresponding author: Professor Natalie Pattison, Florence Nightingale Foundation Clinical Professor of Nursing, University of Hertfordshire/East & North Herts NHS Trust
Natalie.pattison@nhs.net

Co-authors: Dr Nishkantha Arulkumaran*, University College London, UK; Geraldine O'Gara, Royal Marsden Foundation NHS Trust, London, UK; Dr Bronwen Connolly*, Guys and St Thomas' NHS Foundation Trust/Intensive Care National Audit and Research Centre (ICNARC), London, UK; Sally Humphreys, West Suffolk NHS Trust, Suffolk, UK; Professor Tim Walsh*, University of Edinburgh, Edinburgh, UK; Dr Phillip Hopkins*, Kings College Hospital, London, UK; Professor Paul Dark*, University of Manchester, Manchester, UK.
*Former/current members of the NIHR CRN Specialty Group for Critical Care

Abstract:

Conducting clinical trials in critical care is integral to improving patient care. Unique practical and ethical considerations exist in this patient population that make patient recruitment challenging, including narrow recruitment timeframes and obtaining patient consent often in time-critical situations. Units currently vary significantly in their ability to recruit according to infrastructure and level of research activity.

Aim

To identify variability in the research infrastructure of UK intensive care units (ICUs) and their ability to conduct research and recruit patients into clinical trials.

Design

We evaluated factors related to intensive care patient enrolment into clinical trials in the UK. This consisted of a qualitative synthesis carried out with two datasets of in-depth interviews (distinct participants across the two datasets) conducted with 27 intensive care consultants (n=9), research nurses (n=17) and trial coordinators (n=1) from 27 units across the UK. Primary and secondary analysis of two datasets (one dataset had been analysed previously) was undertaken in the thematic analysis.

Findings

The synthesis yielded an overarching core theme of Normalising Research, characterised by motivations for promoting research and fostering research-active cultures within resource constraints, with six themes under this to explain the factors influencing critical care research capacity: Organisational, Human, Study, Practical resources, Clinician, and Patient/family factors. There was a strong sense of integrating research in routine clinical practice, and recommendations are outlined.

Conclusions

The central and transferable tenet of Normalising Research advocates the importance of developing a culture where research is inclusive alongside clinical practice in routine patient care and is requisite for all healthcare individuals from organisational to direct patient contact level.

Keywords: Qualitative synthesis; critical care trials; access to research; barriers; facilitators; normalising research

Revised word count: 4688

Article Summary

Strengths and limitations:

Strengths

- This qualitative synthesis uniquely draws together two datasets exploring the factors that enable or hinder critical care research and presents an overarching theme of normalising research, outlining factors necessary to achieve this.
- The dataset and purposive sample encompasses 14 out of 16 of the National Institute for Health's Clinical Research Networks across England and Wales, reflecting a broad range of research experiences in critical care units.
- The synthesis builds on previous research and highlights how integration and normalisation of research in clinical practice requires several interrelated factors including training, cultural receptivity, adequate funding, flexible study designs, good communication and interdisciplinary working at all levels, and a flexible staffing approach.

Limitations

- While we noted some similar challenges to study outside the UK, this study used two datasets solely from the UK, which has a robust critical care research infrastructure and may differ from other challenges across the world.
- This study focussed on samples from both research-active and non-research active units, however the qualitative purposive sampling, and small sample size (n=27) may have led to a sampling bias, meaning that the issues raised do not reflect all the issues encountered in practice.

Funding: This project was supported with infrastructure from the National Institute for Health Research Comprehensive Research Network in Critical Care (NIHR Theme Hub C King's College London).

Competing interests: The authors have none to declare.

Background

Clinical trials in critical care are integral to improving patient care, albeit unique practical and ethical challenges exist including the time-sensitive nature of treatment and enrolling patients who lack capacity.[1] Data exploring barriers to conducting clinical trials in this setting are scarce, but include managing changing clinical courses, communication breakdowns, and requests for more time for consent [2]. Our previous study, focussing on research active centres,[3] described enhanced patient recruitment in centres valuing research with equal importance to clinical care, with the most commonly cited barriers insufficient human and financial resource, inadequate personnel funding, and limited career opportunities impeding staff retention.[3] Several additional factors may also preclude recruitment, such as lack of clinician equipoise and competing clinical commitments.

Implications for the NIHR

The UK National Institute for Health and Research (NIHR) is the government-funded research arm of the National Health Service (NHS), responsible for driving bench-to-bedside research with tangible patient benefit [4]. Unique infrastructure, including the national coordinated Clinical Research Network (CRN) and specialty groups (SG) with oversight for

specific clinical areas such as critical care (CC), enhance the UK's national and international position to deliver high quality clinical trials. Research teams invest significantly in recruitment to critical care trials with emphasis on mitigating modifiable factors. In particular understanding barriers and facilitators in institutions which are less research-active, such as non-university-affiliated hospitals, is crucial to enhance trial recruitment across the NIHR CRN.

Our objective was therefore to identify examples of these potential barriers and facilitators to patient enrolment in order to inform strategies to enhance future critical care trial recruitment, and identify how research staff could be supported in these organisations.

Methods

Design

A qualitative synthesis was conducted [5], involving two datasets comprising in-depth interviews (n=27) with critical care consultants (n=9), research nurses (n=17), and trial coordinators (n=1) across England and Wales (26 hospitals; 27 units). Dataset 1 included 10 participants and is reported in detail elsewhere [3]. For that dataset a sampling frame across the CRNs was used to represent a mix of smaller and larger ICUs, from teaching hospitals and district general type hospital ICUs, including one person within each CRN to ensure region-wide representation. Dataset 2, a follow-on study, included a further 17 participants from different backgrounds/units, with the aim of specifically exploring issues in less research-active critical care units. Service evaluation and quality improvement methods underpinned the projects.[6] Therefore, this synthesis involved both primary and secondary data analysis. Qualitative synthesis is a well-established method that draws together findings to reach over-arching themes.[5], ensuring similar research can be reliably compared.[7,8,9]

Patient public involvement

Patient/public were not involved in the design of this study since the focus is on research infrastructure.

Data collection

Individual telephone, digitally audio-recorded, interviews were conducted with participants, using a pre-determined semi-structured interview schedule agreed by team consensus. The aim of the second set of interviews was to understand how to engage and promote research activity and increase trial recruitment in critical care units that find it challenging to recruit to trials. Interview questions included: *What can you tell me about how the unit decides whether to participate in a research project? Tell me about the infrastructure in your critical care unit to support research.* See Supplementary file 1 for interview questions. Written and verbal information about the project was provided and confidentiality was assured. Transcripts were anonymised prior to analysis. Team review of both the interview structure, which was refined as interviews progressed in both datasets (including more targeted questions to elicit nuances such as local capacity to conduct research) and also informed refinement of the framework analysis, [10] enhanced dependability in research findings and qualitative rigour through developing credibility and transferability.[11]

Ethical considerations

The study was supported and facilitated by the NIHR Critical Care Specialty Group (NIHR CCSG). No ethical approval or written consent, as per the UK Health Research Authority, was required since only anonymised data with staff were used. No local institutional Research & Development approval was deemed necessary, since this was a project to represent views on behalf of the NIHR CCSG and recruitment did not take place via institutions. Demographic data about each critical care unit's research activity and staffing were also collected. Participation was voluntary and verbal consent was obtained both before and after the interview, to allow interviewees the opportunity to withdraw/withhold any data discussed.

Settings

Two purposive samples were recruited, with the aim of representing different regions and professional grades (critical care nurses, trainees, trial co-ordinators and consultants) across

the UK. The purposive sampling technique involved maximum variation sampling,[12] using UK trial accrual and activity data from the NIHR. The aim was to include clinicians representing critical care units across the 16 CRNs (15 in England, one in Wales). Specifically, the second dataset focused on units with limited trial recruitment, or engaged in few trials. We did not ascribe a set value to define 'less research active', but focused on unit-level activity in terms of participants recruited and active studies, according to NIHR yearly summary data. The NIHR centralises this information in a 'portfolio', and all sites are required to submit this information. Invites were circulated via the NIHR network using established mailing lists, and targeted recruitment to ensure unbiased representation. Using the principles of theoretical sampling (as used most commonly in Grounded Theory),[13,14] a sample size of 20-30 interviews was deemed sufficient to reach data saturation and build up a comprehensive picture of the UK landscape in relation to factors that influence critical care research provision.

Analysis

Themes were explored at an overall and ICU-specific level. Potential barriers/facilitators within individual critical care units, hospitals, locally and nationally were identified. In both datasets, analysis was conducted using thematic analysis, a technique congruent with different types of qualitative research, [15] aided by principles of framework analysis,[10] where categories were refined as analysis progressed. Data from verbatim transcripts were coded at a line level, with sub-themes derived from those codes applied to a framework, with constant comparison. Datasets were compared and contrasted, and a new framework was devised, and all data were re-analysed according to this. An independent researcher verified the analysis on anonymised data to enhance dependability and we coded to reach consensus in the case of coding differences. The framework provided a further degree of dependability in regards to analysis,[11] and allowed for contextual differences to emerge. The matrix provided detail of within case and cross-case analysis,[14] which was developed into themes.

Findings

In Dataset 1 (collected in 2015), 10 interviews were conducted across nine CRN regions across England (n=8) and Wales (n=1). Dataset 2 (collected 2016/17) included 17 interviews conducted across 12 English CRNs. Two CRNs were not represented due to lack of response. Interviews ranged from 29-81 minutes (mean length was 45.2 mins). The framework analysis for each studies yielded six main themes. Demographics are supplied in Table 1, Supplementary file 2.

Overarching findings from synthesis

There was an overarching theme of *Normalising Research*, describing the notion that critical care research should be entrenched in routine practice. Six sub-themes existed around this central tenet: *Organisational, Human* and *Unit Resources, Study, Clinician,* and *Patient/family factors.* Resource issues permeated each theme to a different extent and were evident throughout the organisational, unit, study, or trial level, and at a human, individual level. Resources could be managed and influenced at an individual level, for instance. In centres, units, and teams where research activity was regarded with equal importance as clinical activity, research was considered routine practice. In turn, teams and individuals with a strong sense of integrating research in routine practice acted as the motivating driving force fostering a research culture, whether in primary, translational biomedical, or applied health services streams. A broader cultural influence from organisations was also evident, where research was seen as critical to organisational values, up to executive level, which in turn contributed to enhanced research activity. Barriers and enablers to trial recruitment and conduct are outlined in each theme below. A summary of these factors is outlined in Supplementary file 3, Table 1 and represented in Figure 1.

Organisational factors

This theme related to the organisational system in which units were situated, and incorporated Trust or Board level factors; perceived priority of research; infrastructure; trial planning; funding and external links, such as academia. Research-active and less research-active institutions contrasted with regards prioritisation of research activity by senior management, with the latter placing lower profile on the support and conduct of research.

This was particularly marked at challenging times e.g. during care failure reports, or financial or bed crises, even though these could be opportune periods for potential trial enrolment.

> "Research and development is not high profile. At an organisational level it is service driven, research is seen as an aside and there is no support for it." (Research nurse 2, study 2)

Despite income-generating research activity, such as involvement in commercial studies, increased demand on resources posed a limitation to engagement. Some critical care research leads had to seek executive and/or Research and Development Department (R&D) approval prior to confirming participation, while others could make these decisions unilaterally. Centre factors also determined how trials were embedded through initiatives that increased engagement such as simulated trial runs. Embedding research into routine, or what was perceived as 'normal', care required a conceptual shift.

> "No, research is not a priority. New [intensive care unit] ICU consultants very keen, as are research [specialist registrars] SpRs. The resistance mainly comes from nurses. It is about perceived additional work or disagreement with the protocol. . .it's not part of routine care" (Research nurse 4, study 1)

> "Research should be part of everyone's job. If prescribed it should be given, regardless of it is [part of] research or not." (Research nurse 3, study 2)

> "The Trust don't adequately prioritise research; the management don't 'get it' and [the] financial position takes precedence." (Consultant intensivist 13, study 2)

The nature of funding for research nurses, primarily funded via the CRNs and dependent on trial activity levels, created significant challenges to research conduct, given the lack of continuity. Some units ensured varied funding sources beyond the NIHR, to include commercial and higher education, and internally managed their own research budgets. This successfully allowed flexibility in deciding which trials to undertake, and managing staffing and out-of-hours support. Planning for future trials was evidently problematic on occasion. During periods with fewer critical care trials, many research teams broadened activity to cover Emergency Department (ED) and anaesthetic trials. Whilst this maintained research activity overall, it also resulted in research teams being stretched across many studies and it

was hard to focus on critical care trials when activity in this area resumed. For university or university-affiliated hospitals, additional support for research overall could be obtained through links with academia.

"We have a historical arrangement with the University that they will fund a unit-based research fellow for a year." (Consultant intensivist 11, study 2)

Human and Unit resources

These sub-themes are reported together since they were closely aligned, and incorporated staffing; reciprocity within research and ICU teams; models of provision; management; research opportunities and career structures (nurses/trainees). Staffing was a factor affecting research delivery. Varied models existed for staffing research teams, from rotational and secondments out of critical care, cross-hospital site and cross-specialty working, to research staffing being managed via the CRN. Most research staff had a clinical critical care background, which facilitated fluid working arrangements and carryover of research skills to non-research staff.

> "We instigated rotation of three months from ICU into the research team for 3 months, introducing fresh people and it invigorated the team." (Research nurse 15, study 2).

Many participants commented that while critical care research staff could cover other specialties, reciprocal cover for critical care was less successful given the unique patient population and the time-limited nature of recruitment, and this was often poorly appreciated by hospital R&D and regional CRN level. Research staff with a clinical background in critical care found communication easier and were able to support clinical staff, thus developing a mutually beneficial working relationships and helping with the normalisation of research. Grading of research nurse positions and lack of career development was identified as problematic; line management (direct management of the individual) was at times with the regional CRN offices, rather than the local critical care unit. Some research-active centres created attractive positions that afforded career progression and mitigated against job insecurity, a common feature of research nurse roles that are primarily funded on a yearly contract basis via the CRNs.

> "The career ladder is limited for them and so they move to management or work in R&D roles, and the use of temporary contracts is demoralising and a disincentive." (Consultant intensivist 1, study 1)

Few consultants received programmed activity (PA) sessions specifically for research, especially within non-university affiliated hospitals. Many clinicians relied upon financial support and time from their organisations to undertake research activity.

> "They do it effectively out of interest, there is nothing in their job plan apart from a reference to research, but no time to actually do it. . .it is voluntary and many don't do it" (Research nurse 4, study 2)

This lack of support overlaps with the organisational theme; allocated time and finances to support research activity was rare, occurring only in centres where research was viewed as core activity. Few medical trainees had the opportunity for research involvement, and again primarily only in research-active centres with novel initiatives designed to engage those interested in research e.g. year-long fellowships where research activity contributed to their training programme. Limited time was also a factor: "we have had less [trainees] over the years, enthusiasm fades and other things take over" (Consultant intensivist 9, study 2). However, short clinical placements precluded meaningful trainee participation in primary research.

> "They mainly don't get involved and when [they do], they don't do their own research" (Research nurse 15, study 2)

Designated trial coordinators were rare in smaller non-university-affiliated hospitals with less opportunity to enrol patients. Unit, staffing and centre factors were closely associated in the two datasets. Unit factors pertained to strategies to enhance engagement, provision, recruitment and delivery of critical care research. These varied from simulated runs of screening, recruitment and intervention, to teaching programmes and incentive schemes. Having a physical presence on the unit was seen as a crucial element for ensuring clinical credibility.

> "You need to be there, being present, going on ward rounds and to handovers…" (Research nurse 14, study 2).

Driven individuals were critical to success in recruitment and study conduct, with both research nurses and consultants assuming principal investigator roles.

Study/trial factors

This sub-theme was characterised by study practicalities and how studies could be actualised within internal and external constraints. There were process and infrastructure issues associated with studies that affected the team's ability to conduct the trial.

Trial complexity appeared a considerable factor contributing to trial success, in terms of acceptance by local staff and potential ability to achieve recruitment targets.

> "The complexity of the study and study information is a problem, for staff as well as families. . . It's easier to explain CTIMPS [Clinical Trials of Investigational Medicinal Products] versus devices and it's easier to gain consent in a complex study with a family who can understand." (Consultant intensivist 2, study 1).

Feasibility and capacity assessment moderated concerns about delivering to time and target, a national metric captured by the NIHR CRN. Studies requiring significant pharmacy support, such as Clinical Trials of Investigational Medicinal Products had variable success with implementation and recruitment. Some units reported pressure from the regional CRN and local R&D departments to undertake high-recruiting studies that yielded maximum income generation, rather than complex studies perceived as interesting but with low recruitment targets that might yield less or insufficient income to cover costs. Demonstrating quick, tangible 'wins' for an organisation and staff, through health service research, helped engagement.

Complex studies were considered problematic for balancing effort against outcomes achieved, in particular around training requirements for staff to implement detailed interventions, and strict eligibility criteria with narrow recruitment windows leading to few, if any, patients enrolled. Studies requiring significant preparation, including co-enrolment agreements, time-scheduling, competing population assessment, and importantly, ensuring unit staff were committed and had clinical equipoise, could be particularly challenging:

"they say they have equipoise, but when it comes down to it, they don't, you get surreptitious opposition and stark persuasion is used in those situations." (Consultant intensivist 1, study 1)

Time associated with daily screening was also a factor influencing success of complex trials, as often this could not be performed remotely and required extensive clinical data review. In keeping with study set-up, funding was rarely allocated for this activity, or for follow-up. In units where research was considered part of routine practice, clinical staff also helped with identification of potential participants.

"There needs to be appropriate costing of studies including NHS support costs, for drugs for example. . .long-term follow-up needs to be considered as well." (Consultant intensivist 6, study 2)

Strategies to facilitate complex trials included engagement with local clinical staff on the relevant unit to integrate the trial procedures with standard care, thereby enabling all staff to contribute to patient screening and enrolment, including out-of-hours. Units could achieve this through training and cross-team working.

Clinician factors

This theme focused on how unit clinicians, nurses, trainees and intensivists, were perceived as engaged in research; this did not appear linked to how research-active an organisation was. Where research staff originated from the unit this was a facilitator, often resulting in good team working from both clinical and research team perspectives.

"We try to pick out staff nurses with initiative and encourage them to apply [for research posts]. We've had some on the team who've worked in ICU, which helps, although where there is history it can create problems." (Research nurse 3, study 2)

"We are line managed by critical care staff, which is good, rather than by R&D and we both then have influence in critical care." (Research nurse 5, study 2)

Where research was viewed as additional activity, rather than integral to patient care, research staff reported cases of open hostility, particularly early on in their roles, until unit staff developed an appreciation for research.

> "I've tried working on the unit and taking patients and doing shifts to build relationships" (Research nurse 7, study 2)

Research resources were factored by unit staff where there was good inter-boundary working. For instance, research staff attended senior nurse meetings to identify local issues that might adversely affect recruitment. Equally, unit staff could help identify barriers to recruitment to certain studies. Creating link roles supported nurse-level engagement and enhanced out-of-hours opportunities for recruitment when research nurses were not present. Very limited funding for out-of-hours cover enforced the need for research nurse flexibility.

Equipoise featured again in this theme; clinicians could undermine research activity by appearing supportive in meetings, but not in practice. Permission to recruit patients had to be negotiated at an individual clinician level, which could compromise unit objectivity toward the study.

> "The consultants are all GCP [Good Clinical Practice] trained but there is mixed interest and support, ranging from active obstruction. . ., to more neutral through to full support." (Consultant intensivist 9, study 2).

> "People believe they have equipoise but on the day people change what they do." (Research nurse 5, study 2).

Investment for trainee engagement arose as an important issue, particularly in those less research-active organisations. Ensuring the next generation of critical care consultants prioritised research activity with clinical practice was recognised as imperative. Many trainees were taught to obtain patient consent. At the time of the study, regional trainee research networks were emerging across the UK. However, according to these participants, in larger portfolio NIHR trials trainee engagement was noted to be minimal, and unit pressures contributed to lack of engagement. Trainee fellowship roles successfully

addressed this in two units, with staff continuing research in their careers as consultants, with an emphasis on personal motivation.

> "we actively encourage fellows not to go onto the [unit] rota so that their role is protected for research." (Consultant intensivist 11, study 2)

Personal commitment was a key factor; research activity often required working beyond allocated hours or sessions, or flexible working out-of-hours. This demonstrated how research teams worked to emphasise the sense that research should be considered the norm, with efforts devoted to successful implementation comparable to efforts in clinical practice. Skills of research nurses was a factor common to both datasets, with the ability (and R&D permission) to consent improving recruitment. Extended skills also meant that a number of research nursing staff were supported to undertake further study, including at doctoral level, fostering motivation, willingness to work flexibly and promoting emergence of independent researchers. Portfolio studies requiring a nurse Principal Investigator particularly motivated nurses. For consultants, feelings were mixed: studies with no personal interest fostered less engagement, unless it was likely to be income-generating.

Patient/family factors

This sub-theme encompassed issues such as participant burden, support available, communication, and anticipating declines to participate. Difficulties communicating information about trial procedures to patients and their families was reported by participants. A positive but realistic attitude was deemed essential. The volume of paperwork was identified as problematic. Ensuring that patients or families fully understood complex research interventions, without overburdening them at a sensitive time, was seen as a central issue.

> "We've got savvier about taking consent and have learnt lessons; you don't gain it by giving more paper." (Consultant intensivist 1, study 1)

Managing clinical uncertainty in the context of clinical trials was difficult. Whilst it did not seem to hinder recruitment, managing the process was challenging for research staff. Many families agreed to assent for patients for altruistic reasons, understanding there may be no

benefit to the patient. An important issue emerged in relation to addressing cultural perspectives. Different attitudes were perceived towards research, centring on trust in healthcare. Immediate dismissal by family members, on behalf of patients, was not uncommon. However, sometimes families were keen, but patients weren't.

> "The patient, who was not intubated [breathing tube for mechanical ventilation], had capacity and her family were keen for her to take part, but she wasn't (Research Nurse 9, study 1).

Conversely, some reported a paternalistic medical attitude still prevailing. Despite efforts to address this, provide more information and demonstrate equipoise, families and patients were reluctant and preferred to defer to doctors' opinions regarding enrolment.

> "I work in a deprived area with a lower level of education compared to the UK average, because of that the cultural norms mean they tend to trust what the doctors say: 'whatever you think doctor'" (Research nurse 11, study 2).

Neither of these opposing views about consent were regarded by participants as hindering recruitment. Units serving a disproportionately elderly or rural population reported difficulties gaining access to relatives for assent, particularly where time-sensitive consent was required. Research teams estimated a third of families were likely to decline participation when calculating recruitment targets and reasons for non-participation appeared to be complex and poorly understood. Where approaches to families were prefaced by an explanation that research was part of normal clinical practice in that particular unit, there was increased receptivity to recruitment. Reported preference for treatment arms was rare, and usually managed through explanation. Facilitating understanding was viewed as crucial when approaching families and patients for consent, with issues related to ongoing assessment of mental capacity also highlighted as difficult.

Discussion

This synthesis outlines six inter-related themes under a new over-arching theme of *Normalising Research*. Research activity was regarded as equally important as clinical work by these participants, albeit this was acknowledged as not a representative view across all organisations or units. Where research was embedded into routine care and considered as

the norm, undertaking screening and recruitment were easier. Emphasising the need for normalcy of research at a unit, as well as organisational level, means cohesive units evolve with the unified aim of improvements in patient care as the driving force. However, there are prerequisites for normalcy, including communication towards a shared understanding [16] in this case, that research is an integral part of everyday patient care. Furthermore, this communication needs to take place at a systems level.[16] Specific issues in the synthesis related to variation in funded time and resources, clinician engagement, individual roles, and perceived gains from research, which proved noteworthy, acting as barriers or facilitators to clinical trial recruitment. Bruce et al,[1] outlined how navigating rapidly changing clinical courses and communication breakdown adversely affected recruitment.[1] That these factors did not emerge in this synthesis may reflect different healthcare systems, funding, and the larger number of hospitals. Similarities emerged related to the challenges of recruitment within a narrow timeframe. Good communication between clinical and research teams was important for successful trial implementation.

Inclusion of data from less research-active organisations strengthens this study providing richer data, more transferable across the NHS and to healthcare systems in other jurisdictions. Our findings will resonate with other international settings where, despite variability in national infrastructure, similar challenges are faced by researchers. The tenet of normalising research transcends unit, institutional and country boundaries. Approaches to improve recruitment included simple incentive schemes to reward clinical staff, broadening the range of clinicians who could take consent. The latter is particularly pertinent to CTIMPs where time-limited recruitment was more relevant.[1,2] Previous work has suggested lack of equipoise as a barrier to enrolment[17,18]. An area for further exploration relates to consent waivers, already explored in some recent research [1,17,19, 20], albeit with less known of patient and family perspectives. 'Overburdening' has been described previously [21] as has concern regarding making initial approaches to families during particularly sensitive times [19-23] but again the patient/family voice in these studies is largely absent.[19-21] This would be an important area for future practice and research.

In keeping with existing literature, competition between trials requiring similar patient cohorts and the number of eligible patients were further barriers to trial recruitment [1,24].

Another factor related to lack of clear professional development opportunities and structured career paths. Recent strategy published by the NIHR offers novel career options for research staff [25-27] such as consultant research nurse models [25]. The emergence of medical trainee networks across the UK have also helped create a case for formalised processes.[28, 29] NIHR initiatives to engender a culture of research in healthcare, with every patient being offered the opportunity to participate in research aimed at improving care [30] are also reflected in these individual participants' motivations to improve care through research. Systematic review and large-scale survey evidence highlight key areas to improve trial recruitment as training site staff, communication with patients, and incentives, albeit some suggestions are not applicable to an ICU setting, such as telephone calls to non-respondents and opt-out procedures.[31,32] There have been significant advances over the past five years in critical care research recruitment.[33] In a current climate of significant fiscal pressures in the UK healthcare system with £22 billion of NHS efficiency savings to be achieved by 2020,[34] there was still a universal desire to undertake critical care research. This was driven by key motivated individuals who viewed research as integral to best practice and normal care provision, as well as deriving evidence to drive and support best use of resources.

This qualitative synthesis draws together two sets of original research findings. Whilst data were not collected simultaneously, both studies complemented each other. The second study built on the first by focusing specifically on a target participant cohort not initially represented in order to generate novel data to further understand the question at hand. Limitations include the timeframe between acquisition of each dataset, which although short (twelve months), might have resulted in practice changes occurring between the two data collection points. Potential sampling bias from recruiting primarily research-active units in the first dataset, was mitigated by employing purposive recruitment in the second dataset from less research-active units. Research-active and less research-active units were defined both on subjective reports from individuals, and standardised objective metrics, however this subjective/objective mix and lack of clarity could have introduced further sampling bias. We also only achieved interviews with 14 out of 16 CRNs, potentially missing important information from the other two CRNs. We also acknowledge the possible introduction of bias through refining the interview schedule as we proceeded through the interviews.

Qualitative research is often criticised for lack of generalisability, due to sample size limitations, but notions of transferability can be considered [8,11] and what Payne and Williams term 'moderatum generalisations'.[35] This is where core conceptual principles from the research, which would make sense across setting can be applied. Figure 1. outlines a summary of the main points and four key areas for learning. The core concept of Normalising Research can feasibly be applied beyond critical care trials recruitment, across the full spectrum of clinical specialties represented within the NIHR, as well as internationally.

Conclusion

This qualitative synthesis integrating two original datasets has yielded recommendations for improving trials recruitment in the unique clinical specialty of critical care. Several suggestions are made from the six themes that emerged: Organisational, Human, Study, Practical resources, Clinician, and Patient/family factors, under the overarching theme of Normalising Research, that relate to enhanced staffing, training, trial design and communication. Fostering a culture where research is considered part of routine patient care must be the ultimate goal for those working at all levels, from organisational to bedside.

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contributed to the design. SH and BC contributed to data collection, analysis and manuscript preparation. All authors have reviewed and contributed to the manuscript. NP is the custodian of the intellectual integrity and property arising from this project.

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Data access: All data pertaining to this project are reported here. Please contact the authors regarding accessing aggregated data analysis. Raw data is not available to be shared since this could lead to identification.

Figure 1. Normalising Research

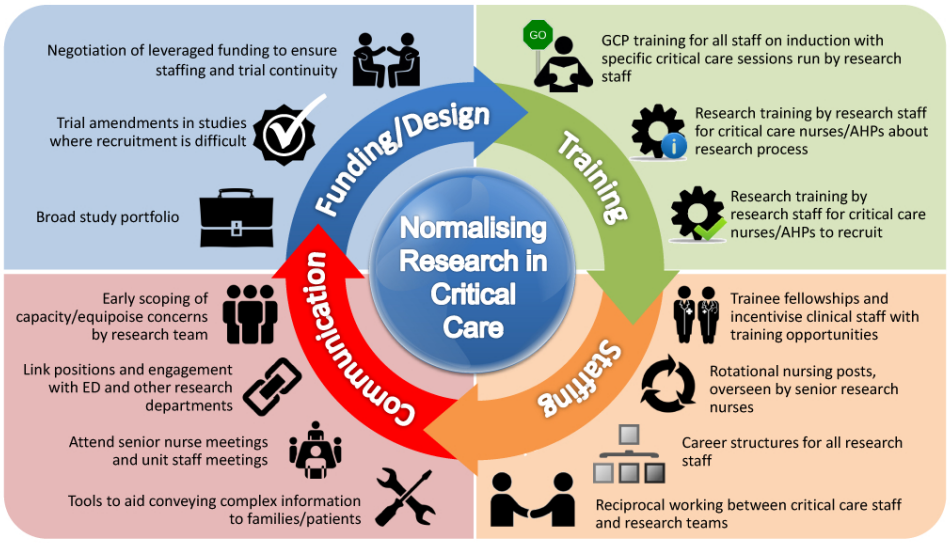

Figure 1. Normalising Research

Supplementary file 1. Interview Questions – exemplars/guide

(Questions drawn from across both studies - Dataset 1 and Dataset 2)

Opening questions

- How is research organised in your critical care unit?
- Tell me about the infrastructure in your critical care unit to support research.
- What can you tell me about your research infrastructure in your organisation?
- How is this supported at different levels (*prompts*: local (unit)/division/board levels)?
- Can you explain what you see as the barriers, or facilitators to recruitment in NIHR trials? (*prompts*: Are there specific examples* you can give me in your unit?)

Culture -

- How do you embed a new (NIHR) study in your unit?
- How is research prioritised in your unit?
- What can you tell me about how the unit decides whether to participate in a research project? (prompts: any specific authorisation needed? e.g. clinical unit head/equipoise issues)

Local/National -

- What do you see as barriers/facilitators at a network level? (*prompts:* Or outside of unit/organisational control?)
- What do you see as local recruitment barriers/facilitators (*prompts*: give examples - clinician buy-in/behaviour)?
- How do you embed research in your unit, and organisation?

Process/Studies/People factors –

- Can you describe where study recruitment has gone well/not so well*? (*prompts*: examples)
- What is your experience of how screening affects study recruitment? Tell me about how you screen patients for studies?
- Can you describe any patient/participant/family* factors that facilitate/inhibit recruitment? (*prompts*: explore burdens/scheduling/demands of study)
- Tell me about how you recruit patients for studies? (*prompts*: families/process/infrastructure)
- What kinds of concerns have patients/relatives raised to you regarding study participation (*prompts:* related to placebo/randomization/uncertainty)?

- Can you describe any study factors that facilitate/hinder recruitment? (*prompts:* examples)
- Tell me about your experience in conveying complex information and gaining consent (*prompts:* complexity of information/experience of team obtaining consent/language or cultural barrier)?
- For randomised trials, have you encountered patient/family preference for a particular therapy? If so, can you talk me through the issues encountered.

- Can you describe any clinician factors (nurse or doctor) that inhibit/facilitate trial recruitment in your experience?
- Tell me about the process for consent in patients without capacity? How does this affect recruitment to trials?
- What can you tell me about recruitment to studies out-of-hours? (*prompts:* who supports this?/Team working)
- What is your experience of recruiting to time-limited critical care trials?

- What is the research staff infrastructure? How does this align with the clinical teams?
- What is the experience of trainees in terms of research in the unit? (*prompts*: structures, training opportunities)?
- How are trainees and nurses/AHPs supported to engage with research (*prompts*: portfolio and non-portfolio; time/support to do 'own' research)?

Are there any barriers we have not yet discussed?

What suggestions do you have for enhancing study recruitment?

Is there anything else you'd like to talk about in terms of facilitating research in critical care?

How else can research be facilitated/supported in critical care?

Supplementary File 2. Table 1. Participants/units

Profession and Area	Level 3/2 beds†	Annual admissions	General /Specialist unit	Research staff numbers including whole time equivalent (WTE)	Research team working patterns	Consultant numbers and funded consultant time (Professional Activity session [PA]) †† for research	Number (total) of ongoing clinical trials (both NIHR and non-NIHR/in set-up)
Nurse/ CRN Eastern	14	1000	General	**1** (work with Emergency Department [ED]); (1 WTE)	5 days/week 8-4pm (flexible)	**7** 1 PA	**6**
Nurse/CRN Yorkshire and Humber	24	1600	General	**2**; (2 WTE)	5 days (flexible – 9 hour cover)	**13** 0.5 PA (shared)	**5**
Nurse/ CRN West Midlands	25	1600	General	**1** (was 4); (1 WTE)	5 days/week; 8-4pm	*Data not provided/ unknown* 1 PA	**6**
Consultant/ CRN Wessex	12	900	General	**2** (across all Division 6*, not just ICU); 1 WTE)	5 days/week; 8-4pm	*Data not provided/ unknown* 2 PAs	**6**
Trial co-ordinator/ CRN London South	63	3100	General/trauma	**6** across ED/ICU; *(Data not provided/ unknown)*	5 days/week (and on-call at weekends/nights as required)	**>50** (exact number unknown) 0 PA	**5**
Consultant/ CRN North West London	44	2600	General/ Trauma/ Neuro	**2** fellows + **5** nurses; (2 fellows at 2 WTE; 5 nurses at 4.5 WTE. 1 WTE research assistant)	7 days/week	**21** 1 PA	**4**
Nurse/ CRN Greater Manchester	40	2000	General	**4** (across ED); (4 WTE)	8-8pm 5 days/week (and on-call at weekends/nights as required)	**22** 1 PA	**8**/ 2 in set-up
Nurse/ CRN TV and South Midlands	9	500	General	**0.5**; (0.5 WTE)	part/time (early/late shift pattern; weekdays)	**10** 0.5 PA	**2**
Consultant/ CRN Wessex	11	750	General	**4 + 0.5** trainee; (2.5 WTE + 0.5 WTE trainee)	7 days/week (plus trainee shifts)	**6** 0 PA	**4**
Consultant/ CRN West Midlands	102	4000	General/ Cardiac/ Trauma/ Burns/ Neuro	**7** (across ED/Trauma and ICU); (6 WTE including Trial Coordinator and administrators)	7 days/week	**34** 1 PA	**7**/ 2 in set-up
Consultant/ CRN North West Coast	33	1550	General	**3 + 0.5** trainee; (2.5 WTE + 0.5 WTE trainee)	5 days/week (flexible)	**17** 1 PA	**3**/ 1 in set-up
Consultant/ CRN West of England	15	5-600	General	**0**	n/a	**18** 0.5 PA	**1**/ 2 in set-up

Consultant/ CRN West of England	15	5-600	General	**0****	n/a	**18** 0.5 PA	**1/** 2 in set-up
Nurse/ CRN South West Peninsula	28	1700	General/trauma/ Neuro/ Cardiac	**1** (across dermatology/ neuro); (1 WTE)	8-4pm; 5 days/week	**14** *Data not provided /unknown*	**0**/ 1 in set-up
Nurse/ CRN West of England	20	1300	General	**9**; 5 WTE + 4 rotational posts	7-7pm; 7 days a week	***Data not provided /unknown*** 2 PAs (shared)	**10**
Nurse/ CRN East Midlands	69	4000	General/trauma/ Neuro	**6** (covering ED) – split site; (4.2 WTE)	7-7pm; 7 days/week	***Data not provided /unknown*** 0 PA	**13**
Nurse/ CRN Norfolk	19	850	General	**2** *; (1.45 WTE)	8-4pm 5 days/week (and on-call at weekends/nights as required)	***Data not provided /unknown*** 0 PA	**4**/ 1 in set-up
Nurse/ Wales	33	1500	General/ Neuro	**5**; (4 WTE)	8-4pm 5 days/week	**14** 1 PA	**6**
Nurse/ CRN North West Coast	35	1880	General	**2**; (1 WTE nurse at band[+] 7 shared and 4 x nurse at band 6 at 0.8 WTE)	7.30-3.30pm 5 days/week	**13** 0 PA	**9**
Nurse/ CRN South West Peninsula	26	1580	General/ Neuro	**1**; (*Data not provided /unknown)*	8-4pm 5 days/week	**14** 0 PA	**7**
Nurse/ CRN North East North Cumbria	18	1000	General	**2**; (1 nurse at band 3 research assistant; 1 nurse at band 6 WTE)	9-5pm 5 days/week	**9** 0 PA	8
Nurse/ CRN East Midlands	19	1200	General	**3**; (2.8 WTE)	8-7pm	***Data not provided /unknown*** 2 PAs	**11**
Nurse/ CRN Eastern	20	1890	General	**4**; *(Data not provided/unknown)*	8-8pm	***Data not provided /unknown*** 1 PA	**7**
Nurse/ CRN Greater Manchester	19	1700	General	**0.8**; (0.8 WTE)	8-4pm	**12** 0 PA	**4**
Consultant/ CRN Wessex	24	1200	General	**3**; (1.6 WTE + 2 WTE for 3 month rotations)	8am-12pm 7 days a week	**14** 2 PAs	**5**
Consultant/ CRN London South	63	3500	General/ Neuro	**9**; (2 nurse at band 7; 7 nurse at band 6* WTE)	8-8pm	***Data not provided /unknown*** *1 PA*	**10**
Nurse/ CRN West of England	21	2000	General	**5**; (4 WTE (1 nurse at band 7; remainder nurse at band 6)	7-7pm	**12** *Data not provided /unknown*	**8**

[+] Level 2 beds are where patients require more detailed observation or intervention including support for a single failing organ system or post-operative care and those 'stepping down' from higher levels of care Level 3 beds only. Level 3 care is defined as patients needing advanced respiratory support alone or support of at least two organ systems. Note basic respiratory and basic cardiovascular support occurring on one day count as one organ. This level includes beds for all complex patients requiring support for multi-organ failure. Flexible critical care beds where there is a mix of level 2 and level 3 beds (NHS data dictionary: https://www.datadictionary.nhs.uk/data_dictionary/attributes/u/unit_bed_configuration_de.asp?shownav=1) ††PAs=Professional Activities Sessions are four hour weekly sessions for consultants only *Working across all Division 6 studies, not limited to critical care; Division 6 is one of six NIHR overarching divisions that encompasses critical care, anaesthesia/peri-operative/pain, emergency care/injuries, surgery, respiratory,

gastroenterology, infectious diseases/microbiology, hepatology, ophthalmology, ENT and **Able to access other Division 6 nurses when studies are active. + Band refers to the grade of nurse/research assistant as per Agenda for Change https://www.nhsemployers.org/pay-pensions-and-reward/agenda-for-change/pay-scales/annual. Band 7 is considered a senior nurse.

Supplementary File 3. Table 1. Summary and Recommendations

Recommendations for normalising research in critical care
Organisational factors:
○ Training: Offer Good Clinical Practice (GCP)/research training for all staff on induction; Research staff running GCP sessions for critical care staff ○ Offer research training by research staff for critical care nurses/AHPs to recruit/learn about research processes ○ Negotiation of leveraged funding to ensuring staffing and trial continuity; maintain a broad study portfolio ○ Work on engagement and links with ED and other research departments in the same NIHR divisions to support teams
Human and Unit resources
○ Offer trainee fellowships to support medical trainees wanting a career in research ○ Create rotational nursing posts in critical care, overseen by senior research nurses ○ Facilitate reciprocal working between ICU staff and research teams; research staff working in ICU to enhance links and recruitment opportunities ○ Create more career structures for doctors, AHPs and nurses working in critical care research (through each of the bands, so there is an identified progression ladder up to the most senior grade) ○ Incentivise clinical staff with training opportunities (e.g. create and offer free study opportunities in a clinical area associated with the relevant study)
Clinician factors
○ Communication and interdisciplinary working: Attend senior nurse/clinical meetings in critical care ○ Create link nurse positions (to be extended to link trainee positions) ○ Ensure early scoping of capacity/equipoise concerns by research team
Study/trial factors ○ Consider/request trial amendments in studies that are difficult to recruit to ○ Engage with and attend unit staff meetings early on in study planning to identify potential study barriers (such as out of hours pharmacy provision
Patient/family factors ○ Create tools/training/peer review to aid conveying complex information to families and patients
○ Have visible evidence of research activity in the unit (e.g posters) so it is apparent that research is part of routine care

Reporting checklist for qualitative study.

Based on the SRQR guidelines.

Instructions to authors

Complete this checklist by entering the page numbers from your manuscript where readers will find each of the items listed below.

Your article may not currently address all the items on the checklist. Please modify your text to include the missing information. If you are certain that an item does not apply, please write "n/a" and provide a short explanation.

Upload your completed checklist as an extra file when you submit to a journal.

In your methods section, say that you used the SRQR reporting guidelines, and cite them as:

O'Brien BC, Harris IB, Beckman TJ, Reed DA, Cook DA. Standards for reporting qualitative research: a synthesis of recommendations. Acad Med. 2014;89(9):1245-1251.

		Reporting Item	Page Number
	#1	Concise description of the nature and topic of the study identifying the study as qualitative or indicating the approach (e.g. ethnography, grounded theory) or data collection methods (e.g. interview, focus group) is recommended	1
	#2	Summary of the key elements of the study using the abstract format of the intended publication; typically includes background, purpose, methods, results and conclusions	1
Problem formulation	#3	Description and signifcance of the problem / phenomenon studied: review of relevant theory and empirical work; problem statement	3
Purpose or research question	#4	Purpose of the study and specific objectives or questions	3
Qualitative approach and research paradigm	#5	Qualitative approach (e.g. ethnography, grounded theory, case study, phenomenolgy, narrative research)	4

		and guiding theory if appropriate; identifying the research paradigm (e.g. postpositivist, constructivist / interpretivist) is also recommended; rationale. The rationale should briefly discuss the justification for choosing that theory, approach, method or technique rather than other options available; the assumptions and limitations implicit in those choices and how those choices influence study conclusions and transferability. As appropriate the rationale for several items might be discussed together.	
Researcher characteristics and reflexivity	#6	Researchers' characteristics that may influence the research, including personal attributes, qualifications / experience, relationship with participants, assumptions and / or presuppositions; potential or actual interaction between researchers' characteristics and the research questions, approach, methods, results and / or transferability	4
Context	#7	Setting / site and salient contextual factors; rationale	4
Sampling strategy	#8	How and why research participants, documents, or events were selected; criteria for deciding when no further sampling was necessary (e.g. sampling saturation); rationale	4
Ethical issues pertaining to human subjects	#9	Documentation of approval by an appropriate ethics review board and participant consent, or explanation for lack thereof; other confidentiality and data security issues	4
Data collection methods	#10	Types of data collected; details of data collection procedures including (as appropriate) start and stop dates of data collection and analysis, iterative process, triangulation of sources / methods, and modification of procedures in response to evolving study findings; rationale	4
Data collection instruments and technologies	#11	Description of instruments (e.g. interview guides, questionnaires) and devices (e.g. audio recorders) used for data collection; if / how the instruments(s) changed over the course of the study	4

Units of study	#12	Number and relevant characteristics of participants, documents, or events included in the study; level of participation (could be reported in results)	5
Data processing	#13	Methods for processing data prior to and during analysis, including transcription, data entry, data management and security, verification of data integrity, data coding, and anonymisation / deidentification of excerpts	4
Data analysis	#14	Process by which inferences, themes, etc. were identified and developed, including the researchers involved in data analysis; usually references a specific paradigm or approach; rationale	4
Techniques to enhance trustworthiness	#15	Techniques to enhance trustworthiness and credibility of data analysis (e.g. member checking, audit trail, triangulation); rationale	4
Syntheses and interpretation	#16	Main findings (e.g. interpretations, inferences, and themes); might include development of a theory or model, or integration with prior research or theory	5
Links to empirical data	#17	Evidence (e.g. quotes, field notes, text excerpts, photographs) to substantiate analytic findings	6
Intergration with prior work, implications, transferability and contribution(s) to the field	#18	Short summary of main findings; explanation of how findings and conclusions connect to, support, elaborate on, or challenge conclusions of earlier scholarship; discussion of scope of application / generalizability; identification of unique contributions(s) to scholarship in a discipline or field	10
Limitations	#19	Trustworthiness and limitations of findings	11
Conflicts of interest	#20	Potential sources of influence of perceived influence on study conduct and conclusions; how these were managed	2
Funding	#21	Sources of funding and other support; role of funders in data collection, interpretation and reporting	2

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