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Implementing early rehabilitation and mobilisation for children in UK paediatric intensive care units: the PERMIT feasibility study

Barnaby R Scholefield[1,2*] Julie C Menzies[2] Jennifer McAnuff[3,4] Jacqueline Y Thompson[1] Joseph C Manning[5,6] Richard G Feltbower[7] Michelle Geary[8] Sophie Lockley,[9] Kevin P Morris[2] David Moore[10] Nazima Pathan[11] Fenella Kirkham[8] Robert Forsyth[12] and Tim Rapley[4]

[1]Birmingham Acute Care Research Group, Institute of Inflammation and Ageing, University of Birmingham, Birmingham, UK
[2]Paediatric Intensive Care, Birmingham Women's and Children's NHS Foundation Trust, Birmingham, UK
[3]Population Health Sciences Institute, Newcastle University, Newcastle, UK
[4]Department of Social Work, Education and Community Wellbeing, Northumbria University, Newcastle, UK
[5]Nottingham Children's Hospital, Nottingham University Hospitals NHS Trust, Nottingham, UK
[6]Children and Young People Health Research, School of Health Sciences, The University of Nottingham, Nottingham, UK
[7]Leeds Institute for Data Analytics, School of Medicine, University of Leeds, Leeds, UK
[8]Child Health, University Hospital Southampton NHS Foundation Trust, Southampton, UK
[9]PPIE Representative, Birmingham Women's and Children's NHS Foundation Trust, Birmingham, UK
[10]Institute of Applied Health, University of Birmingham, Birmingham, UK
[11]Department of Paediatrics, University of Cambridge, Cambridge, UK
[12]Translational and Clinical Research Institute, Newcastle University, Newcastle, UK

[*]Corresponding author

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This report

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Abstract

Implementing early rehabilitation and mobilisation for children in UK paediatric intensive care units: the PERMIT feasibility study

Barnaby R Scholefield,[1,2*] Julie C Menzies,[2] Jennifer McAnuff,[3,4] Jacqueline Y Thompson,[1] Joseph C Manning,[5,6] Richard G Feltbower,[7] Michelle Geary,[8] Sophie Lockley,[9] Kevin P Morris,[2] David Moore,[10] Nazima Pathan,[11] Fenella Kirkham,[8] Robert Forsyth[12] and Tim Rapley[4]

[1]Birmingham Acute Care Research Group, Institute of Inflammation and Ageing, University of Birmingham, Birmingham, UK
[2]Paediatric Intensive Care, Birmingham Women's and Children's NHS Foundation Trust, Birmingham, UK
[3]Population Health Sciences Institute, Newcastle University, Newcastle, UK
[4]Department of Social Work, Education and Community Wellbeing, Northumbria University, Newcastle, UK
[5]Nottingham Children's Hospital, Nottingham University Hospitals NHS Trust, Nottingham, UK
[6]Children and Young People Health Research, School of Health Sciences, The University of Nottingham, Nottingham, UK
[7]Leeds Institute for Data Analytics, School of Medicine, University of Leeds, Leeds, UK
[8]Child Health, University Hospital Southampton NHS Foundation Trust, Southampton, UK
[9]PPIE Representative, Birmingham Women's and Children's NHS Foundation Trust, Birmingham, UK
[10]Institute of Applied Health, University of Birmingham, Birmingham, UK
[11]Department of Paediatrics, University of Cambridge, Cambridge, UK
[12]Translational and Clinical Research Institute, Newcastle University, Newcastle, UK

[*]Corresponding author Barney.scholefield@sickkids.ca

Background: Early rehabilitation and mobilisation encompass patient-tailored interventions, delivered within intensive care, but there are few studies in children and young people within paediatric intensive care units.

Objectives: To explore how healthcare professionals currently practise early rehabilitation and mobilisation using qualitative and quantitative approaches; co-design the Paediatric Early Rehabilitation and Mobilisation during InTensive care manual of early rehabilitation and mobilisation interventions, with primary and secondary patient-centred outcomes; explore feasibility and acceptability of implementing the Paediatric Early Rehabilitation and Mobilisation during InTensive care manual within three paediatric intensive care units.

Design: Mixed-methods feasibility with five interlinked studies (scoping review, survey, observational study, codesign workshops, feasibility study) in three phases.

Setting: United Kingdom paediatric intensive care units.

Participants: Children and young people aged 0–16 years remaining within paediatric intensive care on day 3, their parents/guardians and healthcare professionals.

Interventions: In Phase 3, unit-wide implementation of manualised early rehabilitation and mobilisation.

Main outcome measures: Phase 1 observational study: prevalence of any early rehabilitation and mobilisation on day 3. Phase 3 feasibility study: acceptability of early rehabilitation and mobilisation intervention; adverse events; acceptability of study design; acceptability of outcome measures.

Data sources: Searched Excerpta Medica Database, Cumulative Index to Nursing and Allied Health Literature, MEDLINE, PEDro, Open grey and Cochrane CENTRAL databases.

Review methods: Narrative synthesis.

Results: In the scoping review we identified 36 full-text reports evaluating rehabilitation initiated within 7 days of paediatric intensive care unit admission, outlining non-mobility and mobility early rehabilitation and mobilisation interventions from 24 to 72 hours and delivered twice daily. With the survey, 124/191 (65%) responded from 26/29 (90%) United Kingdom paediatric intensive care units; the majority considered early rehabilitation and mobilisation a priority. The observational study followed 169 patients from 15 units; prevalence of any early rehabilitation and mobilisation on day 3 was 95.3%. We then developed a manualised early rehabilitation and mobilisation intervention informed by current evidence, experience and theory. All three sites implemented the Paediatric Early Rehabilitation and Mobilisation during InTensive care manual successfully, recruited to target (30 patients recruited) and followed up the patients until day 30 or discharge; 21/30 parents consented to complete additional outcome measures.

Limitations: The findings represent the views of National Health Service staff but may not be generalisable. We were unable to conduct workshops and interviews with children, young people and parents to support the Paediatric Early Rehabilitation and Mobilisation during InTensive care manual development due to pandemic restrictions.

Conclusions: A randomised controlled trial is recommended to assess the effectiveness of the manualised early rehabilitation and mobilisation intervention.

Future work: A definitive cluster randomised trial of early rehabilitation and mobilisation in paediatric intensive care requires selection of outcome measure and health economic evaluation.

Study registration: The study is registered as PROSPERO CRD42019151050. The Phase 1 observational study is registered Clinicaltrials.gov NCT04110938 (Phase 1) (registered 1 October 2019) and the Phase 3 feasibility study is registered NCT04909762 (Phase 3) (registered 2 June 2021).

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Contents

List of tables

List of figures

List of abbreviations

AE	adverse event
aOR	adjusted odds ratio
BCH	Birmingham Children's Hospital
BIPAP	bilevel positive airway pressure
CAC	cluster autocorrelation
CAPD	Cornell assessment of paediatric delirium
CERT	consensus on exercise reporting template
CI	confidence interval
CINAHL	cumulative index to nursing and allied health literature
COVID	coronavirus disease
CPAP	continuous positive airway pressure
CRF	case report form
CRN	clinical research networks
CVC	central venous line
CYP	children and young people
ECMO	extracorporeal membrane oxygenation
EMPATHIC	empowerment of parents in the intensive care
ERIC	expert recommendations for implementing change
ERM	early rehabilitation and mobilisation
ETT	endotracheal tube
EU-PACK	European Prevalence of Acute Rehabilitation for Kids in the PICU
HCP	healthcare practitioners
HRA	Health Research Association
ICC	intracluster correlations
ICU	intensive care unit
IQR	interquartile range
LOS	length of stay
LOV	length of ventilation
MRC	Medical Research Council
MDT	multidisciplinary team
MED	median
MV	mechanical ventilation
NIHR	National Institute for Health and Care Research
NoMAD	normalisation measure development
NPT	normalisation process theory
OR	odds ratio
OT	occupational therapist
PBA	person-based approach
PCPC	paediatric cerebral performance category
PedsQL	Pediatric Quality of Life Inventory
PEDI-CAT	paediatric evaluation of disability inventory-computer adaptive test
PELOD	pediatric logistic organ dysfunction
PERMIT	paediatric early rehabilitation and mobilisation during intensive care
PHQ-4	Patient Health Questionnaire-4
PCCS-SG	paediatric critical care society – study group
PICU-AW	paediatric intensive care acquired weakness
PIS	patient information sheet
POPC	paediatric overall performance category
PPIE	patient and public involvement and engagement

PRISM	paediatric risk of mortality	ROM	range of movement
PT	physiotherapy	SANDWICH	sedation and weaning in children trial
QoL	quality of life	SIV	site initiation visit
REC	Regional Ethics Committee	SLT	speech and language therapist
REDCAP	research electronic data capture	TFA	theoretical framework of acceptability
ROBINS-I	risk of bias in non-randomised studies – of interventions		

Plain language summary

Why study early rehabilitation and mobilisation?

Early rehabilitation and mobilisation, within the first week of intensive care admission, can improve the speed of recovery from illness or injury in adults. However, there is a lack of evidence about whether critically unwell children benefit from early rehabilitation and mobilisation.

What did we want to find out?

We aimed to identify which patients may benefit from early rehabilitation and mobilisation. Also, to develop and test a manual of early rehabilitation and mobilisation using the best evidence and expertise – called the Paediatric Early Rehabilitation and Mobilisation during InTensive care manual. Then evaluate whether the manual could be implemented safely in paediatric intensive care units and was acceptable to staff and families.

What did we do?

We undertook in respect of early rehabilitation and mobilisation:

- review of existing research;
- national survey of practice (124 staff);
- gathered information about current conduct (15 paediatric intensive care units, 169 patients);
- spoke to experts (18 people);
- developed the Paediatric Early Rehabilitation and Mobilisation during InTensive care manual to guide paediatric intensive care unit staff;
- Tested the Paediatric Early Rehabilitation and Mobilisation during InTensive care manual in three paediatric intensive care units with 30 patients;
- gathered feedback from healthcare professionals via weekly 'debriefs' (47), interviews (13) and surveys (118), and from parents via parent-completed questionnaires (21) and interviews (14).

What did we find?

Despite being regarded as important, currently early rehabilitation and mobilisation practice is inconsistent, not considered 'early' enough and often focuses on low-risk activities conducted on the bed. Introducing the Paediatric Early Rehabilitation and Mobilisation during InTensive care manual as part of a trial was acceptable and feasible and helps standardise delivery to unwell children. Measuring child and parent reported outcomes was acceptable but follow-up at 30 days was incomplete.

What does this mean?

A larger trial of early rehabilitation and mobilisation, involving more paediatric intensive care units, is feasible and required to demonstrate benefit to children.

Scientific summary

Background

Annually in the UK, 20,000 children (0–<18 years) require life-sustaining treatment for critical illness and injury in paediatric intensive care units (PICU). As more than 96% of admissions to PICU survive, morbidity in survivors is now a major concern. The impact of being critically ill can manifest itself in weakness, cognitive impairment, organ dysfunction and psychological problems. Unfortunately, many children and young people (CYP) experience significant and residual physical, cognitive and psychosocial morbidities following PICU that impact on their quality of life (QoL). Our focus is to minimise iatrogenic harm of critical care and maximise patient outcomes through the development, testing and implementation of novel interventions.

Early rehabilitation and mobilisation (ERM) can include individual patient-tailored interventions, or packages of care, provided by health professionals from multiple disciplines and caregivers within intensive care settings. ERM aims to promote physical (e.g. movement, functional activities, ambulation) and non-physical (e.g. speech, play, psychological, cognitive) recovery. Benefits have been demonstrated in the use of ERM in adult intensive care unit (ICU) populations in relation to patient outcomes as well as healthcare utilisation. The use of ERM in the paediatric ICU population offers significant potential to prevent morbidities associated with being critically ill, facilitate recovery and improve patient outcomes. With practical interventions appropriate to the CYP condition, age and severity of illness (referred to as 'acuity' throughout this report), there is potential to positively impact the emotional, behavioural, cognitive and functional outcomes of CYP and to benefit their caregivers' QoL across the NHS. Challenges to ERM in critically ill children include the wide age range, heterogeneous disease processes and a high proportion of children with chronic comorbidities.

While there is good evidence to support the safe and effective use of ERM in adult ICU populations, there is insufficient evidence of such an effect in children. Several international studies have demonstrated feasibility, acceptability and safety of ERM in this population using physiotherapy (PT), occupational therapy, video games and exercise equipment (e.g. in bed cycling). However, the evidence base for ERM in the paediatric ICU population in a UK context is scant. Some NHS PICUs are reported to have implemented ERM into their clinical practice, albeit that this does not always appear to have been undertaken systematically, nor has the impact on patient outcomes, service utilisation or resources been evaluated. Existing uncertainties around ERM are its current use in the UK, how best to operationalise and implement it, and its potential effectiveness. In this study, we explored current paediatric ERM practice, developed a manualised ERM intervention, then assessed feasibility of proposed ERM intervention and outcome measures in order to prepare for a definitive PICU ERM trial.

Aims

To prepare for a definitive paediatric ERM trial, we will: (1) identify current ERM practice, (2) specify the content of an ERM intervention, (3) establish the patient population for whom ERM may be appropriate, (4) determine patient-centred outcomes of ERM, and appropriate measures and (5) explore the feasibility and acceptability of an ERM future trial.

Study objectives

Understand current practice:

- to review the literature supporting current paediatric ERM practice;
- to define, identify and describe current ERM practice in UK PICs and assess capability of UK PICs to deliver ERM;
- to establish and model how many/which CYP would be appropriate for ERM in the PIC population.

Develop an ERM intervention and select patient-centred outcomes:

- to co-design manual of ERM interventions;
- to identify relevant primary and secondary patient-centred outcomes and assessment tools.

Assessment of feasibility of proposed ERM intervention and outcome measures:

- to explore feasibility and acceptability of manualised ERM intervention in a three-centre, non-randomised feasibility study.

Synthesise data and report findings:

- to combine population, intervention and standard care and outcome definitions for future trial evaluation proposal;
- to build consensus on intervention for feasible/acceptable ERM trial and explore methodological approaches and future trial design.

Methods

A mixed-methods study with three phases and five interlinked studies.

Phase 1a: scoping review of literature

Studies [randomised controlled trials (RCTs) and observational studies] of CYP (≤18 years), admitted to PICU, receiving early (within 7 days) rehabilitation and mobilisation and measuring an outcome (participants' health and well-being, health service utilisation, feasibility, acceptability or intervention implementation) were identified in electronic bibliographic databases from inception to November 2021. Study selection, data extraction and risk of bias assessment [using the Cochrane RoB tool; Risk of Bias in Non-randomised Studies – of Interventions (ROBINS-I)] were undertaken by reviewers independently. Findings were narratively synthesised.

Phase 1b: survey of current practice

An electronic web-based survey administered to healthcare professionals selected from UK PICUs to describe components of ERM, establish current ERM practice and understand barriers and facilitators to implementing ERM.

Phase 1c: observation study of current practice

All paediatric patients admitted to 14 UK PICUs and who remained in PICU at 9 a.m. on the third day were observed for up to 7 days or until PICU discharge or death (if sooner) over a 2-week observation period. Prevalence of early (day 3–day 10 post PICU admission) ERM delivery, adverse events (AEs) related to ERM delivery, clinical acuity and patient level outcomes were recorded.

Phase 2: manual development

Workshops with NHS healthcare professionals and international experts. Reviewed existing literature to identify available concepts, tools and resources and discussed ideas with healthcare professionals to develop and shape the form and specify the content of a prototype ERM intervention [the Paediatric Early Rehabilitation and Mobilisation during InTensive care (PERMIT) manual].

Phase 3: feasibility study with embedded process evaluation

This was an implementation study of a PICU-wide ERM programme, described in the PERMIT manual. The study was conducted in three PICUs. The manual describes the six steps of implementing the programme with qualitative (via debriefing weekly meetings, and HCP interviews) and quantitative (via normalisation measure development e-survey, study set-up observation) evaluation of these implementation steps and observation of feasibility and acceptability of consent model, ERM delivery and AE reporting of ERM usage in eligible PICU patients.

Phase 4: consensus study and trial design meetings

Virtual meeting with parents/family members from Phase 3 feasibility study was convened. Meeting was recorded and, with a summary leaflet of key findings, distributed to all members with accompanying questionnaire on future study design including consent model. Study management group and clinical trials methodologists developed a proposal for a future trial.

Results

Phase 1a: scoping review

We identified 36 articles that met the study eligibility criteria; 18 were full-text studies, mostly conducted in North America. There were only two RCTs; both were pilot studies confirming trial feasibility. Multicomponent 'non-mobility' and 'mobility' ERM interventions were feasible and safe. Most interventions involved physical therapy, occupational therapy and speech and language therapy.

Children under 3 years old were more likely to receive ERM interventions such as cuddles or in-bed mobilisation, whereas non-ventilated children or those aged 3 years and older were more likely to receive mobility interventions involving physical or occupational therapy. Family involvement appeared crucial when considering non-mobility ERM for children under 3 years old.

In 15/18 studies, judged to be of poor methodological quality, there was no benefit with regard to mechanical ventilation, hospital length of stay (LOS) and functional outcomes. Twelve of 18 studies provided some detail to aid replication and used qualified providers for supervision and tailored interventions. Although training and organisational strategies were sometimes applied, reporting was poor and complex intervention theories were rarely incorporated.

Phase 1b: survey of current practice

A strong multidisciplinary involvement in initiating ERM was reported. ERM was defined by participants as consisting of tailored, multidisciplinary rehabilitation packages, focused on promoting recovery. All age groups were considered for ERM. Over half of respondents favoured delivering ERM after physiological stability had been achieved (n = 69, 56%) with ERM more likely to be delivered to patients when PICU length of stay exceeded 28 days, among patients with acquired brain injury or severe developmental delay. The most commonly identified barriers were: insufficient resources and equipment (69%), limited staffing (79%), lack of recognition of patient readiness (67%), patient suitability (63%), physiological instability (81%) and sedation requirement (73%). Respondents ranked 'reduction in PICU length of stay' (74%) and 'improvement in psychological outcomes' (73%) as the most important benefits of ERM.

Phase 1c: observational study of ERM practice

We observed ERM practice in 169 patients across 15 PICUs who reached 9 a.m. on day 3 after PICU admission in our 14-day observation period. Ninety per cent of eligible patients were enrolled using an opt-out consent model. On the first study day (day 3 after PICU admission) 162/169 (96%) of patients received an ERM activity; 87% involved a mobility and 38% an out-of-bed mobility activity. The rate of ERM activities for patients remained constant across the subsequent 7 days of their PICU admission (or until PICU discharge).

Over the observation period, 3696 ERM episodes delivered 4978 ERM activities across all PICUs. Most were delivered by registered nurse or parent/family member. Positioning with and without mobility elements accounted for nearly half of all ERM activities. A wide range of ERM activities were reported but were more likely to be passive or enrichment activities rather than active ERM. 'Cuddles' by a family member/nursing staff were most frequent out-of-bed activity. We identified that family presence significantly increased out-of-bed ERM. Presence of an ERM protocol did not impact chance of out-of-bed mobility. However, some ERM was delivered to nearly all patients, including those of all ages, admission diagnoses and with the full range of organ dysfunction or organ support, including the highest level. ERM was delivered safely with a low (<3%) reported rate of AEs per ERM activity. Most AEs did not require any corrective intervention.

Phase 2: manual development

The synthesis of Phase 1 results showed that ERM is currently defined and enacted in multiple ways and that people see the potential value for the diverse patient populations within PICU and are willing to support the safe delivery of ERM but are uncertain how best to deliver it. The workshops with NHS healthcare professionals (n = 18) and with international experts (n = 3) helped generate some core guiding principles around the potential shape and content of the intervention. For example, everyone in PICU, doctors, nurses, physiotherapists and parents, are all essential for ERM delivery – everyone should take ownership. Also, ERM needs to be as inclusive as possible, with a focus on promoting movement and mobility as early as possible and with progressive increases over time. The review of existing ERM protocols and discussions with healthcare professionals enabled us to develop the prototype PERMIT manual that is focused both on the safe delivery of ERM for each patient, as well as the introduction and embedding of an ERM approach within a PICU. The PERMIT manual is informed by current evidence, experience and theory. It offers a flexible, progressive approach to the delivery of ERM, with resources including essential clinical materials – the 'bedside bundle' – that consist of an ERM daily flowchart, patient acuity levels, ERM activity levels, and pause and re-assess criteria. It also includes a step-by-step guide to putting ERM into practice – the 'implementation toolkit' – that focuses on building ERM leadership, generating staff buy-in, making ERM workable, and keeping it going over time.

Phase 3: feasibility study with embedded process evaluation

All sites implemented the PERMIT programme following the guidance in the manual. The families were positive about the study recruitment process. All sites successfully recruited the 10-patient target. All patients had an acuity level scored and these were repeated on 84% of ward rounds. The acuity level was correctly linked to ERM activity prescription and then subsequently to ERM activity delivered. The level of activity was broadly representative of the acuity level. A large number of potentially clinically relevant patient outcomes were measured through validated tools. All patients received ERM activities safely using the pause and assess criteria with only two trial reported AEs and no severe AEs. ERM was important for the physical and psychological recovery of the CYP, as well as the psychological well-being of parents/carers supporting their involvement in their child's care. Having access to research delivery support was central to support recruitment, data collection and data entry. PERMIT was seen by health professionals and parents as worthwhile, feasible and acceptable. Measuring child- and parent-reported outcomes was acceptable but follow-up at 30 days was incomplete.

Phase 4: consensus study and trial design

With input from members of the Patient and Public Involvement and Engagement (PPIE) group, parent/family members participating in PERMIT and multidisciplinary members of the study management group reviewed the findings from Phases 1, 2 and 3. We confirmed that a future PERMIT ERM clinical trial was necessary, acceptable and feasible. The most suitable trial design is a clustered stepped-wedge randomised control trial within PICUs across the NHS. The primary outcome of length of ventilation is a pragmatic compromise on measurable PICU outcome and probably accurate measure of improvement in critical illness recovery. However, further consensus work in developing the primary outcome will be required with the UK Paediatric critical care society study group and trialists prior to a definitive study proposal.

Conclusion and recommendations for future research

A definitive trial of ERM in PICU appears feasible. ERM is a complex intervention requiring institutional, departmental and multidisciplinary involvement. We have demonstrated that implementation of the PERMIT manual is acceptable, feasible and can deliver ERM safely to critically unwell and injured infants and CYP within the PICU. Further research in a definitive trial with economic assessment and demonstration of improvement in patient-related outcomes is required.

Ethics approval

- Phase 1b survey: University of Birmingham, 5 February 2019: Ref: BMS_1819_03.
- Phase 1c observational study: Regional Ethics Committee (REC) approval: 2 September 2019. East of Scotland Research Ethics Service. Health Research Association (HRA) ref: 19/ES/0102.
- Phase 2 manual development workshop: healthcare professionals: Newcastle University, 1 September 2019: Ref 14224/2018. Parents, CYP: REC approval: 28 February 2020 19/LO/1987 (substudy stopped because of coronavirus disease pandemic).
- Phase 3 feasibility study: REC approval: 26 April 2021. Berkshire Research Ethics Service. HRA ref: 21/SC/0127.

Trial oversight committee

A study oversight committee and data-monitoring ethics committee were recruited to oversee the study processes and results (see *Appendix 1*).

Study registration

The study is registered as PROSPERO CRD42019151050. The Phase 1 observational study is registered NCT04110938 (Phase 1) (registered 1 October 2019) and the Phase 3 feasibility study is registered NCT04909762 (Phase 3) (registered 2 June 2021).

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Chapter 1 Phase 1a: scoping review of literature

Introduction

This review aimed to evaluate early mobilisation and rehabilitation (ERM) within paediatric intensive care as reported within the published literature. We characterised the evidence base using a narrative synthesis approach to understand features of ERM associated with effectiveness and successful implementation within paediatric intensive care units (PICU).

Study management

The work package was led by BRS. The study management group was responsible for defining and reviewing scope of search. JYT performed searches, data extraction, risk of bias assessment, evidence synthesis and first draft of chapter. Second screening of articles, data extraction and risk of bias performed by Dr Olivia Craw, JMc and JMen. Methodological expertise provided by DM and BRS.

Objectives

Our primary objective was to summarise the types and effectiveness of ERM interventions and outcome measures delivered to children admitted to PICUs.

Our secondary objective was to thematically identify subpopulations (if any) that benefit most from ERM or experience associated adverse or clinical events, and any patterns or gaps during implementation.

Methods

Search strategy

Searches were conducted in the bibliographic databases [Excerpta Medica Database (Embase) (via OVID), Cumulative Index to Nursing and Allied Health Literature (CINAHL) (via EBSCO), MEDLINE (via OVID), PEDro, Open grey or Cochrane CENTRAL)]. Original search was from inception to 12 October 2019 and an updated search was performed 1 November 2021, using strategies that combined, where relevant, free text and index terms for:

(1) children and young people (CYP);
(2) admitted to paediatric critical care settings;
(3) receiving early (within 7 days) rehabilitation and mobilisation.

The search strategy was developed in MEDLINE (via OVID) (see *Appendix 2*) and adapted for other databases.

Database of Abstracts of Reviews of Effects, National Health Service (NHS) Economic Evaluation Database and Health Technology Assessment database (all via Centre for Reviews and Dissemination) were searched for relevant systematic reviews to identify primary studies for the review. These were supplemented by relevant websites using hand-searching for mobilization-network.org and search terms for clinicaltrials.gov or Chinese clinical trial registry, checking reference lists of relevant studies, and forward citation-checking of included studies in Web of Science. We screened reference lists to identify relevant primary studies and contacted primary authors to find full texts of incomplete records.

Eligibility criteria

We included all completed studies published in English that met the following criteria:

1. Study participants: critically ill infants, children or young people aged ≤18 years, admitted to PICUs, who received an intervention described as rehabilitation or mobilisation delivered by any health professional within ≤7 days after admission. Rehabilitation or mobilisation interventions could include but were not limited to physiotherapy (PT), occupational therapy, speech and language therapy (SLT) and bundled interventions; these included ABCDEFH bundles (spontaneous awakening and breathing trials; choice of sedation and analgesia, delirium prevention, surveillance and management; early mobilisation and exercise programmes with or without adjuncts; family engagement and empowerment; proper nutrition and humanism) so long as their application was considered within the first 7 days of admission; AND
2. Outcome: at least one outcome was related to participants' health and well-being, health service utilisation, feasibility, acceptability or intervention implementation.
3. Study design: primary research studies of any designs, with >10 participants to synthesise evidence on intervention effectiveness. Case reports, case series with ≤10 patients, qualitative studies and systematic reviews were excluded if relevant primary studies were not identified in the references. Abstracts or ongoing studies identified from clinical trial registries were used to highlight the presence of future emerging research.

Screening and selection

Records identified were imported into a bibliographic referencing software programme (EndNote X9, Thomson Reuters, San Francisco, CA, USA), and duplicates were removed. One PT researcher (JT) and one clinical academic (BS or JMen) independently screened titles and abstracts for relevance against the eligibility criteria within Rayyan systematic review software.[1] The full texts of relevant articles were obtained and assessed against the selection criteria by two reviewers independently (JT, Dr Olivia Craw). A wider range of publication types (abstracts and full texts) were selected to identify all possible lists of ERM interventions but were not analysed to summarise types of ERM. Reasons for exclusion were noted. Discrepancies were discussed via consensus meeting with a third author (JMc).

Data extraction

Data were extracted using a standardised, piloted data-extraction form in Excel. Information within the following domains was extracted:

- *Study* – author, year of publication, country, study design using an algorithm for classifying studies.[2]
- *Patient demographics* – age, sex, admission diagnosis, the severity of illness and, comorbidity using established criteria[3] or paediatric scoring tools such as Pediatric risk of mortality (PRISM III), the Pediatric logistic organ dysfunction (PELOD), the Pediatric Cerebral Performance Category (PCPC) and the Pediatric Overall Performance Category (POPC). We also considered the following prognostic factors when assessing non-randomised studies: age, sex, weight or body mass index (BMI) in percentile, baseline severity, comorbidities and admission diagnosis on the intervention.
- *Intervention details* – definition of ERM, type of interventions, the volume of ERM (time-to-initiation, duration, number of sessions), implementation strategies such as safety and progression criteria, involvement of health professionals or availability of organisational support.
- *Study comparators and outcome* – components of usual care, primary and secondary outcomes (where specified) and assessment time points. When outcome measures were not specified or reported, the outcomes most proximal to the health domain were considered the primary outcome.

Data were extracted (JT) and independently verified by co-authors (Dr Olivia Craw, JMc and JMen). We used all eligible studies, abstracts or full texts that reported any intervention to summarise types of interventions. We only included full-text reports where ERM was initiated within the first 7 days of admission to PICU to synthesise ERM outcomes.

Quality assessment of individual studies

Risk of bias was assessed in randomised controlled trials (RCTs) the using Cochrane Risk of Bias tool version 2[4] and in non-randomised studies using the Risk Of Bias In Non-randomised Studies – of Interventions (ROBINS-I) tool.[5] One reviewer (JT) assessed the methodological quality of studies and this was independently verified by a second (Dr Olivia Craw, JMc).

We evaluated the reporting quality of studies using the Consensus on Exercise Reporting Template (CERT).[6] Due to the nature of the study interventions included in this review, participants, providers and assessors were aware of the intervention, which can affect compliance, outcome assessment or intervention fidelity. To understand implementation, we grouped studies that provided information on different aspects of delivering ERM, such as core content of ERM, who commonly delivers it, mode, timing, frequency of delivery, and the adaptation process for tailoring ERM.

Data synthesis

A narrative synthesis of all included studies was undertaken. Due to the heterogeneous nature of paediatric populations and interventions, meta-analysis was not appropriate. All outcomes were grouped as short-term (≤6 months post-discharge) or intermediate-term (≥6 months post-discharge) outcomes.

Results

Characteristics of included studies

As shown in *Figure 1*, 2580 unique records were screened for relevance, and 62 relevant full-text articles were assessed for inclusion. Twenty-six of these were excluded, mainly due to the ineligibility of the study design or outcomes. Eighteen of the 36 studies that met the eligibility criteria were abstracts, and 18 had full-text reports. Most were conducted in North America,[7–25] Australia,[26] Belgium,[27,28] Brazil,[29,30]

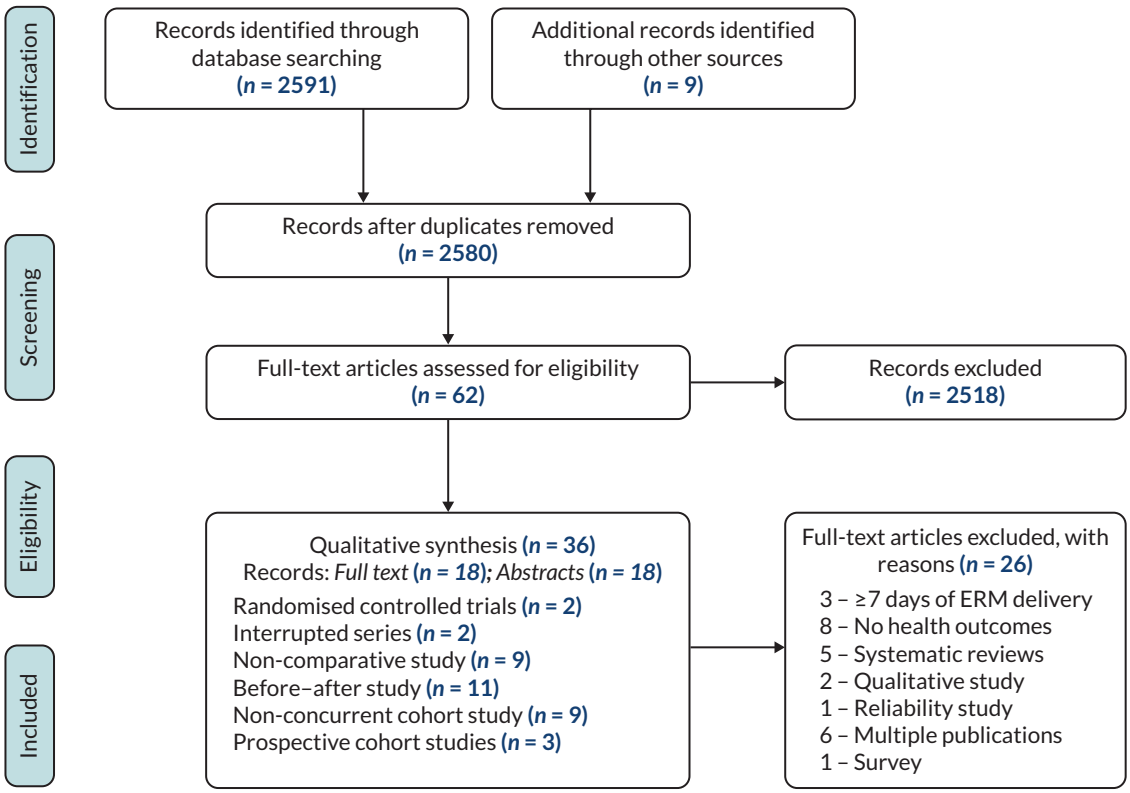

FIGURE 1 PRISMA diagram.

Italy,[31] Japan,[32–34] the Netherlands,[35] Turkey[36,37] and the UK.[38–41] One study was conducted across 15 countries in Europe[42] (see *Appendix 2*, *Table 32*).

Five studies[15,18,21,22,24] were conducted across multiple PICUs, and two studies[15,43] used controlled designs. Three studies were prospective cohorts,[24,41,42] 2 were interrupted-time series,[7,27] 9 non-comparative studies,[8,10,13,22,30,31,34,36,40] 11 before–after studies[9,11,12,17,23,25,32,33,35,38,44] and 9 non-concurrent cohort studies.[14,16,18,19,21,26,28,37,45]

Types of interventions identified

Of the 36 studies that evaluated PICU rehabilitation, we identified two broad categories of early rehabilitation or mobilisation (ERM): non-mobility and mobility interventions. Non-mobility interventions mentioned in included studies were pain and agitation assessment,[23] sleep hygiene/delirium screening,[17,22,23,35] ERM screening checklist,[26] cuddles,[18,40] SLT[8,12,15,21] and chest PT.[21] The majority were mobility interventions and included mobility goals/orders,[22,23,35,40,41] out-of-bed exercises,[15,17] in-bed cycling,[11,19,20,46] edge-of-bed mobility,[40] bed-mobility exercises,[15,17,21,32] interactive boxing,[7] physical therapy[8,10,12–16,18,21,30,32] and OT.[8,10,12–16,18,21,30] When usual care[15,20,24] was used as a comparison, it consisted of positioning,

Interventions were commonly administered from 24 to 72 hours after PICU admission. The volume of sessions varied widely, but most sessions were delivered twice daily. In some situations,[32] information on initiating ERM delivery was unavailable. Five studies[7,11,19,26,43] used single-component interventions. One study[13] reported the number of encounters or admissions but provided no information about patient characteristics. Multicomponent interventions (12/16 studies) consisting of PT, OT and SLT were more commonly explored.

Patient and study characteristics

Out of the 36 studies that met our eligibility criteria, 18 full-text records evaluated at least one ERM outcome (as defined by the study authors) within 7 days after admission; the results reported here are for these 18 full-text publications. The study population consisted of day-old children to ≤18 years, with sample sizes of 12–722 participants. In almost all studies (n = 17/18), patients were admitted with a mixture of medical and surgical diagnoses – respiratory, neurological and cardiac conditions.

Outcomes

Among 18 studies that evaluated ERM, the feasibility and safety of ERM alongside process outcomes were the most frequent outcomes considered. See *Appendix 2*, *Table 32*.

Adverse events

Fifteen studies[7,10–14,17–19,24,25,32,36,42,43] provided information on adverse events (AEs). The most common event was tachycardia/desaturation.[13,14,24,42] Three studies reported haemodynamic changes[7,15,42] or tube removals.[7,10,42] Other events mentioned include pain,[7] fall,[7] behavioural changes,[24] excessive secretions[24] and discontinuation of therapy.[14,15,43]

Evaluation of early rehabilitation and mobilisation interventions

Feasibility in randomised controlled designs

Only two studies used randomised controlled designs, both judged as having a moderate risk of bias.[15,43] These studies[15,43] evaluated the feasibility of ERM as a primary outcome. The consent rates were 60%[15] and 94%.[43] One RCT, in 58 children aged 3–17 years with brain injury, showed that physical therapy was delivered 80% of the time in the usual-care arm and 100% among patients receiving early protocolised ERM.[15] In addition, patients receiving early protocolised rehabilitation received less post-PICU rehabilitation, but there were no differences in functional or quality of life (QoL) outcomes at 6 months.[15]

In a pilot randomised trial with 30 children aged 3–17 years,[43] the primary end point was feasibility defined as (1) the ability to enrol at least 75% of eligible patients, (2) an accrual rate of 1–2 patients a month and (3) a 30-day follow-up of >75%. The consent rate was 94%, and the 30-day follow-up rate was 87%. The median time from randomisation to delivery of mobility PT was not different between patients in the control standard mobilisation group [2.3 hours, interquartile range (IQR) 1–20] and standard mobilisation plus in-bed cycling (2.5 hours, IQR 0.9–11 hours). In this study,[43] the authors found no difference between arms (0.17, IQR −0.01–0.36) among 24/30 patients (80%) who developed new functional difficulties in PICU [Paediatric Evaluation of Disability Inventory-Computer Adaptive test (PEDI-CAT)]. In the usual-care arm 7/10 (70%) did with median of 0.4 (IQR: 0.3–0.6), compared with 17/20 (85%) in the cycling arm (median: 0.6, IQR: 0.4–0.7). Overall, only 10% of these patients fully recovered functional ability at 1 month, and mobility was the slowest to return.[43] No differences were identified for other outcomes evaluated in these studies.[15,43]

Feasibility/prevalence of early rehabilitation and mobilisation in observational prospective and retrospective studies

Single-centre studies

Most studies (n = 16) reported improvements in early mobilisation rates, demonstrating the feasibility of ERM. One study completed enrolment 1 month earlier than anticipated with an 85% consent rate.[19] Another study[12] reported more PT and OT ERM consultations. Betters *et al.*[10] also reported higher ERM consultations (median 30, IQR 29–45 minutes). Alqaqaa *et al.*[8] reported higher mobilisation rates among non-ventilated patients (mean difference of a day) compared to no change for mechanically ventilated patients. In another study,[17] mobilisation and OT consultation rates increased, but this change was not significantly different for PT consultations.

Choong and colleagues[11] showed higher lower-limb activity during in-bed cycling [mean ± standard deviation (SD) 266.47 ± 166.12] versus during non-intervention times (mean ± SD 20.94 ± 15.26, counts/20 minutes, $p < 0.001$) different to baseline. In another study,[21] the median time to mobilisation was 2 days (IQR 1–6) compared to 1 day for non-mobility interventions (IQR 1–3). Likewise, the frequency of physical therapy improved in another study,[32] with more patients achieving their rehabilitation goals.

Multicentre studies

In a multicountry study,[42] the prevalence of PT- and/or OT-provided mobility was 39% [95% confidence interval (CI) 34.7 to 43.9%] and did not differ according to baseline neurodevelopmental function level (PCPC ≤ 2.22% vs. PCPC ≥ 3.26%, $p = 0.331$), while PT or OT consultations were higher in a different study, ordered in 68/128 (49.6%) within 2 days (1–5 days) after PICU admission.[24] The prevalence of out-of-bed mobility was nearly two-thirds (87/110; 63.5%), passive range-of-motion 13.9% and no activity 19.7%. Out-of-bed mobility was common among non-mechanically ventilated children (48/56; 85.7%) and those under 3 years (71/100; 71%), while older children (18/37; 48.6%) were commonly not actively mobilised.[24] Similarly, consultations for all admissions were increased from 25% pre-implementation to 56% ($p < 0.001$) post implementation,[25] while consultations within 2 days increased from 34% to 67% ($p < 0.001$) and within 3 days, from 21% to 30% ($p = 0.02$) for at least one PT and/or OT mobility or 29% to 35% ($p = 0.29$) for mobilisations.

In another multicentre study, ~70% of children[18] received at least one mobilisation intervention. For children on mechanical ventilation (MV), one-third of those <3 years and ~50% of those ≥3 years were mobilised using passive range of movement (ROM) (72%).[18] Out-of-bed mobility was achieved 70% of the time, but less frequently among mechanically ventilated children, 47% (95% CI 44% to 49%).

Secondary or clinical outcomes in observational prospective and retrospective studies

Single-centre studies

Choong *et al.*[19] found improved functional ability measured using PEDI among 28% and 42% of participants at 3 and 6 months. Only 22% of those with a pre-existing chronic condition and 14% with functional limitations returned to baseline levels at 6 months. In comparison, 60% of previously healthy children and 58% of children with normal baseline function regained full functional abilities. The overall mortality rate was 3/33 (9%), and 19/33 (63%) were readmitted within 6 months after PICU discharge.[19]

Alqaqaa *et al.*[16] reported small improvements in length of stay [LOS; average LOS pre-WeeMove = 6.25 days vs. post-WeeMove LOS = 5.23 days] and time spent intubated (pre-WeeMove was 27.86 hours, post-WeeMove = 25.09 hours).[16] In contrast, Abdulsatar and co-authors[7] noted that PCPC scores were worse (mean ± SD change of 1.08 ± 1.0, $p = 0.02$) among two-thirds of patients who received ERM.[7] There was no improvement in grip strength or physiological status, despite increased activity levels (mean ± SD, upper-limb (UL) activity pre: 9.36 ± 4.12 vs. post: 57.12 ± 46.60 counts) and higher carer satisfaction.[7]

Colwell and co-authors reported higher adherence among younger patients ($p = 0.04$), with higher baseline severity of illness ($p < 0.001$) when mobilisation sessions were goal-directed ($p < 0.001$). However, there were no significant differences in mobilisation rates (pre: mean = 0.86 vs. post: = 0.84) or AEs 14/560 (2.5%, $p = 0.18$).[13] In the study by Wieczorek *et al.*, nearly half of the children (48/100) received at least one ERM intervention by day 3 of admission, and the proportion of children receiving at least one in-bed activity increased by 18% from post intervention ($p < 0.001$).[17] However, there was no change in passive ROM, only an increase in active interventions (57% vs. 26%; $p < 0.001$), especially among children ≥3 years. There was also a slight increase from 0% (0/39) ambulation while orally intubated to 10% (4/40) post intervention.[17]

Multicentre observational studies

Studies described a lower amount of mobilisation among younger patients with higher baseline disability[13,17,18] or severity of illness on admission.[13,18] One study[21] showed that older, less sick children admitted during the winter who were not mechanically ventilated, sedated or receiving neuromuscular blockade were more likely to receive mobility interventions. Similarly, consultations within 3 days were higher among males, older children and those with lower baseline function, without an indwelling endotracheal tube (ETT) or urinary catheter, who had adequate family support.[18]

Predictors of early rehabilitation and mobilisation

Three studies evaluated predictors of ERM using multivariate analysis.[18,24,42] The adjusted odds ratio (aOR) for out-of-bed mobility was negatively associated with the presence of an ETT (aOR, 0.13; 95% CI 0.08 to 0.2), a urinary catheter (aOR, 0.28; 95% CI 0.14 to 0.57), opioid infusion (0.42; 95% CI 0.24 to 0.73) and severe baseline disability (PCPC 4 vs. 1) (aOR, 0.59; 95% CI 0.4 to 0.87). Longer PICU LOS and lower nurse-to-patient ratio (1.82; 95% CI 1.2 to 2.8) increase the odds of out-of-bed mobilisation. For children <3 years old, family presence was associated with out-of-bed mobility (aOR, 4.55; 95% CI 3.1 to 6.6) while being older predicted PT or OT (aOR, 3.1; 95% CI 2.01 to 4.79).[18] In another study,[24] the presence of ETT or infusion among children ≤3 years reduced the likelihood of receiving therapist-provided out-of-bed mobility [odds ratio (OR) 3.62; 95% CI 1.49 to 8.82]. However, this improved when the family were present.[24]

Ista and colleagues[42] showed that older age (2.28, 95% CI 1.23 to 4.22), moderate baseline disability (defined as PCPC: 3 vs. 1) (2.12, 95% CI 1.02 to 4.56), severe baseline disability (PCPC: 4 vs. 1) (2.24, 95% CI 1.14 to 4.40), having a central venous line (CVC) in place (aOR 1.63, 95% CI 1.02 to 2.62) and family presence (aOR 5.13, 95% CI 2.55 to 10.32) increased the odds of receiving a mobility session. However, the presence of a urinary catheter reduced the chance of mobilisation (aOR 0.46, 95% CI 0.22 to 0.92). MV through an ETT (aOR 0.29, 95% CI 0.12 to 0.68), being admitted for a surgical reason

(aOR 0.58, 95% CI 0.35 to 0.95) and the presence of a urinary catheter (aOR 0.39, 95% CI 0.19 to 0.81) reduced odds of out-of-bed mobility, but this improved with family presence (aOR 7.83, 95% CI 3.09 to 19.79).[42]

Quality assessment

Controlled trials

Two studies[15,43] randomly assigned participants into groups and were assessed using RoB v2. One study[43] ensured allocation concealment using a computer-generated sequence and reported adequate sample size considerations. In the other study,[43] sample size calculations were not applicable; consequently, outcomes were possibly underpowered. We did not identify attrition bias for both studies, outcomes assessment was similar at baseline, and co-interventions were similar across groups.

Prospective and retrospective studies

We used the ROBINS-I tool to assess the quality of observational studies (see *Appendix 2*, *Table 33*). Overall, most studies were judged to have a serious or critical risk of bias. Three studies (3/18)[18,24,42] were judged to have a low risk of bias. Nine[10,12,13,15,19–21,25,32] were judged to be at moderate risk of bias, while in four there was serious risk.[11,14,16,31] In some studies bias was judged as critical,[8] or information reported was insufficient[17] and could not be assessed (*Figure 2*).

The primary reason for downgrading studies was bias due to blinding or poor consideration of baseline confounding. There was no indication of selection bias during enrolment; studies were judged as adequate except in three retrospective studies.[14,17,31] The lack of a clear definition of ERM hierarchy limited the evaluation of demonstrable effects on objective clinical outcome measures. This made it challenging to determine intervention superiority. Broadly, intervention categories of non-mobility and mobility were consistent across studies, which were judged to be at risk of misclassification bias half of the time (9/18). We assessed the impact of bias due to deviations from the intended response as adequate in most studies. In some studies,[7,8,10,11,13,14,16,17,21,32] the technique for handling missing data was unclear or not reported. We did not identify any evidence of selective outcome reporting or errors due to outcome measurements. Most studies demonstrated congruence between previously defined analyses and outcomes reported. However, none of the studies published a protocol. Overall, most studies did not provide definitive evidence of the effects of the intervention. However, consistent evidence across all studies supports the feasibility of ERM as an intervention in PICU, while physical therapy was the most common intervention considered.

Quality of consensus on exercise reporting

We described techniques considered during intervention design and excluded items not relevant to this review. These items included item no. 3 (descriptions of individual or group exercises), item no. 9 (use of home equipment; discharge interventions were not considered) and item no. 12 (setting of exercise delivery; all studies were conducted in PICUs). See *Appendix 2*, *Table 34* for details.

Quality of consensus on exercise reporting reporting

Most studies (12/18)[7,10,16–18,20,21,24,25,31,32,42] provided details on the type of ERM intervention to aid replication. Some studies (4/18)[18,21,25,32] provided training or engaged multidisciplinary teams (MDTs) to facilitate ERM delivery. Organisational strategies were sometimes applied across MDTs to facilitate PICU culture change. Some studies (12/18) explicitly mentioned using qualified providers such as physiotherapists, nurses or other therapists to supervise sessions and ensure intervention fidelity.[10,11,13–15,17,18,21,24,25,42,43] However, the detail provided was insufficient to explain how differences in experience levels, treatment approaches and therapists' behaviour in these circumstances influence outcomes.

Intervention components were generally tailored and not standardised. Sometimes, it was unclear what aspects of the interventions were usual practice or complementary during ERM delivery. In most studies,

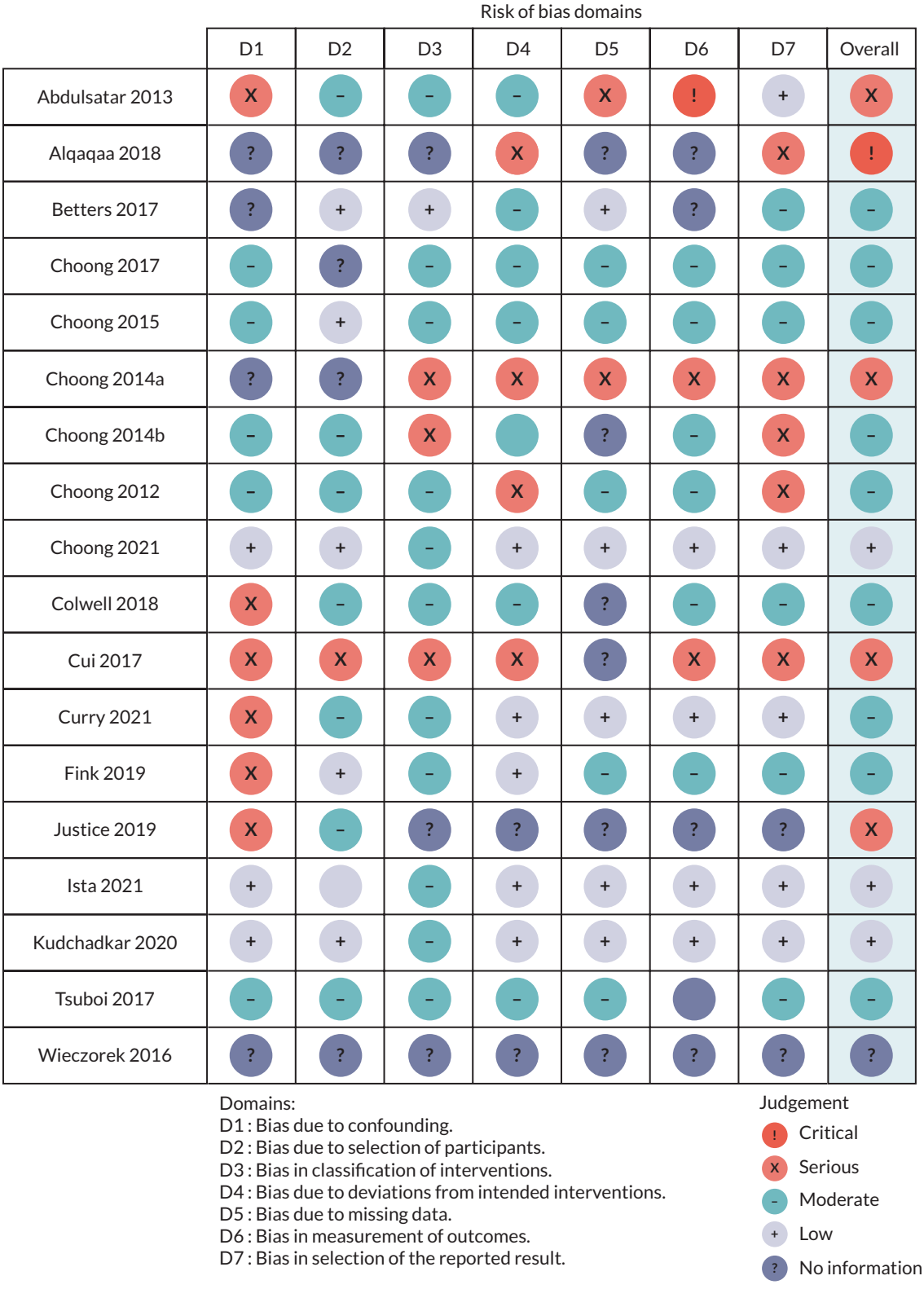

FIGURE 2 Pictorial presentation of quality assessment using ROBINS-I.

information on how deviations from study protocols were handled (i.e. regression or progression) and how these events may have affected outcomes was unavailable. Personalising the volume of ERM was a common concept across studies used to improve compliance. However, since interventions were tailored to tolerance levels, we did not assess intervention fidelity. Some studies provided a detailed description of how compliance or adherence was measured. Strategies mentioned include rehabilitation

sheets[11,19,20,32] and electronic records during PICU ward rounds.[17,18] Two studies[7,11] used an objective outcome to measure compliance – ACTi-graph accelerometers. This outcome measure can be used as a benchmark for future studies, incorporating routinely collected outcomes to increase transferability.[47] Labour-intensive or ad hoc approaches for determining adherence or compliance, such as caregiver verbal confirmation following direct observation, charts or checklists, may limit the implementation of rehabilitation and future attempts at service evaluation.

Early rehabilitation and mobilisation change techniques

No study provided explicit details about applying complex intervention theories when designing interventions, while details on the implementation processes were inconsistently reported. Therefore, it is unclear to what extent interactions between intervention volume of ERM and health systems produce positive effects. It is not impossible to envisage a situation where contextual factors such as how the intervention works, for example the presence of a local champion or an ERM enthusiast, staff turnover, population demographics, or existing PICU culture, affect outcomes, either positively or negatively. No study provided details on motivation strategies or precise details on how interventions were personalised. Safety guidelines (underpinned by clinical stability), verbal feedback and tolerance levels to determine progression were commonly used across studies. Eight studies[10,14,17,18,21,24,25,42] provided information to enable replication. Hence, these studies can be used as a springboard to undertake detailed intervention mapping when designing ERM manuals. Overall, key aspects of intervention delivery were poorly reported, such as co-interventions, strategies for tailoring interventions and motivating patients.

Discussion

This review aimed to summarise evidence on the effectiveness of ERM research within PICUs. We narratively synthesised evidence to improve interpretation of effectiveness given variation in ERM implementation. We identified a broad range of activities, categorised as non-mobility and mobility interventions. Other interventions identified but not considered in this review include undefined ERM,[48–50] music therapy[51] and neuro-psychological training.[52] This review suggests that interdisciplinary multicomponent interventions, sometimes delivered as a bundle, are feasible, safe, acceptable and possibly beneficial to patients. The programmes mainly were designed using safety criteria, were goal-directed and tailored. Although the rate of intervention-related AE reporting across all studies was low, we cannot rule out selective reporting as none of the included studies had published their statistical analysis plan a priori.

Given the limited description of interventions, intervention manuals and process data would be essential to understand the complexity of ERM. There are also organisational factors that need to be considered when implementing ERM. What remains unclear is the number of organisational levels that should be targeted and how. Other issues to consider include mechanisms of effect (moderators – participants' responses to and interactions with the intervention and mediators that affect intervention outcomes in unexpected ways). Administering staff training was a common feature we identified across studies to ensure consistency. However, nursing capacity required to deliver the intervention and family involvement need to be carefully considered. Family involvement is crucial when considering non-mobility ERM for children under 3 years old.

Evidence

We found that children under 3 years of age admitted to PICU tend to be given passive and active in-bed activities. Children 3 years and older were primarily involved in out-of-bed activities when this was considered safe. In addition, one study[18] reported higher ERM incidence among male children, but this finding was not consistent across studies. Hence, it is unclear what interventions should be administered to these age groups and whether certain combinations of interventions are superior to those given to their older counterparts.

We found equivocal evidence suggesting that other factors such as time to admission, tube presence, MV, or sedation also influenced developmental or mobility goals. Only four studies[13,18,24,42] evaluated baseline severity of illness (measured using validated tools) and comorbidities that affected clinical and functional outcomes in multivariate models. Consequently, the effect of residual confounding or chance on the estimated intervention effect remains unknown. Overall, the evidence about subgroup effectiveness was indicative of clinical pragmatism but otherwise inconclusive.

Comparison with the broader literature

Our findings reflect the evidence in previous systematic reviews of ERM interventions within adult and paediatric PICU.[53–56] The evidence emerged from North American PICU contexts, and its transferability to the UK settings remains uncertain.[38,39,46,57] Besides variation in practice, interactions within complex health systems have additional issues. As an additional complexity, due to the nature of interventions considered in this review, it is difficult to determine if intervention effects are additive, multiplicative (biologically plausible) when combined or neutralise each other and plateau.

Most outcomes of feasibility or acceptability were exploratory findings, and the strength of the evidence for objective clinical or functional outcomes remains unclear. Nevertheless, PT and OT, sometimes with SLT, were frequently implicated in the exposure-mechanism-outcome pathway. Furthermore, barriers reported reflect previous literature and support the need for activity orders.

Summary of findings to inform the paediatric early rehabilitation and mobilisation during intensive care study

- Optimal aspects of intervention delivery – timing, content, active ingredients, dose–response relationships, progression and implementation strategies – have yet to be established.
- Improvements in functional independence (though small and sometimes inconsistent) have not been matched with improved PICU-acquired weakness or survival measures. ERM appears safe but requires long-term studies.
- Standardised definitions for ERM, safety and core outcome measures will improve comparability across studies. Authors should consider the effect of an intervention on core outcome sets recommended for paediatric critical care. These include four domains: global cognition, emotional, physical and overall health. Four child-specific outcomes of health-related QoL, pain, survival and communication have also been recommended.[47] Benefits so far indicate some improvement in QoL.
- ERM has been demonstrated to be feasible and acceptable within PICU. There are still uncertainties about the effectiveness of ERM interventions; only two studies used randomised designs. The evidence uncertainty is worse for objective outcomes such as PICU LOS. Overall, non-mobility rather than mobility interventions seem to be preferred in children 3 years and younger compared to their older counterparts.
- The lack of a well-defined ERM protocol is a significant barrier to ERM implementation. There is no clear evidence on the impact of bundles of care or behavioural interventions incorporated with ERM. We identified several studies that evaluated the feasibility of ERM in PICU, some of which report improved QoL as a longer-term outcome. However, the evidence for effectiveness is inconsistent, uncertain and needs further testing. Most studies were quality-improvement studies, which may be the best methodology for evaluating ERM within PICU until a better consensus on intervention components is achieved. As an alternative, nested controlled trials embedded within longitudinal studies or routine data collection can be used to evaluate the effectiveness of these interventions. Data from such studies might also enable mediation analysis to understand key intervention components and mechanisms of action.

Chapter 2 Phase 1b: national survey to establish standard practice

Introduction

This study involved a national electronic web-based survey for paediatric intensive care healthcare professionals to understand the context and professional perspectives of delivering early rehabilitation and mobilisation (ERM) within UK PICUs.

Study management

The work package was led by BRS. JYT co-ordinated survey responses and developed the on-line tool. The study management group provided input into survey questions and designs. The study was piloted in Birmingham and Nottingham by JYT, Emily Brush and Francesca Ryde. Statistical analysis of the full survey was undertaken by JYT, BRS, JMen, JMan and JMc. Qualitative analysis of the free-text responses was undertaken by JYT.

Aims and objectives

To explore how healthcare professionals describe ERM, identify current ERM practice and understand perceived barriers and facilitators of ERM.

Methods

A web-based survey (administered through www.smartsurvey.co.uk) was developed that included 25 questions that related to the study aims. The survey was piloted with multidisciplinary teams of health professionals (n = 40) at two PICUs to assess acceptability and comprehensiveness. Minor changes to improve question clarity were made. Pilot responses were excluded from main survey analysis.

The University of Birmingham granted institutional ethical approval on 5 February 2019 (reference ERN_18-1134). Consent was implied through survey completion.

The survey was administered using a chain-referral method. A UK Paediatric Critical Care Society Study Group (PCCS-SG) member from each UK PICU (n = 29) was contacted via e-mail and requested to identify and cascade an invitation e-mail to members of their local MDT (including at least one physiotherapist, doctor and nurse). Participating PICUs were sent a survey link between May and August 2019 to distribute. Three follow-up reminders were sent at weekly intervals to PICUs that had not responded.

Statistical analysis was performed using R version x64 3.5.1 (R Foundation for Statistical Computing, Vienna, Austria). Data were analysed using descriptive statistics, with categorical responses expressed as numbers (percentage), with Likert scales (median IQR) used to express the frequency of practice or level of agreement. Ranking of perceived ERM benefits was calculated using the sum of ranked scores of respondents' top five important benefits (five points for first, reducing to one point for fifth placed).

Free-text data from the open-ended responses were analysed using a qualitative content analysis approach.[58] Two researchers independently familiarised themselves with the data and conducted open-coding, utilising NVivo™ (QSR International, Warrington, UK) software for data management. Codes were then discussed, summarised and organised.[59,60] Anonymised, free-text quotes from respondents are used in the reporting of this analysis to add context and clarity.[61]

Results

Demographics

We received responses from PCCS-SG link members in 26/29 (90%) UK PICUs. A total of 191 health-care professionals opened the survey link with 124 (65%) submitting responses, with a median of 4.5 participants (IQR 3–6) per PICU.

Most respondents were nurses (*n* = 34, 27%), physiotherapists (*n* = 28, 23%) and doctors (*n* = 22, 18%) (see *Appendix 3*, *Table 36*). Respondents also included occupational therapists (OT) (*n* = 19, 15%), play therapists (*n* = 7, 6%), psychologists (*n* = 7, 6%), dieticians (*n* = 6, 5%) and SLTs (*n* = 1, 1%). Almost three-quarters of health professionals had ≥5 years' experience, with 48 (39%) ≥15 years.

Description of early rehabilitation and mobilisation

We invited participants to describe ERM in their own terms, with 104 (84%) responding. Participant definitions of ERM aligned to four categories, 'Activity-focused', 'Tailored', 'Promote recovery' and 'Timing of ERM' (*Table 1*). Overall ERM was an individualised package of graded interventions, based on an activity-focused programme, to reduce the sequelae of critical illness or injury. However, responses differed for when ERM should be initiated, often emphasising the need for individualisation.

Most respondents considered ERM to be a priority, either crucial 15 (12%), very important 67 (55%) or important 35 (29%) in the care of PICU patients (see *Appendix 3*, *Table 37*).

Availability of established early rehabilitation and mobilisation protocols

Respondents were asked to describe the content of established ERM protocols within their PICU. Only 12 (10%) participants from 5/26 PICUs reported having an established ERM protocol. The most common components of ERM protocols were 'physical therapy not requiring additional equipment' (9/12, 75%) and 'OT interventions' (8/12, 67%). Only 4/12 (33%) referred to play therapy or SLT, and no ERM protocol specified input from psychologists or psychiatrists.

All participants were asked about the content of non-ERM protocols in their PICU. Only 18/124 (15%) participants reported that guidance for physical or OT activities existed in other, non-ERM protocols that were used in the PICU setting (see *Appendix 3*, *Table 35*).

Recipients of early rehabilitation and mobilisation

Despite the paucity of ERM protocols, 51 (41%) respondents reported that all PICU patients 'always' or 'very often' received ERM (*Table 2*). ERM was reported to be more likely to be delivered to patients when PICU LOS exceeded 28 days. Patients admitted for 28 days or more were more likely (91, 75%) to 'always' or 'very often' receive ERM in comparison to only 17 (13%) of those reported to stay fewer than 3 days. Participants reported that patients with acquired brain injury (75, 60%) and severe developmental delay (54, 44%) were 'always' or 'very often' likely to receive ERM.

Perceived benefits of early rehabilitation and mobilisation

Participants ranked the 5 most important potential benefits of ERM out of 13 options (*Figure 3*). The most important outcomes identified were: (1) reduced PICU LOS, (2) improved psychological outcomes for patients after PICU, (3) reduced days of MV, (4) improved participation in activities of daily living and (5) improved patient satisfaction.

Initiation and delivery of early rehabilitation and mobilisation

The decision for ERM initiation was perceived by respondents to be primarily led by physiotherapists (96, 77%), doctors (92, 74%) and bedside nurses (64, 52%). Parents were felt to initiate ERM by only 24 (19%) of respondents (see *Appendix 3*, *Table 38*).

TABLE 1 Descriptions of ERM

Category	Subcategories	Examples
Activity-focused ERM is activity-focused, with consideration of seating and equipment, primarily delivered by nursing and allied healthcare professionals with optimised sedation management to promote patient engagement. There is a lack of consensus on what is routine care compared with purposeful ERM activity	Activity – mobilising, positioning, stretching	'ERM provided includes – passive movements of limbs, periodic change of position, use of splints on extremities and if stable in the long-term patients – sitting up in tumble form chair and mobilising out of bed.' (Doctor, 67) 'We aim to get the children sitting upright, either over the edge of the bed or in appropriate seating as soon as possible.' (OT, 001) 'Nursing staff are taught the importance of regular position changes for patient … and positioning to maintain ranges of movement and prevent foot drop.' (Nurse, 017)
	Core healthcare professional involvement – physiotherapist, nurse, OT	'We try and mobilise patients as soon as able when not invasively ventilated – physio led.' (Doctor, 058) 'As physiotherapists, we work with the OT and nursing staff to either re-position, sit up in bed, sit on the edge of the bed or stand whilst on the ventilators.' (Physiotherapist, 069)
	Additional healthcare professional involvement – psychology, dietician, play therapist, SLTs	'Speech and language therapy become involved usually when nursing or medical staff identify a need for referral.' (Doctor, 003) 'We have a Play Specialist on PICU, who assists with communication tools/toys.' (Nurse, 082)
	Seating and equipment	'Specialist seating need – linking in with OT to ensure appropriate seating available.' (Physiotherapist, 019) 'We have also in the past asked adult (services) to use their moto-med bike and used this with teenagers, but this can be a challenge as it is very far from PICU and it is often in use.' (Physiotherapist, 014)
	Sedation management	'Working with the medics to wean sedation as quickly as possible. This promotes faster ability to mobilise and progress in their rehabilitation.' (Nurse, 034)
	'Routine care' vs. 'purposeful ERM package'	'Some centres define ERM as passive range of movement, repositioning or providing splints. We would deem this as essential core cares rather than ERM; the large majority of our patients will have positioning and movement plan from day 1 of admission.' (Physiotherapist, 111)
Tailored Following the assessment of needs and patient and family preference, ERM activities are personalised to the individual patient	Assessment of need	'We have a programme where patients are categorised to one of 3 levels. Each level provides nursing and therapy staff with activities aligned to the acuity of the patient.' (Nurse, 040)
	Individual preference	'Parents will tell us what their child enjoys doing and make suggestions, often provide toys/games from home.' (Nurse, 076) 'Discuss with parents what patient enjoys doing, watching etc. Discuss options regarding taking patients "out" where possible if long-term patients.' (Nurse, 015)

continued

TABLE 1 Descriptions of ERM (*continued*)

Category	Subcategories	Examples
Promote recovery The purpose of ERM is to normalise the PICU environment, to create an environment that addresses holistic needs, sustains or promotes development and supports recovery from critical illness	Normalising PICU environment	'Provide activities they would use for their enjoyment. This enables them to be more relaxed and less aware of what is going on with/around them.' (Play specialist, 102) 'Being in PICU can be a frightening experience. Not only is a child/young person away from home, but also away from their usual environment, family and friends. There are unfamiliar sounds, smells, equipment and people. The play specialist can help to make the stay much more enjoyable and children/young people to cope and understand.' (Play specialist, 055)
	Sustain/promote child development	'Encouraging the patient to regain or further their development in a therapeutic fun manner.' (Play therapist,102)
	Restoration/recovery	'Interventions aim to promote physical recovery – movement, and ability to engage in activities and psychological recovery – orientation, speech, ability to play and attend school.' (Nurse, 021)
Timing of ERM The optimal timing of ERM initiation is challenging for healthcare professionals to define, although likelihood perceived to increase with increased LOS. Influenced by the perceived stability of patients and the balance of risk to benefit	'Early' poorly defined	'I like to think we consider it within 2–3 days we have a better idea of the patients' PICU journey and how long they are going to stay. The reality is it's usually longer … usually week 2 of admission if they are still on the unit.' (Physiotherapist, 090) 'There is no formal plan for who decides if a patient should start ERM and when …. Currently the delivery of ERM is fairly ad hoc, based on what is highlighted from daily handover each morning.' (Physiotherapist, 083) 'We provide ERM as a structured programme … every patient after 24 hours of admission is considered for ERM.' (Doctor, 012)
	Patient stability, risk and benefit	'Members of the PICU team with less experience of early rehab can deem ERM "unsafe" which can occasionally act as a barrier.' (Physiotherapist, 016) 'Usually ERM activity is not considered until patients can physiologically tolerate movement and are stable with observations.' (Nurse, 008)
	'Long-stay'	'ERM is often thought about as a patient comes up to extubation or has failed extubation, and we feel that the reason for failure may be because of critical care weakness.' (Physiotherapist, 031) 'We provide very little ERM on PICU, other than for long-term patients, which is often, in my opinion, delayed.' (Nurse, 007)

TABLE 2 Reported frequency of receiving or being involved in ERM by age groups, length of PICU stay, diagnostic category and healthcare professional or parental/family role (*n* = 124 respondents)[a]

By age group	Always, *n*, (%)	Very often, *n*, (%)	Sometimes, *n*, (%)	Seldom, *n*, (%)	Never, *n*, (%)	Don't know, *n*, (%)	Not applicable,[b] *n*
All PICU patients (any age)	6 (5)	45 (36)	48 (39)	14 (11)	0 (0)	11 (9)	0
>10–18 years old	18 (15)	40 (32)	43 (35)	8 (6)	1 (1)	14 (11)	0
>4–10 years old	16 (13)	42 (34)	41 (33)	10 (8)	1 (1)	14 (11)	0
1–4 years old	13 (10)	42 (34)	39 (31)	13 (10)	1 (1)	16 (13)	0
Infants and <1 year old	6 (5)	47 (38)	32 (26)	20 (16)	3 (2)	16 (13)	0
By LOS in PICU							
PICU > 28 days	43 (35)	48 (39)	14 (11)	4 (3)	0 (0)	15 (12)	0
PICU > 7–28 days	27 (22)	46 (37)	26 (21)	8 (6)	0 (0)	17 (14)	0
PICU 3–7 days	12 (10)	32 (26)	40 (32)	19 (15)	5 (4)	16 (13)	0
PICU < 3 days	3 (2)	14 (11)	39 (31)	33 (27)	17 (14)	18 (15)	0
By diagnostic category							
Acquired brain injury	36 (29)	39 (31)	16 (13)	11 (9)	4 (3)	18 (15)	0
Severe developmental delay	11 (9)	43 (35)	39 (31)	12 (10)	3 (2)	16 (13)	0
Cancer	11 (9)	24 (19)	36 (29)	14 (11)	4 (3)	35 (28)	0
Pre-existing physical morbidity	9 (7)	38 (31)	44 (35)	12 (10)	4 (3)	17 (14)	0
Mechanically ventilated	9 (7)	38 (31)	39 (31)	18 (15)	5 (4)	15 (12)	0
Congenital heart disease	9 (7)	24 (19)	39 (31)	15 (12)	6 (5)	31 (25)	0
Respiratory illness	7 (6)	35 (28)	39 (31)	22 (18)	3 (2)	18 (15)	0
Sepsis	7 (6)	28 (23)	44 (35)	20 (16)	5 (4)	20 (16)	0
Multiorgan failure	5 (4)	14 (11)	32 (26)	35 (28)	12 (10)	26 (21)	0
Mechanically supported (e.g. extracorporeal life support)	4 (3)	8 (6)	14 (11)	13 (10)	47 (38)	38 (31)	0

continued

TABLE 2 Reported frequency of receiving or being involved in ERM by age groups, length of PICU stay, diagnostic category and healthcare professional or parental/family role (*n* = 124 respondents)[a] (*continued*)

By age group	Always, *n*, (%)	Very often, *n*, (%)	Sometimes, *n*, (%)	Seldom, *n*, (%)	Never, *n*, (%)	Don't know, *n*, (%)	Not applicable,[b] *n*
Healthcare professional team members and parent or family member(s) involvement in ERM (when applicable[b])							
Physiotherapist	86 (70)	27 (22)	4 (3)	2 (2)	0 (0)	4 (3)	1
Nurse	54 (44)	49 (40)	9 (7)	5 (4)	0 (0)	6 (5)	1
Parent or family member	36 (29)	56 (46)	19 (15)	7 (6)	1 (1)	4 (3)	1
OT	23 (19)	34 (29)	29 (24)	20 (17)	6 (5)	7 (6)	5
Doctor	22 (18)	20 (16)	26 (21)	30 (24)	13 (11)	12 (10)	1
Play therapist	12 (10)	24 (21)	39 (34)	26 (23)	9 (8)	5 (4)	9
Dietician	10 (8)	20 (17)	12 (10)	29 (24)	37 (31)	13 (11)	3
SLT	4 (3)	11 (9)	40 (33)	35 (29)	20 (17)	10 (8)	4
Psychologist	3 (3)	11 (10)	24 (23)	32 (30)	30 (28)	6 (6)	18

a Percentages may not total 100 due to rounding. Data present as number (per cent).
b Not applicable (e.g. not available in PICU) responses excluded from per cent calculation.

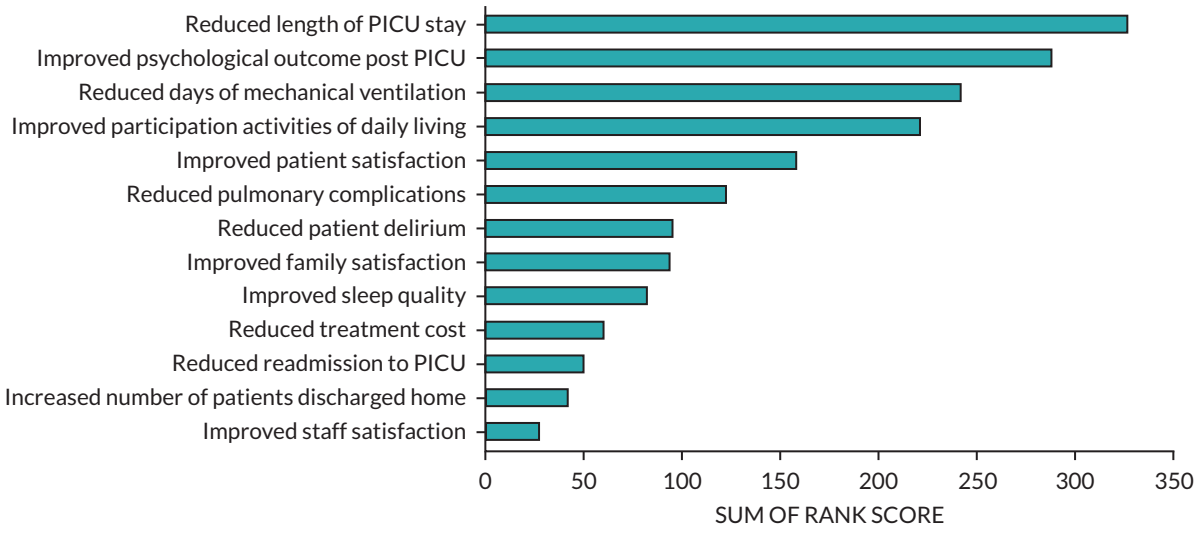

FIGURE 3 Perceived benefits of ERM. Ranking of participants' potential top five perceived benefits of delivering ERM within PICUs. Sum of rank score: ranking of top five (1–5) (first-placed rank scored five points to fifth placed scored one point). Ranked scores of 121/124 (98%) participants.

Factors that influenced ERM initiation included patient stability (69, 56%) and LOS, specifically within 3 days of admission (31, 25%). Five (4%) respondents reported they would not consider ERM at all. The influence of perceived clinical stability is demonstrated in respondents' free-text comments:

> *We are involved as early as required depending on the child/young person medical stability and their rehabilitation needs.*
>
> *(OT, 033)*

> *Usually, ERM activity is not considered until patients can physiologically tolerate movement and are cardio-vascularly stable.*
>
> *(Nurse, 008)*

Assessment of patient stability and tolerance of ERM were less well described. Most respondents (98, 79%) provided subjective cues or informal clinical criteria. These included monitoring of vital signs, physiological changes, observation of behavioural changes and documentation of AEs.

Physiotherapists (113, 92%), nurses (103, 84%) and parents or family members (92, 75%) were 'always' or 'very often' involved in the ongoing delivery of ERM, with less frequent input from other members of the MDTs (see *Table 2*).

Barriers to early rehabilitation and mobilisation implementation

Figure 4 presents the perceived barriers of ERM. The most significant factors identified as barriers at the institutional levels were insufficient resources/equipment (83, 69%) and inadequate funding (73, 61%). Participants provided examples of resources having to be shared across organisations or having to be specially ordered to deliver ERM to patients.

> *All equipment shared with the whole therapy department at present, therefore dependent on availability.*
>
> *(OT, 010)*

Most PICUs had access to standard lifting 22/26 (85%) and specialist static seating equipment 25/26 (96%). However, bedside or in-bed cycling machines were only available in 10 (38%) of PICUs (see *Appendix 3*, *Table 39*).

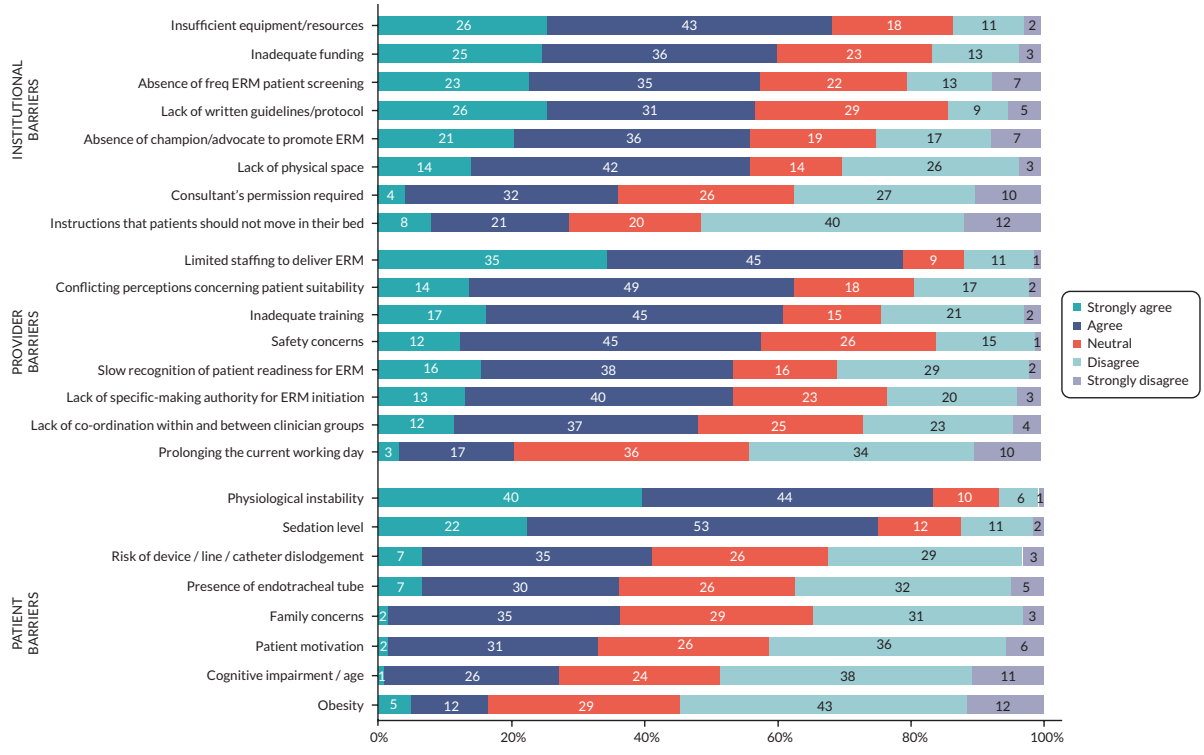

FIGURE 4 Perceived barriers of ERM.

A lack of established protocols (69, 57%), ERM champions (68, 57%), space (68, 56%) and robust patient-screening processes (63, 58%) were also issues identified by respondents.

Limited staffing was the most frequently reported barrier to ERM being delivered (101, 79%). Approximately half of the respondents agreed issues such as training, patient safety, lack of decision-making authority and delays in recognition of patients' ERM needs were barriers to ERM initiation. However, only 25 (21%) identified that the impact of ERM potentially prolonging the working day was a barrier.

At the patient level, the two most frequently reported barriers to delivering ERM were physiological instability (101, 81%) and sedation (91, 73%).

Institutional, patients and provider barriers to ERM

Table 2 shows the percentage of responses for the categories strongly agree, agree, neutral, disagree and strongly disagree. Responses ranked on the cumulative score of percentage 'strongly agree and agree'.

Summary of findings to inform the PERMIT study

- This national survey of healthcare practitioners (HCPs) from UK PICUs identified the importance of ERM as an intervention which participants believe can improve the physical, psychological and cognitive recovery of critically ill or injured infants and children across all ages.
- Our findings indicate support for ERM, but highlight uncertainty with suitability, variability with the definition of this complex intervention, variation in timing of initiating and which patient groups should receive ERM.
- Key barriers to ERM delivery were identified (e.g. funding and staffing) and potential clinical (e.g. improved psychological outcomes) and economic (e.g. reduced PICU LOS) benefits to patients and PICUs.

- Our results indicate uncertainty and wide variation in time to start ERM (24 hours to over 7 days), increasing agreement for ERM to be considered after longer periods on PICU, and support for the concept of 'as early as the patient's clinical condition allows', which may be much longer.
- The uncertainty of the content of ERM also adds to the challenge for healthcare professionals to appreciate when ERM could be delivered. Understandably, normal bedside nursing care (e.g. functional positioning) may be considered acceptable earlier than more advanced physical therapies requiring multiple staff (e.g. sitting a ventilated child out of bed or in-bed cycling).
- Our survey identified that clinical stability is the most influential patient factor for initiation.
- The reported lack of ERM protocols in most (21/26) UK PICUs reinforces a strong requirement for evidence-based standardised protocols with optimal timing, intensity, frequency and duration of ERM. There is a need for flexible protocols to allow for tailoring rather than prescription.
- ERM was more likely to be delivered to patients admitted for >28 days, among patients with acquired brain injury or severe developmental delay across all age ranges. Most published ERM intervention studies to date have excluded patients <3 years of age.[20,15] However, this represents 60% of the UK PICU patient population,[62] and this age group was as likely to receive ERM as older children in our study. Future ERM trials should include all PICU age groups to ensure ERM content and efficacy are assessed across all potential patients.
- Our results show that within the UK NHS setting, doctors, physiotherapists and nurses have an equally significant role in the decision to initiate ERM.
- Nurses' and parent's roles are also important in both initiation and delivery of ERM. In our study, 91% felt 'involved' in delivery of ERM. However, parents were reported to be the least likely group to initiate ERM (19%), although becoming influential in its ongoing delivery.
- The key barriers to ERM practice were (1) at institutional level: insufficient resources, equipment and funding; (2) at provider level: limited staffing, training, protocols and slow recognition of readiness for ERM; and (3) at patient level: physiological instability, risk of ETT dislodgement and amount of sedation.

Chapter 3 Phase 1c: observational study

Introduction

This chapter describes the observational study to ascertain current ERM practices, as well as barriers and facilitators to ERM delivery, within the PICU setting. Following the scoping review and survey (see *Chapters 1* and *2*), we were interested in the concept of early ERM occurring by day 3 and over the following 7 days of PICU admission, and ERM to include the broad category of any rehabilitation or mobilisation, including both mobility and non-mobility activities. We directly observed current ERM practices within UK PICUs, identify patients who do and do not receive ERM and describe variation between PICUs and factors associated with ERM practices.

Study management

The work package was led by BRS. The study management group provided input into protocol and ethics design. JYT was study co-ordinator and piloted and developed the Research Electronic Data Capture (REDCap) database. Statistical analysis was undertaken by JYT, BRS and James Martin. Data interpretation was by BRS, JYT, JMan and JMen with input from all study management group.

Objectives

- Observe and describe current ERM practice, including barriers and facilitators, in UK PICUs.
- Assess the capability of UK PICUs to deliver ERM.
- Establish and model how many/which CYP may be suitable for ERM in the PICU population using routinely collected data.

Method

Study design

A multicentre prospective observational study.

Target population/setting

All CYP (0 to <16 years) admitted to PICU and remaining on PICU by 9 a.m. on day 3 after PICU admission were eligible to participate. The exclusion criteria included a local decision by PI or treating clinical team not to include patients (e.g. receiving end-of-life care) and parents or guardians who choose to opt out. The broad study inclusion criteria allowed for the observation of all types of patients admitted for PICU care (e.g. planned and unplanned admissions), and all age ranges.

Site and patient selection

The Paediatric Early Rehabilitation and Mobilisation during InTensive care (PERMIT) study was an observational study conducted in 15 UK PICUs across two 21-day periods: (1) 26 November–16 December 2019 and (2) 14 January–3 February 2020. PICUs were identified from the PERMIT survey (see *Chapter 2*). The PICUs selected were of varying sizes (n = 6 large: >800 admissions/year, n = 5 medium: 500–800 admissions/year, n = 3 small: <500 admissions/year) and reported ERM activity of differing levels in the survey.

This study was conducted in two separate time periods to maximise efficiency, overcome recruitment hurdles and meet the target. Ten sites recruited and collected data during period 1, with a further five sites in period 2. Patients were observed on study day 1–14 with a further week to complete follow-up (study day 15–21). Individual patient data collection and observations took place for up to 7 days after patients were recruited or until PICU discharge, whichever was sooner.

Recruitment/enrolment

The study protocol, manual of operation, checklists and case report forms (CRFs) provided details on the study procedures. Staff at participating sites received remote training on research conduct before, and ongoing support sessions during, the study period.

Research staff screened patients admitted to PICU for the PERMIT study using a bespoke study screening log. The daily screening process ensured patients becoming eligible (e.g. the day before their third day) were identified. Designated research co-ordinators entered data on ERM activities recorded by clinical staff in clinical notes on the study proformas. Data were transferred to a secure electronic database (REDCap™), with scanned copies uploaded for data validation. Data were pseudo-anonymised at the local site before secure transfer to the PERMIT trials office.

Consent

As the study was observational, Regional Ethics Committee (REC) approved data collection without seeking prior consent from parents/legal representatives. In addition, this avoided unnecessary burden for parents/legal guardians in approaching consent during a very sensitive time. Information about the study was provided to all eligible patients' families and was displayed within public areas of participating PICUs. This explained the study to parents, family, friends and children who were able to make autonomous decisions. Parents/legal guardians were able to opt the child's data out of the study at any time and were aware that the future care their child would receive would not be affected.

Study procedure and data collection

Site staff collected demographic data on the third day of admission. Clinical and ERM data were collected from enrolment until discharge at the end of the study period. Data were collected twice, between 09.00 and 10.00 and between 14.00 and 15.00, each day.

Patient-level data

Patient characteristics collected at PICU admission included age (in categories); reason for admission; primary diagnosis; the severity of illness using Pediatric Index of Mortality (PIM3) score, with clinical function being assessed at baseline (pre-PICU state) and admission via the PCPC and POPC, which scores from 1 to 6 (1: normal, 2: mild disability, 3: moderate disability, 4: severe disability, 5: vegetative state or coma and 6: death).[63] PICU LOS was also recorded.

Clinical data

Data collected during PICU stay included healthcare interventions; requirement for MV; sedation and level of consciousness; presence of delirium; critical care interventions; indicators of physiological status; and individual patient PICU resource use. We calculated PELOD score (PELOD-2),[64] which is a measure to describe the severity of organ dysfunction/illness in critically ill CYP, daily at 9 a.m.

Observed early rehabilitation and mobilisation active interaction

Clinical staff performing ERM activities were instructed to record the planned and delivered ERM activity duration in medical records. A research nurse or co-ordinator used these data to complete the bespoke active interaction CRF, which was submitted to the PERMIT study office. CRFs were completed hourly between 9 a.m. and 5 p.m. by the local site research nurse. A retrospective review of clinical case records of ERM activities that occurred overnight was carried out, with CRFs completed accordingly. Overnight ERM interventions were defined as the time from the end of the observed active interaction period 17.01 until 08.59 before the start of the next period.

We defined a priori ERM as (1) any ERM activity, (2) any mobility ERM activity and (3) mobility activity out of bed, informed by scoping review and survey (see full breakdown of ERM activities, ERM group and level of ERM detailed in *Appendix 3*, *Table 40*). We excluded chest PT, tracheal tube suctioning and routine nursing 'cares' (such as mouth and eye cleaning).

Patients were defined as receiving any ERM intervention if any ERM was recorded on study day. Details on interventions such as type of ERM activity (mobility, non-mobility, out-of-bed, passive, active and psychological) and safety events (such as changes in heart rate, oxygen saturation, removal of tubes or falls) were recorded.

Primary outcome

- the delivery of any ERM activity on day 3 post admission (study day 1).

Secondary outcomes

- the delivery of any ERM activity on days 4–10 post admission (study day 1–7);
- the delivery of ERM involving any mobility activity and out-of-bed mobility ERM on days 3–10;
- the number, type and duration (e.g. dose) of ERM delivered on each day;
- predictive factors related to the delivery of ERM on day 3 post admission.

Data analysis

We reviewed data for errors: missing data, duplicated records and outliers. Extreme values were set to missing if they were deemed impossible, based on their validity range. Continuous variables were reported as mean and SD or median and IQR based on data distribution. Categorical variables were described in numbers and/or percentages.

The prevalence and scope of ERM were described as the proportion of patients provided with any 'active interaction' of any ERM on day 3 post admission. Proportions of eligible patients receiving ERM interventions were analysed for each day. Rate ratios of patients receiving an ERM intervention during the study period were analysed using a Poisson regression model.

Cumulative prevalence for each day in PICU after day 3 up to day 10 post admission was calculated. Cumulative proportion of patients receiving ERM interventions as per prespecified categories during the study period was described graphically using Kaplan–Meier estimation and event rate plots.

We undertook further analysis to understand potential predictive factors associated with ERM and the incidence of ERM. We performed multivariable logistic regression to evaluate predictive factors of ERM provided on day 3. Factors of interest were established following the PERMIT survey and expert group consensus. These included age; baseline PCPC score; unplanned versus emergency admission; ventilation status; requirement of vasoactive infusion, sedative infusion, or neuromuscular blocking drugs; presence of urinary catheter, CVC or arterial line; family member present or participating in ERM activity; and presence of PICU protocol.

We calculated level of mobility activity using a modified progression score previously described in the EU-PACK (European Prevalence of Acute Rehabilitation for Kids in the PICU) study[42] – Level 1: passive ROM, 2: sitting and exercise in bed, 3: sitting edge of bed, 4: held by parent or nurse (cuddle), 5: transfer to chair, 6: mat play, 7: standing, 8: walking in room/PICU, 9: walking out of PICU (see *Appendix 3*, *Table 40*). Further post hoc categorisation of ERM activities as enrichment, passive and active activities was also applied.

Adverse events rates were calculated per ERM activity. For zero rate observed AEs, the upper 95% CI are presented using Hanley's formula.[65]

Patient and public involvement and engagement

For an overview of the approach to patient and public involvement and engagement (PPIE) adopted throughout the study, please see *Chapter 8*. With this element of the study, we explored the potential consent model, especially the acceptability of an 'opt out' approach to consent. There was a study

recruiting at the time on PICU with an 'opt out' approach – the Sedation AND Weaning In Children trial (SANDWICH) trial.[66] At the time, the SANDWICH trial had recruited over 700 patients at Birmingham Children's Hospital (BCH), with only three families choosing to opt out of their child's data being collected. It was therefore regarded as a highly successful approach to consenting.

For the SANDWICH trial, parents were given a leaflet outlining that data collection was taking place on data routinely collected as part of 'normal care' which goes to the national PICU audit.[67] They were told that the SANDWICH team would have access to some of this information. In addition, the research team would also collect information from the child's medical notes and charts. All the data were anonymised and there were no interventions (at the individual level), just data collection. Parents were not asked for their informed consent. They received the Participant Information Sheet (PIS). If they did not want to take part, they then spoke to the clinical staff, who informed the research staff, and this was documented as an 'opt out'.

We spoke to families who had received the information to ask how they had experienced the process of approach for the SANDWICH study. In addition, we approached families who were participating in other research studies known to the PPIE lead (JMen) and whose children had recently been discharged from hospital. We spoke to six parents of four children (aged 0.3–6 years) who had experienced one or more PICU admission(s) and had experience of their child being recruited to research. We also spoke to three young people (aged 17–20) naive to PICU to participate as PPIE participants. Different models of consent were discussed and where there was no intervention then an opt-out model of consent was universally popular (*Table 3*). We also discussed the PISs and poster to inform parents about the observational study with them and they suggested a number of changes to the language, graphics and layout of them.

Results

Eligibility and enrolment

A total of 169 patients were enrolled into the study from 15 PICUs, with each PICU enrolling a median (IQR) of 10.0 (9.5–15.3) patients.

During the 14-day enrolment period, the median census on each PICUs was 10.5 patients (IQR 7.0–17.0; range 3–26). Overall, there was a median (IQR) of 1 patient (0–2) eligible per PICU per study day of whom 1 patient (0–1) was enrolled into the study per PICU per study day. This identified 203/2447 (8.7%) patients within each PICU eligible, of whom 158/203 (77.8%) were enrolled over the 14-day enrolment period (enrolment data were missing from 1 unit which recruited 11 patients). Ineligible patients had either not reached day 3 or had already reached day 4 or greater on day of screening. *Table 4* shows PICU patient census, eligibility and enrolment proportion. During days 8–14,

TABLE 3 Summary of PPIE feedback and impact on observational study

Aspect	PPIE feedback	Impact/changes made
Consent model	Opt-out consent acceptable Informed consent model also acceptable but adds burden at a difficult time	Opt-out consent approach used. Well received with no negative feedback from the 15 sites that participated and no queries or amendments from REC
Participant-facing information	Language: current draft was understandable and clear but few suggestions to change phrasing and shorten sentence length Graphics: would like to see pictures of what was meant by early rehabilitation activities and feedback about the selection of figures used Layout: need larger font, better spacing, figures to break up text	PIS and poster both amended. No negative feedback from the REC or the 15 sites that participated. Used as a template for Phase 3 work

TABLE 4 Number of patients in PICU, eligible and enrolment rate

Study day	Patients in PICU[a]	Eligible, *n*	Eligible (%)	Enrolled, *n*	Enrolled (%)
1	174	11	6	11	100
2	183	15	8	14	93
3	183	14	8	12	86
4	183	20	11	18	90
5	178	16	9	14	88
6	171	15	9	14	93
7	169	17	10	15	88
8	189	16	8	13	81
9	182	12	7	7	58
10	183	19	10	13	68
11	177	9	5	6	67
12	163	15	9	9	60
13	157	9	6	5	56
14	155	15	10	7	47

a 9 a.m. census data from 14/15 PICUs.

some sites reported not enrolling as they had already reached their target of 10 patients. Enrolment rate in study days 1–7 was 98/108 [90.7% (95% CI 83.6% to 95.4%)].

Demographics

Of the 169 patients, 59.2% were male; median age was 4.5 months (IQR 1.1–37.9). The majority (81%) were <4 years with 62.7% <1 year. Only 48 (28.4%) were ambulatory prior to PICU admission (key demographics at admission are in *Table 5*).

The most common admission diagnosis was bronchiolitis in 55 (32.5%). Eighty-four (49.7%) were admitted from another hospital, requiring retrieval into PICU. There were 127 (75.1%) emergency admissions, 150 (89.3%) required invasive ventilation at admission, 5 (3%) extracorporeal membrane oxygenation (ECMO) and 60 (35.5%) required cubicle isolation. Prior to admission, 66% had a PCPC score of 1 or 2 and 50% a POPC score 1 or 2, indicating a high proportion with moderate to severe disability pre-PICU. Admission predicted probability of mortality, as measured by PIM3, was median 1.2% (0.5–4.4%) and 68 (40.2%) children were enrolled in a PICU with an existing ERM protocol (as reported in the PERMIT survey – *Chapter 2*).

Patient clinical status on day 3 of admission (study day 1)

Between PICU admission and study day 1, 12 (7.1%) had surgery, 1 had a cardiac arrest. Most (119; 70%) remained ventilated by an ETT, 40 (23.7%) required vasoactive infusions and 3 remained on ECMO (*Table 6*).

Sedative medications were used in 108 (63.9%); 102 on opiates, 40 on benzodiazepines and 26 (15.3%) were on neuromuscular blocking drugs. In patients who could be assessed and on sedative drugs, comfort B sedation score was median (IQR) 12 (11–14), and 12 (12–15) if not receiving sedation. No patient was screened for delirium in any PICU. PELOD2 severity of illness median score was 4 (IQR 2–6).

TABLE 5 Demographic data – baseline for all, any ERM, mobility ERM and out-of-bed ERM on study day 1

Factor	All	No ERM	Any ERM activity	No mobility ERM	Mobility ERM	Not out-of-bed	Out-of-bed ERM	Missing
N	169	7	162	22	147	105	64	
Age (days), median (IQR)	135 (34–1137)	207 (51–680)	134 (33–1169)	49.5 (10–283)	183 (40–1299)	260 (47–1169)	92.5 (25–734.5)	0
Patient age group								
<1 month	34 (20.1)	0 (0.0)	34 (21.0)	6 (27.3)	28 (19.0)	18 (17.1)	16 (25.0)	0
1–3 months	46 (27.2)	3 (42.9)	43 (26.5)	7 (31.8)	39 (26.5)	26 (24.8)	20 (31.3)	
4–6 months	11 (6.5)	0 (0.0)	11 (6.8)	1 (4.5)	10 (6.8)	6 (5.7)	5 (7.8)	
7–11 months	14 (8.3)	2 (28.6)	12 (7.4)	4 (18.2)	10 (6.8)	9 (8.6)	5 (7.8)	
1–4 years	31 (18.3)	1 (14.3)	30 (18.5)	1 (4.5)	30 (20.4)	26 (24.8)	5 (7.8)	
5–8 years	6 (3.6)	0 (0.0)	6 (3.7)	0 (0.0)	6 (4.1)	2 (1.9)	4 (6.3)	
9–13 years	13 (7.7)	1 (14.3)	12 (7.4)	1 (4.5)	12 (8.2)	10 (9.5)	3 (4.7)	
13–17.9 years	14 (8.3)	0 (0.0)	14 (8.6)	2 (9.1)	12 (8.2)	8 (7.6)	6 (9.4)	
Ethnicity								
White	93 (55.0)	5 (71.4)	88 (54.3)	14 (63.6)	79 (53.7)	56 (53.3)	37 (57.8)	22
Mixed	4 (2.4)	0 (0.0)	4 (2.5)	0 (0.0)	4 (2.7)	2 (1.9)	2 (3.1)	
Asian	18 (10.7)	0 (0.0)	18 (11.1)	0 (0.0)	18 (12.2)	11 (10.5)	7 (10.9)	
Black	12 (7.1)	2 (28.6)	10 (6.2)	3 (13.6)	9 (6.1)	10 (9.5)	2 (3.1)	
Other	2 (1.2)	0 (0.0)	2 (1.2)	0 (0.0)	2 (1.4)	2 (1.9)	0 (0.0)	
Not stated	18 (10.7)	0 (0.0)	18 (11.1)	1 (4.5)	17 (11.6)	11 (10.5)	7 (10.9)	

TABLE 5 Demographic data – baseline for all, any ERM, mobility ERM and out-of-bed ERM on study day 1 (*continued*)

Factor	All	No ERM	Any ERM activity	No mobility ERM	Mobility ERM	Not out-of-bed	Out-of-bed ERM	Missing
Reason for admission								
Post surgery: neurology	5 (3.0)	0 (0.0)	5 (3.1)	0 (0.0)	5 (3.4)	4 (3.8)	1 (1.6)	1
Post cardiac surgery	16 (9.5)	1 (14.3)	15 (9.3)	5 (22.7)	11 (7.5)	9 (8.6)	7 (10.9)	
Other surgery	21 (12.4)	0 (0.0)	21 (13.0)	1 (4.5)	20 (13.6)	13 (12.4)	8 (12.5)	
Haematology/oncology	4 (2.4)	1 (14.3)	3 (1.9)	1 (4.5)	3 (2.0)	2 (1.9)	2 (3.1)	
Cardiac (medical)	16 (9.5)	0 (0.0)	16 (9.9)	1 (4.5)	15 (10.2)	7 (6.7)	9 (14.1)	
Infectious	5 (3.0)	0 (0.0)	5 (3.1)	0 (0.0)	5 (3.4)	3 (2.9)	2 (3.1)	
Neurology	9 (5.3)	1 (14.3)	8 (4.9)	3 (13.6)	6 (4.1)	6 (5.7)	3 (4.7)	
Renal	2 (1.2)	0 (0.0)	2 (1.2)	0 (0.0)	2 (1.4)	1 (1.0)	1 (1.6)	
Respiratory	80 (47.3)	4 (57.1)	76 (46.9)	10 (45.5)	70 (47.6)	51 (48.6)	29 (45.3)	
Trauma	1 (0.6)	0 (0.0)	1 (0.6)	0 (0.0)	1 (0.7)	1 (1.0)	0 (0.0)	
Other medical	9 (5.3)	0 (0.0)	9 (5.6)	1 (4.5)	8 (5.4)	7 (6.7)	2 (3.1)	
POPC								
1. Good	85 (50.3)	5 (71.4)	80 (49.4)	13 (59.1)	72 (49.0)	49 (46.7)	36 (56.3)	1
2. Mild disability	41 (24.3)	1 (14.3)	40 (24.7)	6 (27.3)	35 (23.8)	23 (21.9)	18 (28.1)	
3. Moderate disability	20 (11.8)	0 (0.0)	20 (12.3)	0 (0.0)	20 (13.6)	12 (11.4)	8 (12.5)	
4. Severe disability	21 (12.4)	1 (14.3)	20 (12.3)	2 (9.1)	19 (12.9)	19 (18.1)	2 (3.1)	
5. Coma/vegetative state	1 (0.6)	0 (0.0)	1 (0.6)	1 (4.5)	0 (0.0)	1 (1.0)	0 (0.0)	
PCPC								
1. Good	113 (66.9)	6 (85.7)	107 (66.0)	16 (72.7)	97 (66.0)	64 (61.0)	49 (76.6)	3
2. Mild disability	21 (12.4)	0 (0.0)	21 (13.0)	2 (9.1)	19 (12.9)	11 (10.5)	10 (15.6)	
3. Moderate disability	14 (8.3)	0 (0.0)	14 (8.6)	0 (0.0)	14 (9.5)	11 (10.5)	3 (4.7)	
4. Severe disability	17 (10.1)	1 (14.3)	16 (9.9)	2 (9.1)	15 (10.2)	16 (15.2)	1 (1.6)	
5. Coma/vegetative state	1 (0.6)	0 (0.0)	1 (0.6)	1 (4.5)	0 (0.0)	1 (1.0)	0 (0.0)	

Note
All values are numbers (%) unless other stated.

TABLE 6 Clinical status for all, any ERM, mobility ERM and out-of-bed ERM on study day 1

Factor *n*(%) or median (IQR)	All	No ERM	Any ERM activity	No mobility ERM	Mobility ERM activity	Not out-of-bed	Out-of-bed ERM activity	Missing
n =	169	7	162	23	146	105	64	
PELOD 2 score median (IQR)	4 (2–6) (*n* = 169)	5 (1.5–6) (*n* = 8)	4 (2–6) (*n* = 161)	5 (4–7) (*n* = 23)	4 (1–5) (*n* = 146)	5 (3–6) (*n* = 105)	2.5 (0–5) (*n* = 64)	
Type of ventilation								
No oxygen support	19 (11.2)	1 (12.5)	18 (11.2)	2 (8.7)	17 (11.6)	6 (5.7)	13 (20.3)	
High-frequency oscillator	5 (3.0)	0 (0.0)	5 (3.1)	1 (4.3)	4 (2.7)	5 (4.8)	0 (0.0)	
Conventional ventilation	114 (67.5)	6 (75.0)	108 (67.1)	19 (82.6)	95 (65.1)	86 (81.9)	28 (43.8)	
Non-invasive (CPAP/ BiPAP)	15 (8.9)	1 (12.5)	14 (8.7)	1 (4.3)	14 (9.6)	6 (5.7)	9 (14.1)	
High-flow oxygen	10 (5.9)	0 (0.0)	10 (6.2)	0 (0.0)	10 (6.8)	1 (1.0)	9 (14.1)	
Supplemental oxygen only	6 (3.6)	0 (0.0)	6 (3.7)	0 (0.0)	6 (4.1)	1 (1.0)	5 (7.8)	
Vasoactive infusions	40 (23.7)	3 (37.5)	37 (23.0)	7 (30.4)	33 (22.6)	27 (25.7)	13 (20.3)	1
Neuromuscular blocking drugs	26 (15.4)	4 (50.0)	22 (13.7)	8 (34.8)	18 (12.3)	23 (21.9)	3 (4.7)	1
Sedation medication	108 (63.9)	6 (75.0)	102 (63.4)	20 (87.0)	88 (60.3)	82 (78.1)	26 (40.6)	1
Screened for delirium	0	0	0	0	0	0	0	
ETT								
Oral	82 (48.5)	3 (37.5)	79 (49.1)	12 (52.2)	70 (47.9)	63 (60.0)	19 (29.7)	
Nasal	44 (26.0)	3 (37.5)	41 (25.5)	8 (34.8)	36 (24.7)	30 (28.6)	14 (21.9)	
No tube	43 (25.4)	2 (25.0)	41 (25.5)	3 (13.0)	40 (27.4)	12 (11.4)	31 (48.4)	
Central venous line	103 (60.9)	4 (50.0)	99 (61.5)	13 (56.5)	90 (61.6)	72 (68.6)	31 (48.4)	1
Arterial line	72 (42.6)	5 (62.5)	67 (41.6)	15 (65.2)	57 (39.0)	57 (54.3)	15 (23.4)	2
Haemodialysis catheter	7 (4.1)	0 (0.0)	7 (4.3)	1 (4.3)	6 (4.1)	5 (4.8)	2 (3.1)	2
Extracorporeal membrane oxygenation	3 (1.8)	2 (28.6)	1 (0.6)	3 (13.0)	0 (0.0)	3 (2.9)	0 (0.0)	2
Urinary catheter	103 (60.9)	5 (62.5)	98 (60.9)	16 (69.6)	87 (59.6)	83 (79.0)	20 (31.3)	2
Surgical drain	8 (4.7)	1 (12.5)	7 (4.3)	2 (8.7)	6 (4.1)	5 (4.8)	3 (4.7)	12
Chest tube	15 (8.9)	2 (25.0)	13 (8.1)	6 (26.1)	9 (6.2)	11 (10.5)	4 (6.3)	11
Intracranial pressure monitor	4 (2.4)	0 (0.0)	4 (2.5)	0 (0.0)	4 (2.7)	3 (2.9)	1 (1.6)	2

Note
All values are numbers (%) unless other stated.

Central venous access was used in 103 (60.9%), arterial access in 72 (42.6%), and 103 (60.9%) had a urinary catheter. Pressure ulcers were reported in 6 (3.6%) patients.

Early rehabilitation and mobilisation prevalence

On the first day of PERMIT study (day 3 post-PICU admission) overall 162/169 (95.9%) received at least one ERM activity. A mobility ERM activity was delivered to 147/169 (87.0%) of which an out-of-bed mobility ERM was delivered to 64/169 patients (37.9%).

Figure 5 shows the reduction in number of patients remaining in PICU following enrolment to PERMIT and the prevalence for (1) any ERM, (2) mobility ERM and (3) out-of-bed ERM mobility. Of note, by day 7 post PICU admission, half of patients enrolled into PERMIT had been discharged and by day 9, 113 (67%) had been discharged and 2 (1%) had died.

The rate of receiving ERM during the PERMIT study period, analysed using a Poisson regression model, did not change across the study period. We did not identify a significant trend with rate ratios of (1) any ERM: 0.98 (95% CI 0.92 to 1.05, $p = 0.57$), (2) mobility ERM: 0.97 (95% CI 0.93 to 1.01, $p = 0.14$) and (3) out-of-bed mobility 0.97 (95% CI 0.93 to 1.01; $p = 0.14$).

Cumulative probability of early rehabilitation and mobilisation

Figure 6a shows that while over 95% of enrolled patients were observed to have received an ERM intervention on day 1 of the study period, mobility ERM and out-of-bed ERM were less frequent (see *Figure 6b* and *c*). However, by day 6 of the study, 98% of patients had received a mobility ERM and 80% (see *Figure 6b*) of patients had received an out-of-bed ERM at some point during their observed period (see *Figure 6c*).

Description of early rehabilitation and mobilisation

In total, 3696 ERM episodes capturing 4978 ERM activities occurred during 729 patient days. On the first study day (day 3 post PICU admission), 169 patients received 977 ERM episodes and 1302 ERM activities [median IQR 7 (4–10) ERM activities per patient].

Analysing the whole study period, positioning (which incorporated the mobility element) (1205/4978; 24%) and non-mobility positioning (1177/4978; 23.6%) were the most frequent activities (*Figure 7*). Active mobility was less frequent: the majority were active movement (e.g. rolling, active ROM) and sitting up in bed or transfer out of bed to chair or mat. No in-bed cycling was reported throughout the observation period.

Table 5 compares the baseline characteristics of patients receiving any ERM, mobility ERM or out-of-bed ERM and those who did not on the first study day. Patients receiving mobility ERM tended to be older that those who did not; however, the opposite was seen in out-of-bed mobility, where younger patients (especially <3 months) were more likely to receive mobility out of bed (e.g. cuddles). We identified no difference across ethnicity groups or diagnostic admission group in the proportion of patients receiving

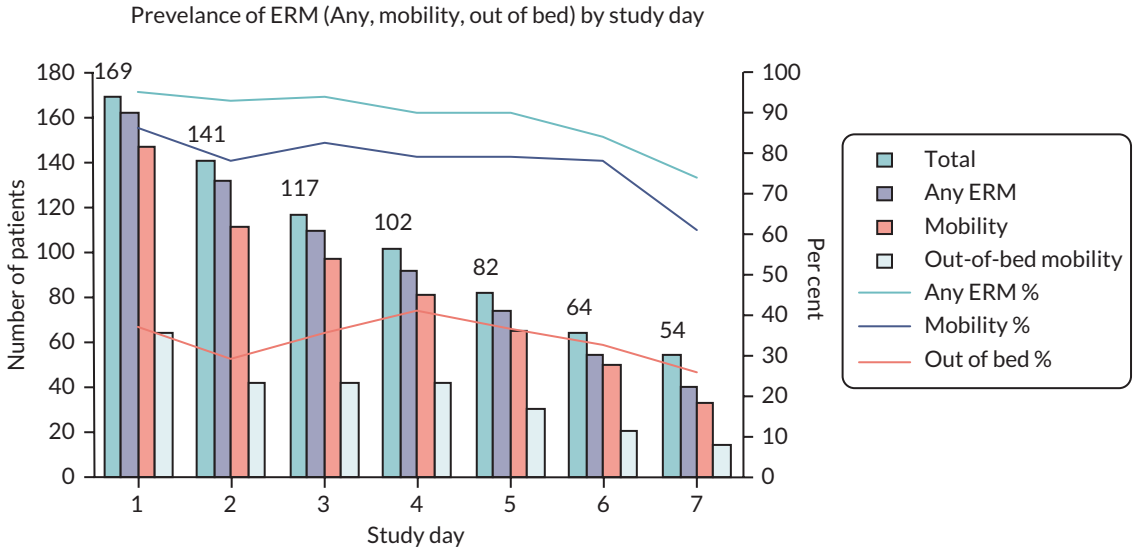

FIGURE 5 Prevalence of ERM for each study day in PICU.

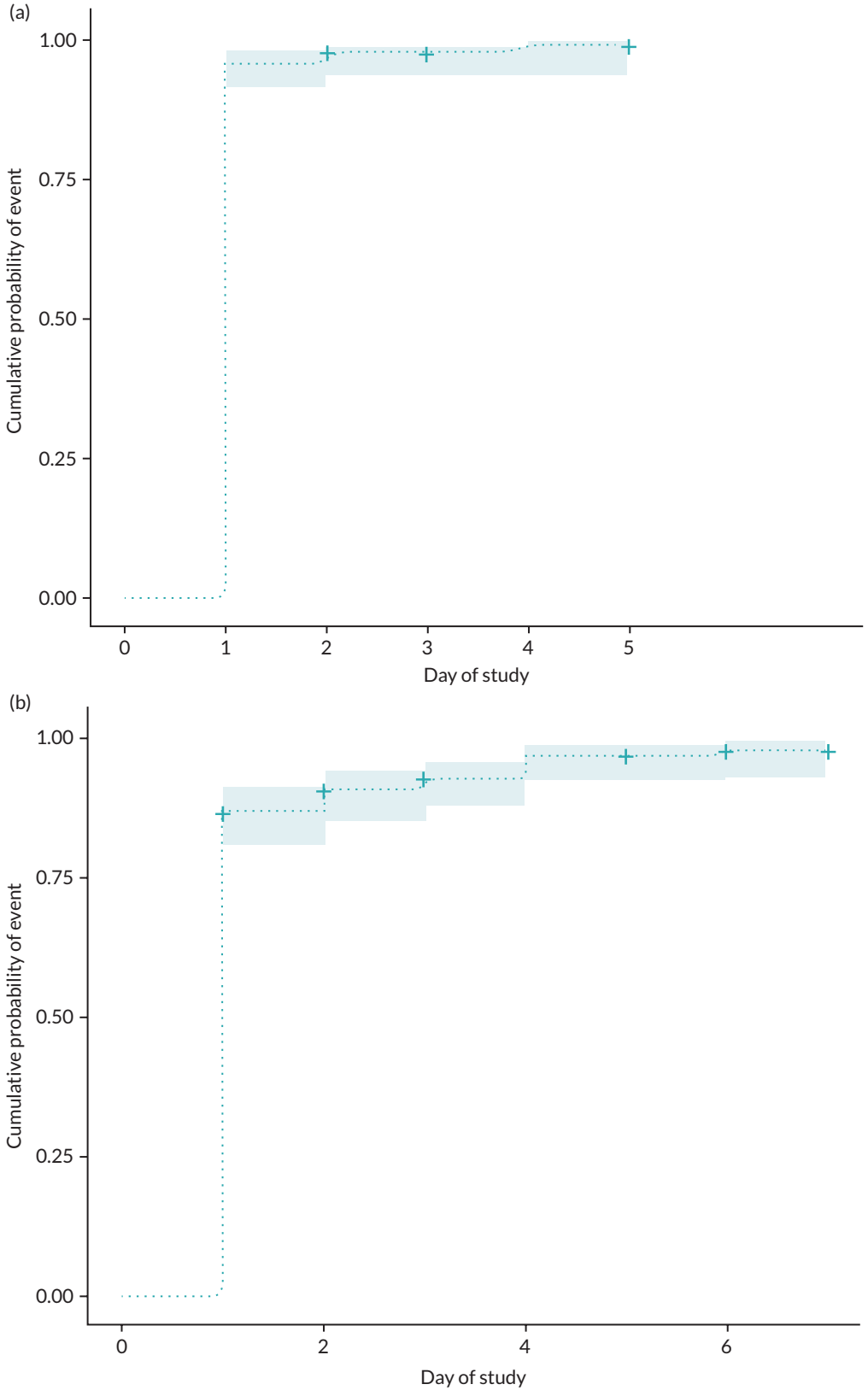

FIGURE 6 Cumulative probability of (a) any ERM, (b) mobility ERM and (c) out-of-bed ERM. (*continued*)

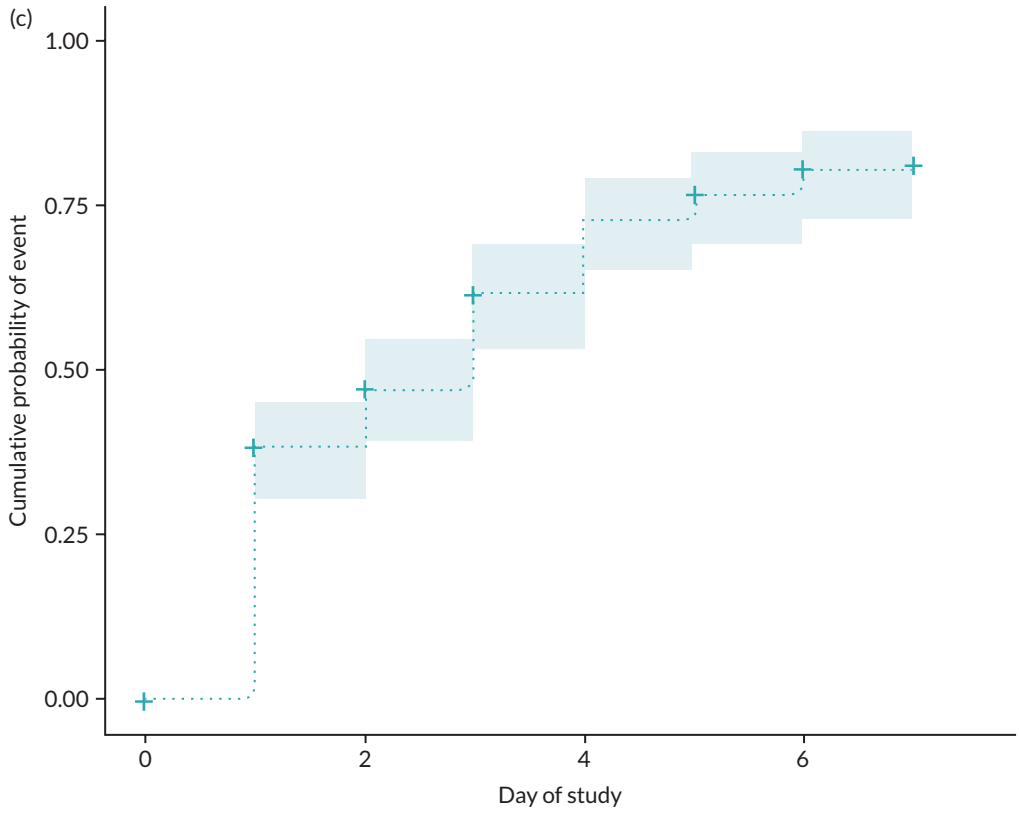

FIGURE 6 Cumulative probability of (a) any ERM, (b) mobility ERM and (c) out-of-bed ERM. (*continued*)

each category of ERM. We did identify that patients with moderate (PCPC 3) or severe disability (PCPC 4) received less out-of-bed mobility.

Table 6 compares the clinical status of patients with ERM type on the first study day. Patients receiving or not receiving any ERM or mobility ERM were similar in respect to the majority of measured clinical status factors. The only differences were between patients receiving out-of-bed mobility or not. There were more patients receiving invasive ventilation (high-frequency oscillation and conventional ventilation), use of neuromuscular blocking drugs, sedative drugs and with additional lines or tubes (e.g. central venous catheter, arterial line, urinary catheter and chest tubes) in the group not receiving out-of-bed mobility. This was also reflected in the higher PELOD2 organ dysfunction score for patients not receiving out-of-bed ERM [5 (IQR 3–6)] versus those who did receive [2.5 (IQR 0–5)].

Mobility activities

Using the ranking scale described by Ista *et al.*[42] on the first day of study 147/169 (87%) had a mobility ERM activity. The ranked activities are shown in *Table 7*. Most were either passive ROM or cuddles. Only 29 (17%) involved ranked 5–9 activities (transferring out of bed, mat play, standing or walking).

Staffing and parental involvement in early rehabilitation and mobilisation

We examined staffing and parent data across all ERM episodes (which may have involved a combination of activities). As shown in *Figure 8*, registered nursing staff were involved with the majority of ERM episodes (3127/3696, 85%). Parents/guardians were present for 1614/3696 (44%) and participated in delivering 1372/3696 (37%). Physiotherapists delivered only a small proportion of ERM episodes (361/3696; 10%).

For individual patients, on the first study day, only 57/162 (35%) of patients received at least one ERM episode delivered by a physiotherapist. Across the duration of the study period this increased to 95/162 (59%) of patients having the input of a physiotherapist for at least one ERM activity. While the majority of ERM episodes were delivered by registered nursing staff or parents, without specialist therapy input there is a risk that ERM activity quality may be low (e.g. not targeted at the patient acuity or developmental age).

Timing and duration of early rehabilitation and mobilisation

ERM episodes were commenced throughout the 24-hour period of PICU with 1855/3730 (49.7%) occurring between 09.00 and 17.00 (*Figure 9*). The median duration of ERM episode was 15 (IQR 10–30) minutes and 37% of ERM episodes were of short duration (1–14 minutes) (*Figure 10*).

As the professional group present at the bedside 24/7, nursing staff delivered 85% of ERM activities and 48% of these activities were commenced outside '9 a.m. to 5 p.m. office hours' and emphasise the need to view ERM as a 24/7 intervention and not just an activity performed during office hours by physiotherapists. Less than 10% of ERM episodes delivered by a physiotherapist were outside 9 a.m. to 5 p.m..

Predictive factors associated with out-of-bed mobility

We created a multivariable logistic regression model to explore predictors of interest for out-of-bed ERM on study day 1 (day 3 of PICU) (*Figure 11*). Factors associated with a decreased odds of out-of-bed mobility included pre-PICU severe disability (PCPC score 4 vs. 1) [OR 0.09 (95% CI 0.01 to 0.61)], invasive ventilation [OR 0.23 (95% CI 0.06 to 0.83)] and presence of a urinary catheter [OR 0.16 (95% CI 0.16 to 0.42)]. The only statistically significant factor associated with increased odds of out-of-bed mobility was the presence of a parent or guardian and/or their involvement in the ERM activity [OR 13.46 (95% CI 1.05 to 172.7)], although the CI was wide. Of note, a vasoactive infusion was associated with increased out-of-bed mobility [OR 1.85 (95% CI 0.5 to 6.82)] and use of neuromuscular blocking drugs was associated with decreased out-of-bed mobility [OR 0.33 (95% CI 0.08 to 1.4)]; however, both of their CIs crossed 1. We were unable to create models for any ERM or mobility ERM because of the high rate of positive events for both on study day 1.

Adverse events

There were 106 recorded AEs during 78 separate ERM episodes (*Table 8*). Overall proportion of ERM activities with an AE was 106/3696 (2.87%; 95% CI 2.35 to 3.45), which equates to 1 in 35 (95% CI 1 in 29 to 1 in 43) ERM activities. The most frequent reported event was desaturation in 38 (1.03%; 1 in 97) of ERM activities and discomfort of patient or tiredness in 18 (0.49%; 1 in 205). There was only one ETT tube dislodged, and seven other tubes dislodged, during the entire study period. Overall ERM delivery was safe, with a very low rate of AEs.

Summary of findings to inform the PERMIT study

- Paediatric intensive care units were able to enrol 90% of eligible patients into the observational study during week 1, using an opt-out consent model.
- All participating UK PICUs delivered some form of ERM to patients. However, the range of ERM delivered is broad, with most of the time and resources delivered to basic patient positioning, family holding of patients and active movement in bed.
- ERM, using its broadest definition, is delivered to nearly all PICU patients on day 3 after admission and throughout their PICU stay. We did not identify a change in the prevalence of ERM delivery across study days. However, mobility and especially out-of-bed mobility was less frequent.

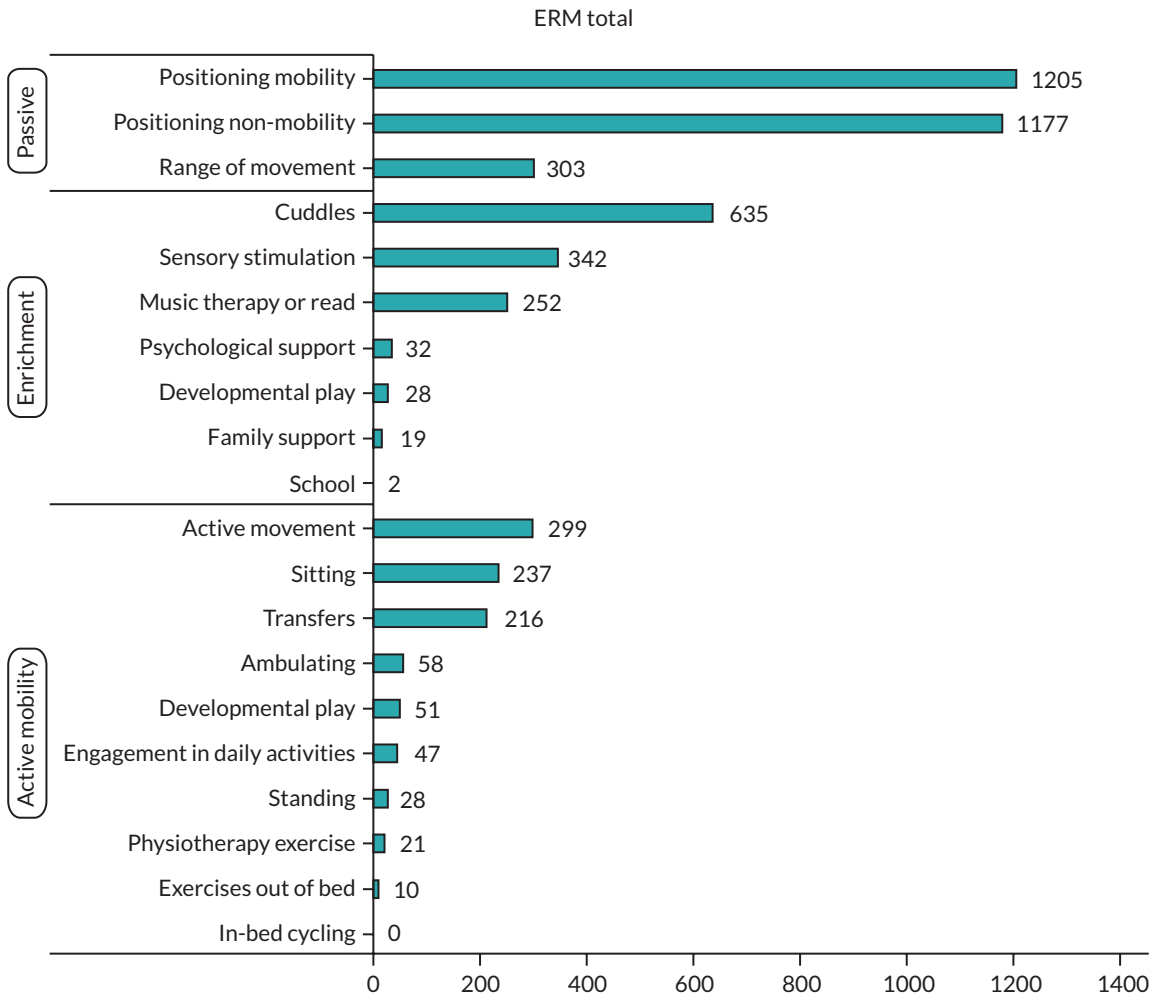

FIGURE 7 All ERM activities ranked by active, enrichment and passive categories.

TABLE 7 Proportion of study day 1 ranked mobility ERM

Rank	Description	Number (%) of patients
1	Passive ROM	38 (25.9)
2	Sitting in bed	21 (14.3)
4	Held/cuddle	59 (40.1)
5	Transfer to chair	17 (11.6)
6	Mat play	2 (1.4)
7	Standing	4 (2.7)
8	Walking in room	6 (4.0)
9	Walking out of room	0 (0)

- We identified some barriers and modifiable factors associated with delivery of out-of-bed mobility (e.g. invasive ventilation, presence of urinary catheter, pre-existing severe disability and parental presence and involvement in ERM). Strategies to address these could improve rates of out-of-bed mobility.

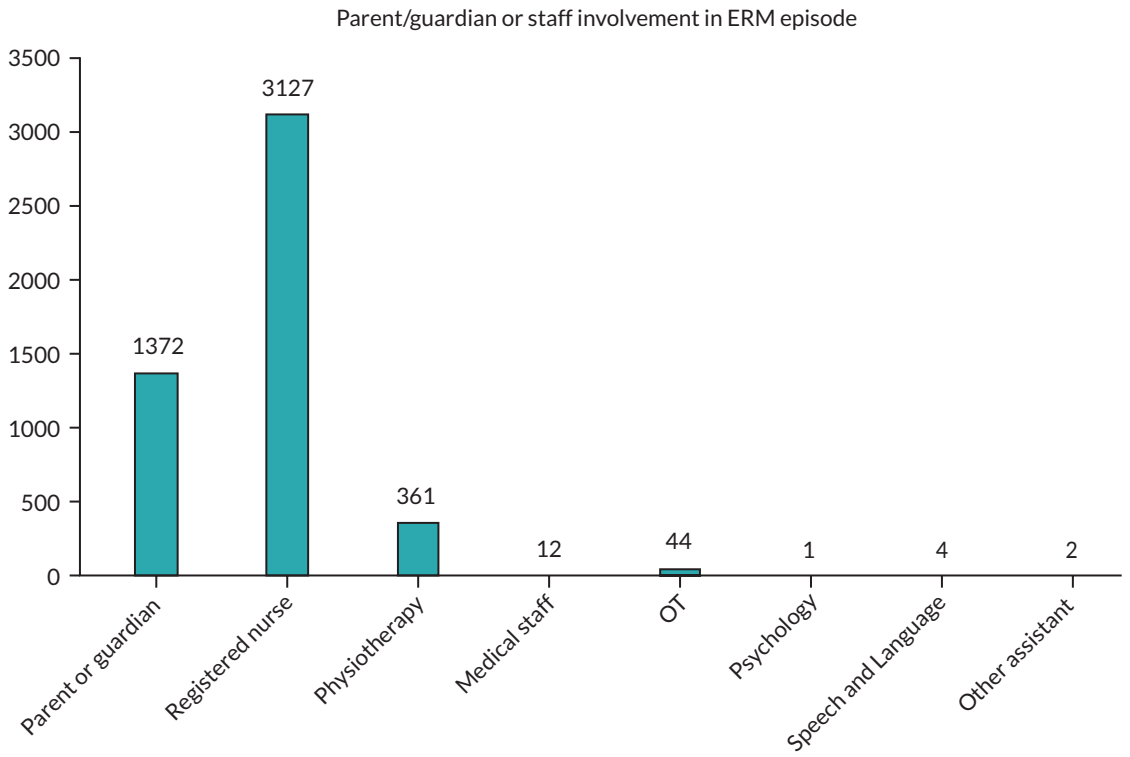

FIGURE 8 Number of parents, guardians or healthcare professionals involved in ERM episodes.

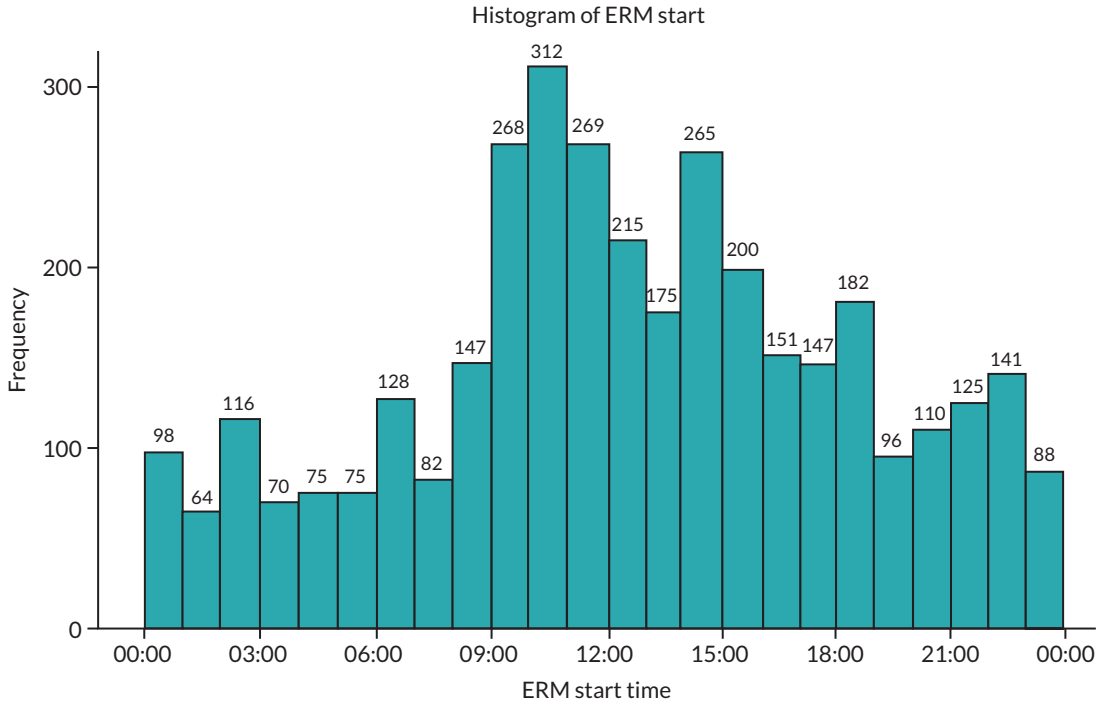

FIGURE 9 Histogram of ERM start time.

- The presence of an existing ERM protocol neither increased nor decreased the odds of receiving out-of-bed mobility.
- Reported safety profile of patients receiving ERM is very good. There is a very low level of incidents, safety events, or physiological effects reported during ERM delivery.

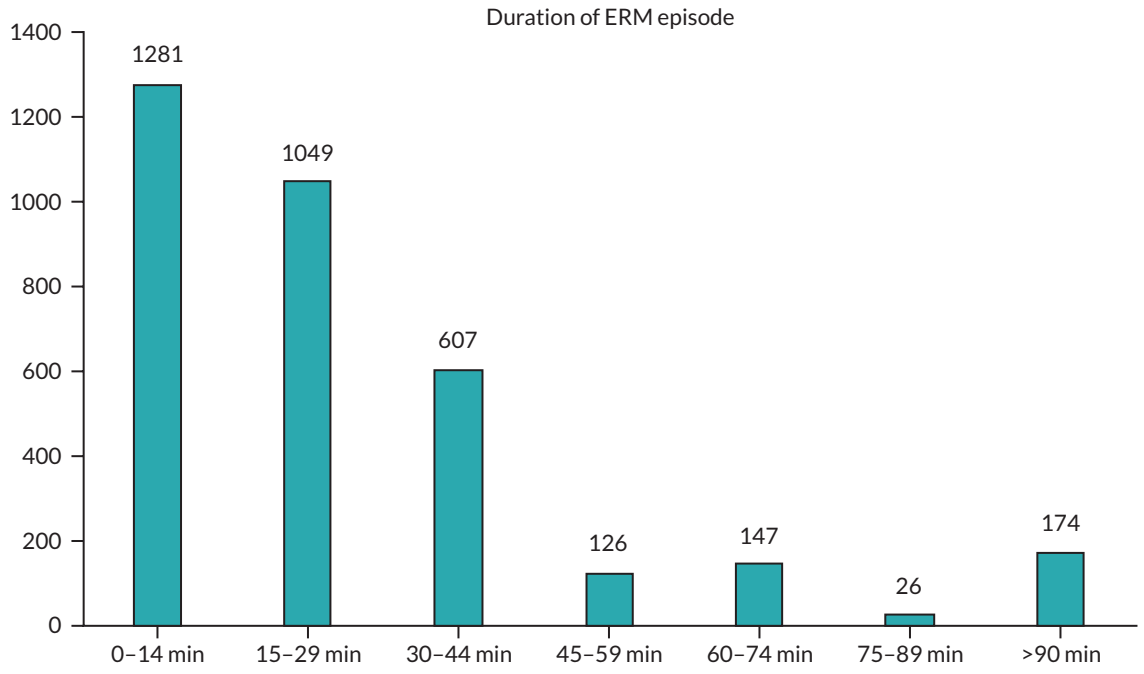

FIGURE 10 Duration of ERM episode (data available *n* = 3410).

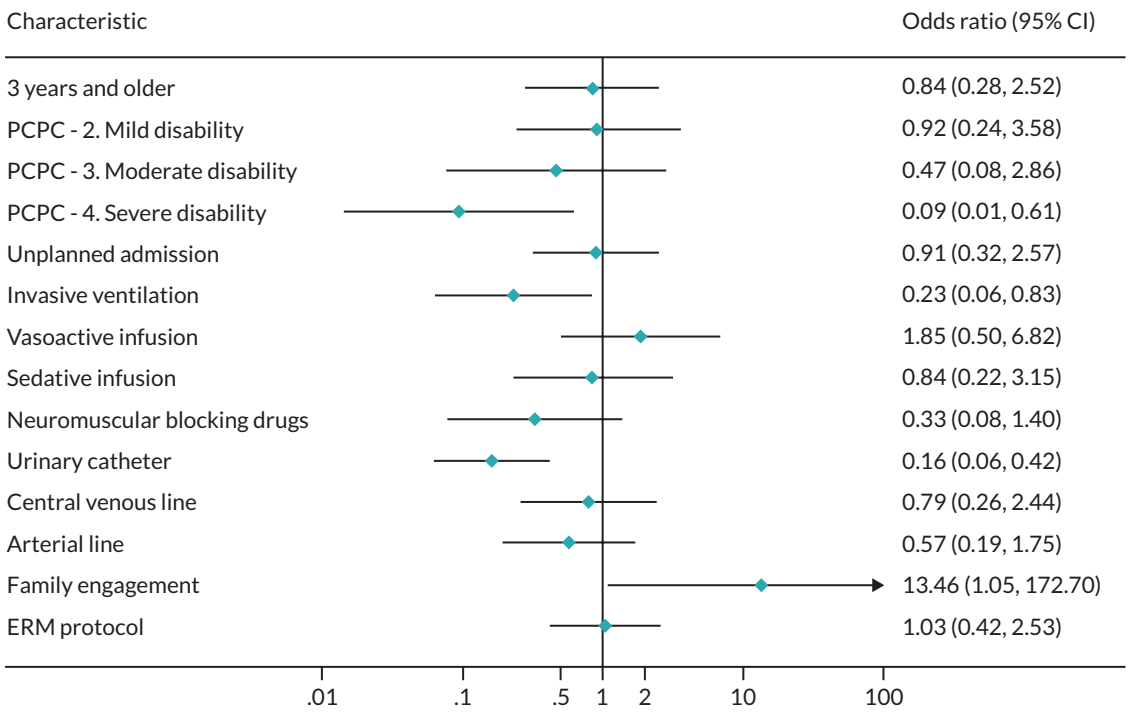

FIGURE 11 Forest plot of odds of out-of-bed mobility on study day 1 by key factors.

- Important information regarding PICU practice was obtained. Delirium screening is universally absent in participating PICUs. Nursing staff and parents deliver the majority of ERM activities throughout the 24-hour period. Physiotherapists only delivered 10% of ERM, although 59% of patients received at least one PT delivered ERM episode at some point. There was minimal input from other medical, therapy, or support staff reported. Any ERM manual or intervention plan will need to utilise available staff.

TABLE 8 Adverse event rates

Adverse events	Number	Per cent of ERM activities (95% CI)	1 in *x* rate
Desaturation (>15% decrease from baseline)	38	1.03	97
Discomfort of patient or tiredness	18	0.49	205
Clinically significant change in heart rate	14	0.38	264
Clinically significant increase in O_2 requirement	8	0.22	462
Line/tube dislodgement or removal	7	0.19	528
Clinically significant change in blood pressure	5	0.14	739
Clinically significant increase in end-tidal CO_2	5	0.14	739
Other tube removal	3	0.08	1232
Asynchrony with ventilator	3	0.08	1232
Clinically significant change in respiratory rate	2	0.05	1848
Dislodgement/unplanned removal ETT	1	0.03	3696
Pain	1	0.03	3696
Arrhythmia	1	0.03	3696
Fall	0	0.00	11,088[a]
Cardiac arrest or CPR	0	0.00	11,088[a]
Changes in mental status	0	0.00	11,088[a]
Total: Any AE	**106**	**2.87 (2.4 to 3.5)**	**35 (29 to 43)**

CPR, cardiopulmonary resuscitation.
a Upper 95% CI estimate using Hanley's formula.[65]

Note
Reported for *n* = 3696. AEs occurred within 78 ERM activities.

Chapter 4 Phase 2: developing early rehabilitation and mobilisation intervention

Introduction

Early rehabilitation and mobilisation in PICU, like most rehabilitation interventions, is a complex intervention, in relation to the diverse actions, reasoning, and resources embedded in enacting ERM in intensive care, as well as the diversity of PICU contexts. Following the Medical Research Council (MRC) guidance on developing complex interventions,[68–70] we anticipated that our intervention development work would involve learning from and adapting elements of existing ERM interventions, as they are already in use in some PICU settings internationally and a few sites in the UK. In this chapter, we show how we used the results from our survey, observational study and scoping review (see *Chapters 1*, *2* and *3*), together with a range of other evidence and expertise, to design the ERM intervention manual, called the PERMIT manual (*Figure 12*). The intervention manual is a detailed prototype specifying the content of ERM for diverse patient populations and setting out how ERM can be implemented in varied paediatric intensive care settings. The feasibility and acceptability of the manual, and core elements of clinical trial designs for evaluating ERM, were subsequently explored across three PICUs (see *Chapter 5*).

Study management

Phase 2 was co-led by co-applicants JMc, RF and TR (the core intervention development team). Two research associates (Dr Laura Cutler and Dr Olivia Craw, Faculty of Medical Sciences, Newcastle University) supported the organisation of the workshops and literature-based work. The study management group provided input into protocol, ethics application design and data interpretation.

Important changes to protocol

The PERMIT protocol planned a Phase 2a, Health Research Association (HRA) approved, workshop with parents and children. In discussion with and approval of National Institute for Healthand Care Research (NIHR) Health Technology Assessment (HTA) funder, this subphase was not started due to the impact of the COVID19 pandemic.

Methods and results

In developing the proposed ERM intervention, alongside the MRC frameworks we also drew on a range of conceptual resources from implementation science – notably Normalisation Process Theory (NPT),[71,72] Theoretical Framework of Acceptability (TFA),[73] Expert Recommendations for Implementing Change (ERIC),[74] behaviour change Theory and Technique Tool[75] – as well as the Person-Based Approach (PBA) to intervention development.[76] PBA emphasises:

> *prioritising and incorporating user perspectives wherever possible, while ensuring the intervention retains all the elements that theory and evidence suggest will be effective.*[77]

In line with PBA, the development of our ERM intervention prototype(s) has been intimately shaped by the involvement of key target users of the manual – multidisciplinary clinical stakeholders. Throughout the development process, we worked with clinical stakeholders within the wider PERMIT research team as well as healthcare professionals across the UK and international PICU clinicians. However, due to the evolving COVID context, planned workshops with parents/carers and CYP were not possible.

As outlined in *Figure 12*, the intervention development process initially involved establishing key messages and areas of uncertainty from our survey, observational study, and scoping review. We

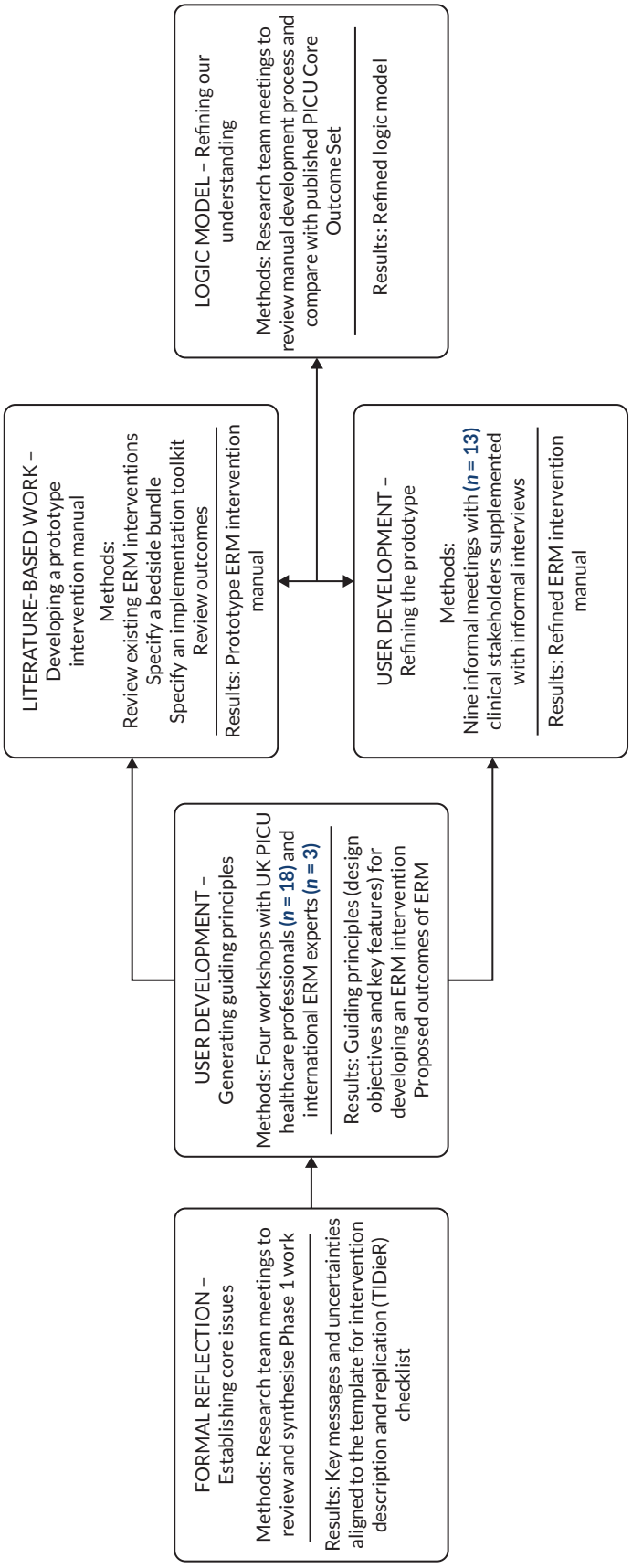

FIGURE 12 Overview of the intervention development process.

then explored the potential dimensions of the intervention with clinical stakeholders and iteratively refined prototypes of the intervention manual in relationship to evidential, practice-based and theoretical ideas.

Patient and public involvement and engagement

For an overview of the approach to PPIE adopted throughout the study, please see *Chapter 8*. Within this intervention development element of the study, PPIE work was only conducted to inform the Research Ethics Submission. We had planned to undertake PPIE work with parents with direct experience of involvement in PICU research studies in relation to discussing potential trial designs as well as patient-centred outcomes, but the research suspension imposed in response to directives to prioritise COVID-related research[78] created a challenge. As outlined in *Chapter 8*, suspension of research recruitment reduced the number of studies which were open and recruiting and reduced researchers' contact with families. Additionally, there were no pre-established local or national groups of parents with experiences of PICU. This created challenges for the PPIE lead to speak to parents with experience of being recruited to research. We decided to delay that element of the PPIE work until the feasibility study in Phase 3.

Formal reflection – establishing core issues

Purpose: to formally describe and synthesise the key messages, assumptions and uncertainties that emerged from our prior Phase 1 work to guide our intervention development work.

Methods: we reviewed the results of the survey, observational study and scoping review (see *Chapters 1*, *2* and *3*), and undertook discussions with the wider PERMIT research team. We further refined and conceptualised the core findings of this process by aligning them to elements of the template for intervention description and replication (TIDieR) checklist.[79]

Results: as outlined in *Table 9*, people see the potential value of ERM for the diverse patient populations within PICU and are willing to support its (safe) delivery but are uncertain how best to deliver it. The current evidence base and analysis of existing practice demonstrate that ERM is defined and enacted in multiple ways, ranging from more formal referral processes (directing patients only to specific allied health professionals), to a range of mobilisation and non-mobilisation activities, to being seen as encompassing everyday standards of good practice in PICU care. Core questions remain unresolved in relation to the conceptualisation of ERM, the pragmatics of operationalisation (e.g. how 'early' should ERM be delivered), and how best to measure the delivery and potential impact of ERM.

User development – generating guiding principles for the intervention

Purpose: to explore clinical stakeholders' views and experiences of ERM for different populations, including feasible and acceptable content, delivery, implementation and important outcomes of ERM.

Methods: we took forward the key messages and uncertainties from Phase 1 into interactive workshops with UK NHS healthcare professionals and international ERM experts. The workshops received ethical approval from Newcastle University (NU Reference 14224/2018). We also planned to conduct workshops and interviews with parents and CYP in Spring 2020. These received HRA approval (IRAS 270791) but were unable to proceed as NHS Research and Development were not allowing non-COVID research at the time.

Sampling and recruitment: we recruited a multidisciplinary group of NHS healthcare professionals with diverse experience of ERM in PICU settings. We recruited from those who had participated in the Phase 1 survey and agreed to be approached about further work. They were approached via e-mail and a total of 18 professionals from 5 PICUs were included – 3 consultant doctors, 3 senior nurses, 5 physiotherapists (including 2 clinical specialists), 5 OTs (including 1 clinical specialist), 1 dietician and 1 play specialist. We also recruited a multidisciplinary group of international experts leading research and quality

TABLE 9 Key messages and uncertainties from Phase 1

What is the underpinning rationale, theory or goal of ERM?

- Wide range of views on what ERM encompasses from a narrow focus on movement and mobilisation to a broader focus on adapting the environment and optimising medication.
- Boundary is not well defined between broader conceptualisations of ERM and 'good general PICU care'.
- Existing specifications are often vague. Where more specificity is provided, underpinning conceptual/theoretical coherence and definition are often lacking.
- No consensus on key mechanisms of action or essential elements/active ingredients of ERM.
- Might be especially challenging to conceptualise ERM and differentiate it from usual care in very young patients.

Which patient populations are eligible for ERM?

- Traditional emphasis on ERM for certain diagnoses (e.g. acute traumatic brain injury). However, this is now acknowledged as too restrictive.
- Desire to bring ERM to (nearly) all patients. However, there is an awareness of extreme heterogeneity and associated challenges:
  (1) Majority of PICU patients are young (<4 years) or very young (<1 year)
  (2) Wide variety of underlying medical conditions and reasons for admission
  (3) Children with pre-existing cognitive and other impairments are over-represented in the PICU population – developmental/cognitive level may be delayed compared to chronological age.
- Disagreement between clinicians about patient suitability is a barrier to ERM both in general and in relation to individual patients and particular patient groups.
- LOS is an important consideration – there is support for use of an (undefined) minimum LOS threshold to 'make ERM worthwhile'.

When is ERM initiated?

- Agreement that consideration of – and consensus on need for – rehabilitation and mobilisation increase with LOS. However, this is at odds with the goal of 'early' rehabilitation and mobilisation.
- Uncertainty and wide variation in suggested time points for starting ERM (24 hours to >7 days).
- Uncertainty as to whether timing should be based on day of admission or clinical recovery milestones (stage in critical illness recovery trajectory). Both are important to people – can these be standardised?
- Support for the idea of a minimum LOS – many patients are discharged within 24–48 hours and the majority have a LOS <7 days. ERM may be unnecessary in very short admissions.
- Support for the concept of 'ERM as early as the patient's clinical condition allows' – physiological stability is seen as the most important patient factor influencing ERM timing. However, there is slow recognition of patient readiness for ERM, which conflicts with this concept.
- Need a decision-making process that includes consideration of whether and when ERM is appropriate/possible for each patient with clarity around responsibility for this decision-making.

What processes and materials are involved in ERM?

- Wide variety of conceptualisations of ERM:
  (1) ERM as 'mere referral' for PT, OT, speech and language (i.e. ERM as an undefined 'black box' intervention). Timing of these referrals seen as a key component of ERM.
  (2) ERM as mobilisation activities and non-mobilisation activities. However, there is enormous variability in terms of wide-ranging activity categories and individual activities.
  (3) Mobilisation activities include a very wide range of in- and out-of-bed exercises. There is a lack of clarity on dimensions such as active versus passive mobilisation activities (e.g. where do positioning, stretching, seating fit?).
  (4) Non-mobilisation activities include sedation protocols, analgesia, sleep hygiene, delirium screening/reduction, cuddles, nutrition, and chest PT. Are these vital 'co-interventions' (often a part of usual care) or are they within the scope of ERM? They are often poorly reported, although they are understood to influence delivery of ERM.
- ERM as 'more than just activities' – important to also normalise and enrich the wider environment.
- Again, lack of clarity over relationship between ERM and 'good general PICU care'. Is ERM different to usual care or is ERM usual care delivered earlier? There is also no consensus on usual care.
- Availability of specialist equipment and resources is very variable and an important constraint.

Where is ERM delivered?

- Physical space in which to deliver ERM (e.g. at bedside) is very variable and an important constraint.

TABLE 9 Key messages and uncertainties from Phase 1 (*continued*)

How much ERM is delivered?

- Clinicians want to be guided by a protocol that is flexible rather than prescriptive and sets out optimal timing, intensity, frequency and duration of ERM. However, no evidence base exists to determine optimal timing, dose or progression of ERM.
- How important is intensity (e.g. minutes/hours per day)? Is it as important as timing (i.e. days since admission)?
- Twice-daily ERM sessions are commonly discussed. However, would this be a realistic goal or minimum standard given major staffing concerns?

How is ERM tailored?

- ERM is typically personalised to the individual patient and not standardised. However, strategies for personalising and tailoring ERM are not clearly reported.
- Clinicians want a protocol that is flexible rather than prescriptive.
- ERM should be graded. However, criteria for how and when to progress ERM (i.e. how to make it more challenging as a patient's condition/tolerance improves) are vague and variable.
- Uncertainty as to how to best monitor tolerance of ERM. Currently, this is done very informally and subjectively based on monitoring of individual patients' physiological parameters, behaviour and AEs.

Who delivers ERM?

- ERM delivery is multidisciplinary. Doctors have a role in assessing appropriateness. Nurses and physiotherapists are especially important in delivery.
- ERM may be viewed as a 'physiotherapist role'. However, nurses are the only profession present 24/7 and they do the majority of ERM delivery, particularly in the context of wider conceptualisations of ERM.
- Depending on the setting, ERM delivery may also include OTs, SLTs, play therapists, psychologists or dieticians.
- Parents are important in ongoing ERM delivery and their role could be enhanced. They are usually present when ERM is happening.
- Staffing is frequently raised as an issue – staff capacity fluctuates and is frequently insufficient.
- Inadequate training is a barrier to ERM delivery.

How is ERM delivered safely?

- Objective data indicate low AE rates in ERM. However, safety is a real concern for people, especially tube and line dislodgement (including accidental extubation) and especially mobility and out-of-bed ERM activities.
- Range of possible safety considerations have been identified – which are most relevant and how can these be monitored and managed?
- Need an approach for stratifying patient acuity levels to guide ERM delivery.
- Need more formal guidelines for assessing patient safety and tolerance.

What other factors influence implementation of ERM?

- Strong support in the UK for ERM – ERM is considered a priority.
- ERM implementation processes have not been described in detail or theorised. However, multiple barriers to ERM delivery and adherence have been reported.
- Clinicians want implementation support to address modifiable barriers to ERM delivery.
- Organisation-wide strategies and culture change may be important for supporting ERM implementation.
- Lack of champions to lead ERM implementation is seen as a barrier.
- A phased approach (i.e. gradually introducing ERM) may be needed to build acceptability.

What are the proposed outcomes of ERM?

- No current agreement on the purpose of ERM/important outcomes.
- A range of patient-centred, clinical, and economic outcomes are important to clinical stakeholders, including reduced LOS in PICU; reduced days of MV; participation, function and activities of daily living; mobility and strength; cognitive, emotional and psychological outcomes; QoL; and family functioning and parent/caregiver stress.

improvement on ERM in paediatric and adult intensive care settings. We recruited individuals who are active in the ERM community, identified from reviewing recent published work and from the team's clinical and research networks. These people were approached via e-mail and a total of three were included from Europe and the USA – a senior clinical academic doctor, a senior clinical academic nurse and a senior physiotherapist.

Data collection: we undertook three face-to-face workshops with NHS healthcare professionals and one online workshop with international experts. Initial workshop plans were designed to explore the key reflections from Phase 1 and examples of existing ERM protocols. Plans evolved through findings from prior workshops shaping the focus of the next. The workshops were audio recorded and transcribed and facilitators recorded contemporaneous fieldnotes. The workshops lasted for between 90 minutes and 2 hours.

Data analysis: we drew on standard procedures from rigorous qualitative analysis[80] including coding, constant comparison, memoing and team debrief sessions. The core intervention development team (JMc, RF, TR) reviewed, discussed, organised and summarised the analytic work. Following ideas from PBA,[76] we focused on generating 'guiding principles' in relation to:

- *Intervention design objectives* – what an ERM manual must do to address the needs of target users and enhance engagement.
- *Key features of the intervention* – how these design objectives may be achieved in practice.

These guiding principles were critically discussed and revised with the wider PERMIT research team.

Results: as outlined in *Table 10* ERM can be conceptualised as patients engaging in progressive movement and mobility in the context of individually meaningful and purposeful activities and a supportive environment that promotes familiar and orientating daily routines. Several discrete interventions can be legitimately conceptualised as either closely related to or a core part of ERM and these topics are being investigated in their own right (e.g. sedation, ventilation, delirium, nutrition and mental health).[66,81–84] A specific focus on progressive movement and mobility within PERMIT would add to the current research and further advance the overall goal of improving PICU care. Clinical stakeholders perceive that ERM is relevant for most patients and can be actively considered from the second morning of admission for those anticipated to still be on the unit the following day. However, clinicians especially require safety guidelines for delivering ERM to the most severely ill and complex patients. Factors influencing the implementation of ERM vary according to unit, team, individual clinician and individual patient. Therefore, both ERM activities and ERM implementation support need to balance flexibility (so they can be highly tailored) and specificity (so they can be differentiated from usual care, implemented and evaluated). Clinicians' views on the potential impact of ERM seem to converge on a small cluster of key clinical, functional, psychological, family-related, QoL and economic outcomes.

Literature-based work – developing a prototype intervention manual

After the workshops, we conducted a range of literature-based work to identify available concepts, tools and resources to develop and shape the form and content of a prototype ERM intervention manual. This work took place alongside formal and informal meetings with clinical members of the wider PERMIT research team (see user development – reported below) and had an iterative relationship.

Reviewing existing ERM interventions

Purpose: to review existing ERM interventions and compare them to our ERM guiding principles.

Methods: we used a rapid pragmatic approach to identify, characterise and understand existing PICU ERM interventions and compared the intervention components to the guiding principles we developed. We identified existing interventions by hand-searching the literature, through topic experts in the wider research team and from the Phase 1b survey (see *Chapter 2*). We focused on coding, memoing and team debrief sessions.

Results: we explored ERM systematic reviews and practice recommendations[55,85,86] along with six UK paediatric ERM protocols provided by participants in the Phase 1 survey, some of which had

TABLE 10 Guiding principles in developing an ERM intervention

Design objectives – what an ERM intervention must do to address the needs of target users and enhance engagement	Key features – how ERM design objectives may be achieved in practice
What is the underpinning rationale, theory, or goal of ERM?	
• Progressive movement and mobility are key active ingredients of ERM. They need to be specified practically and meaningfully for clinicians (the target users). They are also the key mechanism generating patient benefits.	• The International Classification of Functioning, Disability, and Health can be used as a practical starting point for specifying progressive movement and mobility in the context of meaningful and purposeful activities such as sensory experiences, self-care, education, recreation and leisure, play and interaction.
• However, a focus solely on movement and mobility is too narrow for clinicians. ERM needs to convey a holistic perspective and a rehabilitation 'mindset' by: (1) contextualising movement and mobility within activities that are meaningful and purposeful to individual patients, considering their age, developmental level, and reason for admission, and (2) emphasising the role of a supportive environment that enables engagement in movement and mobility in the context of familiar and orientating daily routines.	• Developmental care, neonatal therapy and early intervention can be used as a relevant theoretical and practical starting point for specifying aspects of ERM for very young patients. There are some examples of implementation in paediatric intensive care, providing proof of concept that these approaches may be feasible and acceptable in this setting.
• Adult intensive care has influenced ERM in the PICU setting. However, given the very young age and early developmental level of many paediatric patients, ERM in PICU needs to incorporate developmental approaches.	
• There is a desire amongst clinicians to interpret ERM broadly and include many aspects of wider good clinical practice. This is motivated by a desire that these aspects should not be forgotten or side-lined. But there is also recognition that ERM needs to be carefully differentiated from other aspects of care to enable evaluation and implementation.	• Many interventions related to ERM are being investigated in their own right (e.g. sedation, ventilation, delirium and nutrition). Early and progressive movement and mobility is a core element of ERM. A specific focus on this element can advance the overall goal of improving usual PICU care. However, this will not address all elements of all clinicians' conceptualisations of ERM.
• Several key interventions can be legitimately conceptualised as either closely related to or a core part of ERM (e.g. interventions for pain, sedation, ventilation, delirium, nutrition, sleep, communication, mental health and family support). An ERM intervention manual needs to be explicit about where these interventions fit.	
Which patient populations are eligible for ERM?	
• ERM has potential benefits for most patients. An intervention manual needs to be relevant for diverse patient groups in terms of severity of illness (acuity), age, developmental level and reason for admission.	• ERM is less relevant to the high proportion of patients with very short lengths of stay (24–48 hours).
• Routinely screening all patients for eligibility makes it easier to embed ERM across the whole PICU and make it part of usual care. An intervention manual needs to enable unit-wide implementation.	• ERM is inappropriate for patients receiving palliative or end-of-life care. Although some features of wider good practice typically associated with ERM may be relevant and should be available (e.g. prevention of pain, confusion and agitation) care for these patients is conceptualised differently to ERM and goals are communicated differently to families.
• Patient acuity is the main factor guiding eligibility for ERM. Clinicians need a means of describing acuity levels that enables decision-making about ERM eligibility for individual patients.	

continued

TABLE 10 Guiding principles in developing an ERM intervention (*continued*)

Design objectives – what an ERM intervention must do to address the needs of target users and enhance engagement	Key features – how ERM design objectives may be achieved in practice
• However, ERM is also guided by the experience and intuition of clinicians and parents/carers and the wider unit context (e.g. how confident and skilled staff are with ERM). An intervention manual needs to encourage and enable sensitive, individualised decision-making.	• Several existing ERM protocols describe patient acuity levels in terms of specific central nervous, cardiovascular and respiratory system parameters, and presence of lines, tubes etc. Acuity levels are then linked to specific ERM activities that may be appropriate. This enables team communication and decision-making, is popular with clinicians, and can be further developed.
• Clinicians need explicit guidance on ERM for the most severely ill and complex patients who are thought to have a lot to gain from ERM but for whom implementation is particularly challenging.	• In most PICU settings, the morning ward round can be used as a focal point for building ERM decision-making into the daily routine.
• Patient acuity fluctuates and is not a straightforward trajectory of improvement. The type of ERM that is appropriate (if any) may change daily or more frequently. Clinicians need a routine process for continuously making and reviewing decisions about ERM eligibility.	• Each PICU is unique. Individual units differ in their patient populations, the resources they have available, and their views and practical experience of ERM. Specific guidance needs to be balanced with a flexible approach to implementation as blanket rules and prescriptive approaches are not likely to be feasible or acceptable.
When is ERM initiated?	
• 'Early' initiation of progressive movement and mobility is a critical element that generates benefits for patients and differentiates ERM from usual care. Guidance on when to initiate ERM needs to consider both day of admission and patient acuity level.	• In most PICU settings, the morning ward round can be used as a focal point for building ERM decision-making into the daily routine.
• Clinicians need a routine process for actively screening all patients and making timely decisions about initiating ERM.	• ERM can be actively considered from the second morning of admission for patients anticipated to still be on the unit the following day. This can be legitimately considered 'early' (and is earlier than typical current practice), avoids ERM for very short admissions (24–48 hours), and may be feasible and acceptable in practice. • Existing approaches to acuity levels can be used to guide what ERM can be considered on day 2 of admission even for the most severely ill and complex patients.
What processes and materials are involved in ERM?	
• ERM can be conceptualised as patients engaging in progressive movement and mobility in the context of individually meaningful and purposeful sensory, self-care, education, recreation and leisure, play and interaction activities, and a supportive environment that enables engagement and promotes familiar and orientating daily routines. Clinicians need practical specification of these core ERM concepts.	• The International Classification of Functioning, Disability, and Health can be used as a starting point for specifying progressive movement and mobility in the context of activities such as self-care and play.
• An intervention manual needs to enable clinicians to sensitively select specific ERM activities appropriate to acuity, age, developmental level, the experience and intuition of clinicians and parents/carers, and the wider unit context (e.g. how confident and skilled staff are with ERM).	• The concept of 'progressive' can incorporate several practical aspects that clinicians find important and useful, including passive → active movement, more → less assistance with mobility, and activities in → out of bed.

TABLE 10 Guiding principles in developing an ERM intervention (*continued*)

Design objectives – what an ERM intervention must do to address the needs of target users and enhance engagement	Key features – how ERM design objectives may be achieved in practice
	• Several existing ERM protocols suggest ERM activities that may be appropriate for different levels of patient acuity. This approach provides ERM activities to aim for ('goals'), enables the team to make decisions and select activities, is popular with target users, and can be further developed.
Where is ERM delivered?	
• While ERM is delivered within the PICU setting, it is relevant to and embedded within the wider hospital setting.	• In the first instance, the primary focus for clinicians is enabling delivery within PICU settings.
How much ERM is delivered?	
• Amongst clinicians, there is a general sense of 'any ERM is better than none' but there are no established rules of thumb for dosage of ERM.	• At this point, the primary issues for clinicians are achieving 'early' initiation, enabling safe delivery for the most severely ill and complex patients, and the feasibility of daily implementation in busy PICU settings with no additional staffing capacity.
How is ERM tailored?	
• ERM delivery is highly tailored to the individual patient and ERM implementation is highly tailored to the individual paediatric intensive care setting.	• Clinicians need a flexible intervention manual that sets out which elements of ERM can be tailored (and how) and which should be retained because theory and evidence suggest they will be effective. Specific guidance needs to be balanced with a flexible approach to implementation as blanket rules and prescriptive approaches are not likely to be feasible or acceptable.
Who delivers ERM?	
• Doctors, nurses and physiotherapists are essential to ERM delivery. Doctors create a supportive unit culture, take overall responsibility for safety and include ERM decision-making in morning ward rounds. Nurses are highly sensitised to individual patients and families, are present at the bedside 24/7 and ensure delivery of ERM. Physiotherapists have expertise in progressive movement and mobility and can build confidence and skills in ERM delivery, including with the most severely ill and complex patients.	• Beliefs and traditions about the roles and responsibilities of different professions vary between units and there is variation in which professional groups are available. An intervention manual needs to specify ERM tasks and responsibilities but be flexible about which professional group(s) should carry them out. • Named individual ERM champions leading on implementation is important and useful.
• An intervention manual needs to support the confidence and skills of staff delivering ERM, considering that many units experience a high staff turnover. • Parents/carers and siblings should be given opportunities to participate in ERM as they often feel very impotent in PICU settings. However, sensitivity to their emotional situation is required and wishes not to be involved should be respected.	• Parents/carers – need permission to contribute to ERM and roles to perform but also space and permission to step back if necessary.

continued

TABLE 10 Guiding principles in developing an ERM intervention (*continued*)

Design objectives – what an ERM intervention must do to address the needs of target users and enhance engagement	Key features – how ERM design objectives may be achieved in practice
How is ERM delivered safely?	
• A specific ERM protocol needs to help create a culture in which PICU staff feel safe and feel that they are not doing something wrong. • Clinicians need strategies for addressing negative emotions that restrain ERM delivery (e.g. staff anxiety, fear of causing harm, worry about getting into trouble) and accentuating positive emotions that facilitate delivery (e.g. feeling that ERM is worthwhile, enjoyable, and raises the quality of care).	• A clear and consistent decision-making tool for planning and monitoring ERM could increase confidence and skills for safe delivery. • Safety guidelines could ensure nurses feel confident to implement ERM and should consider the patient diversity and variation in PICU.
What other factors influence implementation of ERM?	
• ERM implementation factors will vary by unit, team, individual clinician and individual patient. Every PICU is different and is at a different point in their implementation journey. Clinicians need implementation support, but this should be able to be highly tailored to the individual unit – flexibility is key to feasibility and acceptability. • Clinicians identified important contextual factors that may influence and/or be influenced by ERM: pain, sedation, delirium, nutrition, sleep and communication.	• ERM implementation can be progressed by getting all stakeholders on board (including funders, managers and sceptics), getting organised to do ERM every day (e.g. by fitting it into existing routines and processes), phasing it in gradually, and working out how it can be sustained in the unit after initial efforts and enthusiasm peter out.
What are the proposed outcomes of ERM?	
• ERM is important for different patients for different reasons. As with many rehabilitation interventions, progressive movement and mobility in ERM generate a wide range of patient benefits. Clinicians need to see this diversity reflected in an intervention manual.	• Clinicians' views seem to converge on a small cluster of key outcome constructs: duration of MV; LOS in paediatric intensive care and hospital overall; movement function and mobility capacity and participation at discharge relative to pre-admission; activities of daily living capacity and participation at discharge relative to pre-admission; body functions (i.e. cognitive, respiratory and muscle functioning/strength); patient and family psychological well-being; QoL; and family satisfaction with care.

been adapted from the PICU Up! early mobilisation programme in the United States.[17] Three key elements emerged:

- *Focus on enabling progressive movement and mobility in diverse patient groups* – several existing interventions involve matching ERM activity levels to a patient's acuity levels, as opposed to focusing on one specific piece of ERM equipment. Many also focus on delivering ERM to diverse population groups over one type of patient. These approaches echo those in the guiding principles. The interventions also offer a range of tried-and-tested materials (e.g. checklists and safety thresholds) that can be used or adapted.
- *Lack of specificity around key activities* – existing practice recommendations specify progressive movement and mobility activities; however, this specificity is often lacking in locally adapted ERM protocols that appear to rely more on tacit knowledge of staff and have been expanded to include elements of usual care. Broad concepts such as neurodevelopmental play and activities of daily have been included as ERM activities; however, the guiding principles outline that PICU teams need practical specification of all core ERM concepts. Existing interventions consistently emphasise the importance of developmentally appropriate and individualised ERM; however, more practical guidance is required on how to operationalise these principles in the context of multidisciplinary delivery of ERM.
- *Implementation support is missing* – existing interventions offer very little guidance or support on how to introduce and embed ERM into a specific setting. The guiding principles outline how clinical stakeholders want and need support with initial implementation work, from getting initial staff buy-in to sustaining ERM over time.

Current ERM interventions offered a useful and important base. However, implementation issues need to be considered as early as possible to improve the design and sustainability of ERM interventions and reduce the chance of implementation failure.[87] Two of the core implementation issues in ERM are making sure that adequate support and guidance are offered in the day-to-day delivery of ERM activities and that all activities are both flexible (to enable tailoring for individual units and patients) and specific (to enable differentiation from usual care, implementation, and evaluation).

Specifying the bedside bundle

Purpose: to specify the essential clinical materials needed to plan and deliver ERM for individual patients.

Methods: we used a rapid pragmatic approach to identify, characterise and understand existing PICU ERM clinical materials. We identified existing materials by hand-searching the literature, through topic experts in the wider research team and from the Phase 1b survey (see *Chapter 2*). We focused on coding, memoing and team debrief sessions.

Results: we identified existing clinical materials that were tried-and-tested for delivering ERM in different PICU contexts and could be adapted to achieve key design objectives within the guiding principles. These were patient acuity levels, ERM activity levels, safety and tolerance criteria and a daily ERM flowchart. They were further developed and specified to form the first part of a prototype ERM intervention manual – the beside bundle (*Table 11*).

Patient acuity levels

Several existing ERM interventions already set out patient acuity levels that describe the full spectrum of clinical stability across diverse patient populations ranging from the least to the most stable. The levels are based on central nervous, cardiovascular and respiratory system parameters, as well as other factors such as the presence of lines or tubes. They are then linked to corresponding levels of ERM activities that may be safe and appropriate. This approach was pioneered in paediatric intensive care by the PICU Up! programme[17] and has been further adapted within UK PICU settings. We compared and contrasted existing patient acuity levels along with specific contraindications, exclusions,

TABLE 11 Overview of the PERMIT ERM intervention manual

Bedside bundle **The essential clinical materials needed to do ERM with individual patients**	**Implementation toolkit** **A step-by-step guide to putting the bedside bundle into practice across a PICU**	**Training and support materials** **Flexible resources for tailoring the bedside bundle and implementation toolkit to an individual unit**
Patient Acuity Levels – a table displaying four levels of patient acuity ranging from the lowest (level 1) to the highest (level 4) level of clinical stability. Levels are based on specific clinical parameters related to the central nervous system, cardiovascular system, respiratory system and other factors (e.g. lines, tubes etc.).	**PICU preparation:** • Take stock – make an overall assessment of the unit's readiness to implement ERM (i.e. where the unit is currently at with ERM and the next steps required to put the bedside bundle into practice).	• Guidance on using and tailoring the patient acuity levels. • Additional explanation of each clinical parameter in the patient acuity levels and their implications for ERM.
ERM Activity Levels – a table displaying four increasingly challenging levels of ERM activity. ERM activity levels focus on patients engaging in progressive movement and mobility in the context of individually meaningful and purposeful activities and a supportive environment that promotes familiar and orientating daily routines.	• Build the team – bring together a group of multidisciplinary ERM champions within the unit. These are people who can support and market ERM, drive it through, and overcome any indifference or resistance.	• Guidance on selecting an individual patient's ERM activity level and specific ERM activities. • Guidance on using and tailoring the ERM activity levels and progressing individual patients towards more challenging ERM activities.
Pause and Re-assess Criteria – a list of clinical parameters that should be monitored before, during and after ERM activities. The criteria should be personalised based on the clinical team's judgement and discretion about acceptable deviations from the individual patient's baseline status.	• Get buy-in – build a shared understanding across the unit of what ERM is all about (i.e. what the bedside bundle involves, how ERM is supposed to work, and what are the potential benefits and intended outcomes for patients).	• Guidance on how the pause and re-assess criteria were developed, how they can be personalised to individual patients and how they can be incorporated into existing checklists in the unit.
Daily ERM Flowchart – a graphic used during ward rounds to prompt key actions for each patient every day 2, including: screen for ERM eligibility, assign patient acuity level, assign ERM activity level, select specific ERM activities, decide who is leading the ERM and how the parent/carer will be involved, and feedback from previous day's ERM activities.	• Get ready – tailor the bedside bundle to make it as workable as possible for the staff and systems already in place in the unit.	• Guidance on using and tailoring the daily ERM flowchart. • Self-assessment checklist for taking stock and assessing the unit's readiness to implement ERM.
	Patient delivery: • Make it work – gradually put the bedside bundle into practice in the unit until it is fully implemented with all patients. This is when the unit goes live with ERM, tests things out and gets feedback on how things are working.	• Resources to help ERM champions present the evidence for ERM, persuade colleagues about the benefits and reassure them about safety. • Slide set to support getting buy-in (e.g. information about ERM to share in team meetings that can be tailored to fit in with how the unit is approaching implementation).
	• Keep it going – come together as a unit to review the bedside bundle, decide how it could be working better and plan how ERM can be sustained over the next 6–12 months.	• Guidance on creating a unique local ERM identity to help increase engagement in, and understanding and recognition of, ERM.

precautions and eligibility criteria from other ERM interventions identified in our literature-based work (reported above).

Based on the existing interventions, we drafted four levels of patient acuity that were further refined by clinical members of the wider PERMIT research team (see user development – reported below). We developed comprehensive guidance for the patient acuity levels that includes an explanation of each clinical parameter and a description of how it should be considered in shaping ERM delivery, including for the most severely ill and complex patients. The guidance encourages tailoring of the patient acuity levels to fit in with practice in a particular unit. For example, it sets out how users can remove clinical parameters that are not relevant to their patient population, add clinical parameters that are particularly relevant, or change parameters to fit in with local practice standards.

ERM activity levels

We set out to specify the three core elements in our conceptualisation of ERM (see *Table 10*) – 'progressive movement and mobility' carried out within a 'supportive environment that promotes familiar and orientating daily routines' and delivered with the context of 'individually meaningful and purposeful activities that into account the patient's age, developmental level and reason for admission'. We extracted practical examples of these elements from the ERM interventions identified in our literature-based work (reported above) and supplemented them with examples from the International Classification of Functioning Disability and Health[88] and adult ERM literature.[89–93] We were mindful of identifying examples that related to the more severely ill and complex patients for whom adaptive positioning in bed and gentle sensory experiences would be most relevant. We were also mindful of the very young age and early developmental level of many paediatric patients and so we drew on examples from developmental care interventions, neonatal therapy and early intervention, specifically about protecting sleep, developmentally supportive activities of daily living, infant positioning, family-centred care and controlling light and noise in the environment.[94–96]

The core intervention development team compared, contrasted and further specified the examples, removing duplicates and prioritising examples more closely aligned to the key design objectives within the guiding principles. Following the tried-and-tested structure of the PICU Up! programme,[17] we arranged this content into four levels of ERM activities to correspond with our four levels of patient acuity. The activity levels were then further refined by clinical members of the wider PERMIT research team (see user development – reported below).

Activity level 1 focuses on positioning the patient to maintain ROM, avoid triggering of maladaptive tonic neurological reflexes, particularly in children with pre-existing neuro-disability, prevent pressure ulcers and other complications of immobility, and optimise respiratory and gut function. Level 2 focuses on assisting the patient to practise different activities. Level 3 focuses on progressing to more challenging activities. Level 4 focuses on preparing the patient for transition off the unit by regaining as much of their pre-admission levels of independence as possible. The levels are progressively more challenging for the patient and each level includes a minimum recommended dosage of ERM activities. Across the levels, there is an emphasis on orientating the patient to themselves, others, place, and time, and on protecting their sleep. We also developed comprehensive guidance for the activity levels that includes:

- An overall explanation of the activity levels and how ERM has been conceptualised in the PERMIT intervention manual.
- An explanation of each of the four activity levels, including the main aim of each level, a description of the type of patient for whom each level is usually appropriate, guidance on specific activities within each level, and suggestions for who may need to lead or be involved in delivering activities at each level (e.g. allied health professional, nurse, parent/carer).

- How to select meaningful and purposeful ERM activities for an individual patient, considering their acuity, pre-admission characteristics (e.g. age, pre-existing developmental level, pre-existing impairments or limitations, favourite toys and activities), the ERM confidence and skills of the multidisciplinary team at that point in time, and parent/carer intuition about what their child enjoys, dislikes, and may be able to tolerate.
- How to progress patients to more challenging activities within a specific level as well as progressing up through the four activity levels.

As with the patient acuity levels, the guidance encourages tailoring of the activity levels to fit in with practice in an individual unit. For example, it sets out how users can specify who should lead certain ERM activities depending on the staff groups that are usually available and users can add specific activities that are available in their unit or add/remove activities they especially do/do not want to be considered for certain patient populations or levels of acuity.

Safety and tolerance criteria

Our literature-based work (reported above) highlighted a range of tried-and-tested safety checklists used just before initiating ERM activities and safety criteria used during activities to monitor patient tolerance and guide decisions about whether ERM should be paused, altered, continued or stopped. These clinical materials include key indicators of cardiorespiratory and central nervous system instability, pain or discomfort, and concern for the integrity of critical lines and tubes. We compared and contrasted safety and tolerance criteria identified through our literature-based work and supplemented these with examples from adult ERM literature.[53,97,98]

Through discussion between the core intervention development team and clinical members of the wider PERMIT research team, we initially considered and ruled out three approaches to specifying safety and tolerance criteria:

(1) Define explicit safety thresholds by age and illness category. Age-related normal values for cardiovascular, respiratory and central nervous system parameters are widely established. However, in a PICU setting many patients' observations will be outside normal thresholds and a priori specification of thresholds in all scenarios would not be feasible given the heterogeneity of the clinical population.
(2) Use a 'triggered alarm' approach. Bedside nurses frequently review and adjust alarm limits for oxygen saturation, heart rate, arterial blood pressure monitoring etc. However, false alarms are common (e.g. brief, insignificant perturbations, particularly in more awake patients) and therefore strict application of a triggered alarm approach may not be feasible.
(3) Define thresholds in terms of percentage change relative to a patient's baseline (e.g. change in heart rate of >20%). While this approach to individualising safety and tolerance criteria is attractive, it may not be feasible to calculate a meaningful and useful baseline. For example, clinicians do not routinely calculate an average heart rate over the last 4 hours and to do so before initiating ERM activities may be burdensome and open to discretion about how to interpret periods of elevated heart rate during procedures over those 4 hours.

We determined that, as part of a routine risk assessment conducted just before ERM activities are carried out, clinicians should use their judgement to prospectively define individualised safety and tolerance criteria that are meaningful and useful for a given patient [e.g. acceptable upper and lower thresholds for heart rate, respiratory rate, saturation, intracranial pressure (ICP)]. If observations exceed these limits the ERM activity should be paused and the appropriateness of further activities should be re-assessed. Our rationale was that clinicians have intuitions of acceptable bounds on physiological parameters for a given patient, based on their routine observations to date, knowledge of the patient's condition etc. Patient acuity level can change rapidly during the day and between procedures. Therefore, clinicians are accustomed to reviewing the appropriateness of any intervention before it is carried out and monitoring how the patient is responding throughout and afterwards. The same principle may apply

to ERM. In the ERM intervention manual, we set out the safety and tolerance ('pause and re-assess') criteria that clinicians should prospectively define and monitor for individual patients before, during and after ERM activities. The manual also includes guidance on incorporating the criteria into a unit's existing documentation and processes and provides a practical example of implementation in one unit (Birmingham Women and Children's NHS Foundation Trust) for clinicians to use as a model.

ERM daily flowchart

Having specified the essential clinical materials needed to deliver ERM, we set out to identify an approach to planning and organising delivery on a daily basis across a PICU. In line with the guiding principles, we needed a mechanism for prompting routine screening of all patients across the unit for ERM eligibility, ensuring timely initiation of ERM on the second morning of admission for patients anticipated to still be on the unit the following day, assigning acuity levels, selecting meaningful and purposeful ERM activities for individual patients, deciding who would support each patient's ERM on a given day and how parents/carers would be involved, and feeding back on the patient's tolerance of ERM to inform subsequent team decision-making.

Our literature-based work identified an existing ERM intervention – MOVE4WARD – that included a tried-and-tested daily flowchart used in the morning ward round to plan and organise ERM delivery. MOVE4WARD is the ERM programme at Birmingham Women and Children's NHS Foundation Trust and was adapted from the PICU Up! programme.[17] We further specified the MOVE4WARD daily flowchart and developed guidance on how to use it and tailor it to fit in with practice in a particular unit. For example, we encourage users to change the design and layout, insert their own language and terminology for local processes and documentation, and add more detail such as the specific people who will be carrying out certain tasks.

Specifying the implementation toolkit

Purpose: to specify the second part of a prototype ERM intervention manual – a step-by-step guide to putting ERM into practice across a unit.

Methods: we used a rapid pragmatic approach to identify, characterise, and understand literature focusing on the implementation of ERM interventions in PICU settings and conceptualised the core findings in relation to implementation theories.

Search strategy and study selection: we included all the papers from the Phase 1 scoping review as well as those that were excluded on the basis of sample size or study design. We updated the searches to identify more recent work in paediatric intensive care. We also identified published systematic reviews, meta-analyses, and scoping reviews of ERM in adult intensive care.

Data extraction: we extracted information on determinants (i.e. barriers and facilitators) to introducing, embedding, and sustaining implementation of ERM as well as strategies used to overcome those identified determinants.

Analysis: we coded the determinants against theoretical concepts from NPT[71,72] and TFA[73] and strategies against those identified by ERIC,[74] and the behaviour change Theory and Technique Tool.[75] We reviewed and discussed the findings. Through an iterative process, we developed a step-by-step toolkit and related resources to support tailored implementation of ERM within individual and diverse units. This was further refined by clinical members of the wider PERMIT research team (see user development – reported below).

Results: *Table 11* includes an overview of the implementation toolkit and related resources. We identified six steps towards ERM implementation – four geared towards preparing the PICU for ERM delivery and two geared towards actual delivery of ERM to patients. PICU preparation involves: taking stock – making an overall assessment of where the unit is currently at with ERM and deciding the

next steps; building the team – bringing together a group of multidisciplinary ERM champions to lead implementation; getting buy-in – building a shared understanding across the unit of what ERM is all about; and getting ready – tailoring the bedside bundle to make it as workable as possible for the staff and systems already in place in the unit. Patient delivery involves: making it work – gradually putting the bedside bundle into practice in the unit until it is fully implemented with all patients; and keeping it going – coming together as a unit to review the bedside bundle, decide how it could be working better, and plan how ERM can be sustained over the next 6–12 months. *Table 12* sets out a more detailed theoretical overview of the implementation toolkit.

The six steps towards implementation form a flexible framework that can enable both those units new to ERM to get started and more experienced units to renew their efforts and build on the ERM they have already been doing. The steps are not conceptualised as a linear or sequential process. We suggest in the intervention manual that it makes sense for users to start off with taking stock and thinking through their unit's readiness for implementing ERM. Otherwise, given that implementation factors vary between units and that every PICU is at a different point in their ERM journey, we envisage that settings will focus their implementation efforts on the steps most in need of attention locally.

Reviewing outcomes

In the workshops with clinical stakeholders, we collected information about potential outcomes of ERM and incorporated these into our guiding principles (see *Table 10*). We planned to conduct a rapid literature review to identify related patient-centred outcome measurement tools and potentially incorporate these into the prototype ERM intervention manual. However, prior to starting the review work, we learnt that Fink *et al.* were developing a PICU core outcome set and core outcome measurement set – a PERMIT co-applicant had been invited to join that study's International Steering Committee.[99] Rather than repeat this work, we reviewed the outcomes within our guiding principles against the published PICU core outcome set[47] (*Table 13*) and developed our ERM logic model accordingly (see logic model – reported below).

User development – refining the prototype intervention manual

Purpose: to refine the prototype ERM intervention manual through exploring clinical stakeholders' views on acceptability and feasibility.

Methods: we took forward key topics and outstanding issues and uncertainties emerging from the ERM intervention manual development process into a series of formal and informal meetings with clinical members of the wider PERMIT research team. These meetings took place alongside the literature-based work (reported above) and had an iterative relationship.

Sampling and recruitment: we worked with existing members of the wider PERMIT research team. They represented a multidisciplinary group of NHS healthcare professionals with diverse experience of ERM in PICU settings. A total of 13 professionals from three PICUs took part in the process – four consultant doctors (three paediatric intensivists and one paediatric neurologist), two senior nurses (one clinical academic and one PICU lead) and seven senior physiotherapists.

Data collection: we undertook nine online group meetings. Meeting focus evolved with findings of literature-based work and insights from prior meetings shaping the focus of the next. The core intervention development team would present materials from the bedside bundle and implementation toolkit and/or facilitate the discussion and the clinical team members would support, refine and challenge elements of the manual. Members of the intervention development team recorded contemporaneous fieldnotes. The meetings lasted for 60 minutes. We also undertook additional formal and informal smaller meetings, with specific people, to further explore or refine difficult issues, as well as to undertake 'walk-throughs' of manual processes and explore reactions.

TABLE 12 Theoretical overview of the PERMIT ERM implementation toolkit

Implementation steps	What does it mean?	Theoretical processes	Why does it matter?	Theoretical processes	What's involved? *(corresponding ERIC strategies)*
TAKE STOCK	Making an overall assessment of where the unit is currently at with ERM and decide the next steps to be taken. Creating a tailored action plan for delivering the bedside bundle across the unit, focusing time and effort on the areas that most need support.	Communal appraisal (NPT) Interactional workability (NPT)	Focusing on a tailored action plan makes ERM feel more manageable for everybody. It is harder to change practice if clinicians believe they are already doing all aspects of ERM. Therefore, it helps to specify exactly where the bedside bundle is not happening or needs to be improved.	Burden (TFA) Differentiation (NPT)	The manual includes a self-assessment checklist for taking stock. (Assess for readiness and identify barriers and facilitators.) From the self-assessment, the next steps for progressing ERM can be prioritised. Be specific about who will do what, with and for whom, and when. This is the action plan. *(Tailor implementation strategies)*
BUILD THE TEAM	Bringing together multidisciplinary champions to support and market ERM, drive it through and overcome any indifference or resistance.	Initiation (NPT)	Leadership from a credible, representative and organised group of multidisciplinary clinicians makes people trust ERM and feel more positive about it. ERM champions with a good understanding of the different roles, expertise and personalities in the unit can allocate tasks and responsibilities to those with the right skills.	Affective attitude (TFA) Relational integration (NPT) Skill-set workability (NPT)	Champions should represent the multidisciplinary team and include a lead doctor, nurse and physiotherapist as a minimum. *(Identify and prepare champions)* The manual includes resources to help champions prepare for presenting the evidence for ERM and persuading colleagues about its benefits and safety. *(Identify and prepare champions)* Champions should organise weekly team meetings to plan, monitor and review ERM and support one another's learning. *(Organise clinician implementation team meetings)*
GET BUY-IN	Building a shared understanding across the unit of what ERM is all about – what the bedside bundle involves, how it is supposed to work, and what are the potential benefits and intended outcomes for patients. Achieving agreement that ERM fits in with the unit's values of providing the best possible care.	Communal specification (NPT) Intervention coherence (TFA) Internalisation (NPT) Ethicality (TFA)	When clinicians buy-in to ERM, they understand how they can contribute to ERM and feel comfortable that it can be done safely. They can see where the bedside bundle is currently working well, where it is not happening, and where it needs to be improved. They are willing to make it happen. When unit managers buy-in, they make it clear that they support ERM.	Legitimation (NPT) Affective attitude (TFA) Differentiation (NPT) Contextual integration (NPT)	Get everybody in the unit involved in discussions about ERM to start building positive feelings and understanding. *(Conduct local consensus discussions)* Get people actively involved in problem-solving around ERM. For example, what are their concerns around patient safety and staffing? How do they think ERM should fit in with sedation and nutrition practices? *(Facilitation)*

continued

TABLE 12 Theoretical overview of the PERMIT ERM implementation toolkit (*continued*)

Implementation steps	What does it mean?	Theoretical processes	Why does it matter?	Theoretical processes	What's involved? *(corresponding ERIC strategies)*
					Share examples of successful ERM and positive patient and parent/carer feedback. *(Obtain and use patient/family feedback)* Ask unit managers to make it clear that ERM is a priority and that they support implementation. *(Mandate change)*
GET READY	Tailoring the bedside bundle to make it workable for the staff and systems already in place in the unit. Specifically, this means allocating ERM tasks and responsibilities appropriately and fitting the bedside bundle into the current ways of ordering, recording, communicating, and monitoring patient care.	Enrolment (NPT) Skill-set workability (NPT) Individual specification (NPT) Systematisation (NPT)	When clinicians understand their role in the bedside bundle and prepare for carrying out their allocated tasks and responsibilities, they feel more confident and positive about ERM. Building the bedside bundle into existing systems makes ERM feel more manageable.	Self-efficacy (TFA) Burden (TFA)	The manual includes guidance on tailoring the bedside bundle to an individual unit. *(Promote adaptability)* It is easier to deliver the bedside bundle if units are specific about who does what and when. *(Revise professional roles)* Consider how to use existing systems (e.g. ward round checklists, electronic records, whiteboards). *(Change record systems)*
					Plan training sessions to show people how the bedside bundle works. Make sessions interactive and tailored to the needs of different clinicians. *(Conduct educational meetings; Make training dynamic)*
MAKE IT WORK	Gradually putting the bedside bundle into practice until it is fully delivered with all patients. The unit tests out ERM and gets feedback on how it is working (e.g. have tasks and responsibilities been allocated appropriately, is it fitting into existing systems?).	Interactional workability (NPT) Skill-set workability (NPT) Systematisation (NPT)	Gradual implementation provides time and space for clinicians to build confidence in their own and each other's skills. As they gain first-hand experience of safe delivery, clinicians feel more positive and less worried about ERM.	Self-efficacy (TFA) Relational integration (NPT) Affective attitude (TFA) Individual appraisal (NPT)	Phase-in the bedside bundle and very gradually move to a unit-wide rollout. *(Stage implementation scale-up)* Consider rostering an ERM champion onto every shift to help implement the bedside bundle, solve problems, and monitor quality. *(Facilitation)*

Implementation steps	What does it mean?	Theoretical processes	Why does it matter?	Theoretical processes	What's involved? *(corresponding ERIC strategies)*
			As they gradually gain more experience, clinicians are able to give feedback about the impact of ERM on themselves, their workload, patients, and the unit overall.		Build in reminders that prompt clinicians about the bedside bundle and help them remember what exactly they need to do. *(Remind clinicians)* Put in place a system for getting feedback about ERM from clinicians, patients (where possible), and parents/carers. *(Obtain and use patient/family feedback)*
KEEP IT GOING	Coming together as a unit to review the bedside bundle, decide how it could be working better, and plan how ERM can be sustained over the next 6–12 months.	Communal appraisal (NPT) Reconfiguration (NPT) Activation (NPT)	Ongoing evaluation of the bedside bundle combined with comprehensive feedback for clinicians builds trust and confidence in the effectiveness of ERM.	Relational integration (NPT) Perceived effectiveness (TFA) Skill-set workability (NPT) Self-efficacy (TFA)	Review how the unit is doing with the bedside bundle. *(Purposely re-examine implementation)* Provide feedback to the overall unit, clinician groups, and individuals about how ERM is going. *(Audit and provide feedback)* Conduct spot checks on different parts of the bedside bundle and provide feedback to the overall unit, clinician groups, and individuals. *(Audit and provide feedback)*
			Staff turnover in the unit means that who is delivering the bedside bundle changes over time. Permanent staff also change as they develop their confidence and skills in ERM. Ongoing evaluation and training should consider these changes.		Plan ongoing training sessions to refresh permanent staff and show new staff how the bedside bundle works. *(Conduct ongoing training)* The manual includes guidance on creating a unique identity for the locally tailored bedside bundle and spreading the word about ERM through posters, newsletters, events and social media to help create a positive buzz and maintain interest. *(Use mass media)*

TABLE 13 Proposed outcomes of ERM and the core outcome set for paediatric critical care[47]

Outcomes of ERM proposed by clinical stakeholders	Corresponding global outcomes considered for the PICU COS	Included in PICU COS	Included in PICU COS – Extended	Excluded from PICU COS	Corresponding specific outcomes considered for the PICU COS	Included in PICU COS	Included in PICU COS – Extended	Excluded from PICU COS
Duration of MV	Healthcare utilisation			X	New technological supports (tracheostomy, gastrostomy tube, oxygen, etc.)			X
LOS in paediatric intensive care and hospital overall	Healthcare utilisation			X	Cost of care			X
Movement function and mobility capacity and participation at discharge relative to pre-admission	Physical function	x			Physical mobility		X	
Activities of daily living capacity and participation at discharge relative to pre-admission	Overall health	X			Activities of daily living			X
	Social function			X	Child participation			X
Body functions – respiratory	Physical function	X			Organ function		X	
Body functions – muscle functioning/strength	Physical function	X			Medical frailty		X	
Body function – cognitive	Cognitive function	X						
Patient psychological well-being	Emotional health and function	X			Mood and feelings		X	
					Post-traumatic stress		X	
Family psychological well-being	Family function		X		Parent/legal guardian emotional function		X	
Patient QoL	Overall health	X			Child QoL	X		
Family satisfaction with care	n/a				n/a			

[47]Fink EL, Maddux AB, Pinto N, Sorenson S, Notterman D, Dean JM, *et al.*, Pediatric Outcomes STudies after PICU (POST-PICU) Investigators of the Pediatric Acute Lung Injury and Sepsis Investigators (PALISI) Network and the Eunice Kennedy Shriver National Institute of Child Health and Human Development Collaborative Pediatric Critical Care Research Network (CPCCRN). A core outcome set for pediatric critical care. *Crit Care Med* 2020;48(12):1819–28. https://doi.org/10.1097/CCM.0000000000004660.

Data analysis: we focused on reviewing fieldnotes, memoing and debrief sessions within the core intervention development team. We reviewed, discussed and summarised the meetings, and worked to adapt the manual in an iterative fashion focusing on maximising potential successful introduction and embedding of the intervention.

Results: *Table 11* summarises the content of the PERMIT ERM intervention manual. The key feedback points that were used to refine the prototype manual and improve its overall feasibility and acceptability can be summarised as follows:

- Introduction and orientation – tell the user what is in the manual, where to start and how to work through the different sections.
- Layout and formatting – introduce the bedside bundle first as this is of primary importance to users. Keep the manual brief, simple and accessible by ensuring that each of the clinical materials in the bedside bundle and each of the steps in the implementation toolkit fits onto one side of A4. Minimise the burden of flipping between sections in the manual by clearly separating the bedside bundle and implementation toolkit from the lengthier training and support materials.
- Language and tone – use labels that are already familiar and acceptable, for example a 'checklist' for implementing the pause and re-assess criteria evokes more confidence and positive emotion than a 'risk assessment'. When providing instructions, ensure the tone comes across as flexible and enabling – clear and straightforward instructions may inadvertently come across as too prescriptive or authoritarian.
- Promote and enable ownership – make it explicit how the bedside bundle builds on systems, processes and expertise that are already in place across a unit. Empower users by highlighting where the intervention manual can be tailored to fit in with local practice and actively encourage them to tailor and take ownership of the materials and resources.
- Minimise extra burdens and manage expectations – remove unnecessary detail from the tables and flowchart within the bedside bundle. Make it clear which training and support materials are provided within the manual and clarify any materials that will need to be developed or tailored locally by the unit. Take advantage of all opportunities to build the manual into existing documentation rather than introducing new paperwork to the unit.
- Create a positive buzz and maintain interest – consider providing branded promotional materials such as pens, stickers etc.

In addition, the wider research team identified several key topics that warranted further exploration in our subsequent feasibility study (see *Chapter 5*): for example, the practicalities around recording ERM intervention data within existing documentation systems and processes, the impact of different clinical perspectives about how to deliver ERM to particular patient populations such as those on ECMO, and the acceptability of our conceptualisation and specification of ERM to diverse stakeholders beyond the PERMIT research team and study participants.

Logic model – refining our understanding

Purpose: to refine a PERMIT ERM logic model.

Methods: we had already developed a preliminary ERM logic model based on current literature and the clinical expertise within the research team. We reviewed and refined our logic model in relation to findings from the manual development process, the correspondence between the outcomes within our guiding principles and the published PICU core outcome set,[47] and through discussions within the wider PERMIT research team.

Results: the refined logic model is presented in *Figure 13*. It provides an overview of the proposed intervention components and implementation processes set out in the refined ERM intervention manual, as well as the proposed outcomes of ERM and the key contextual factors thought to influence its implementation and potential effectiveness.

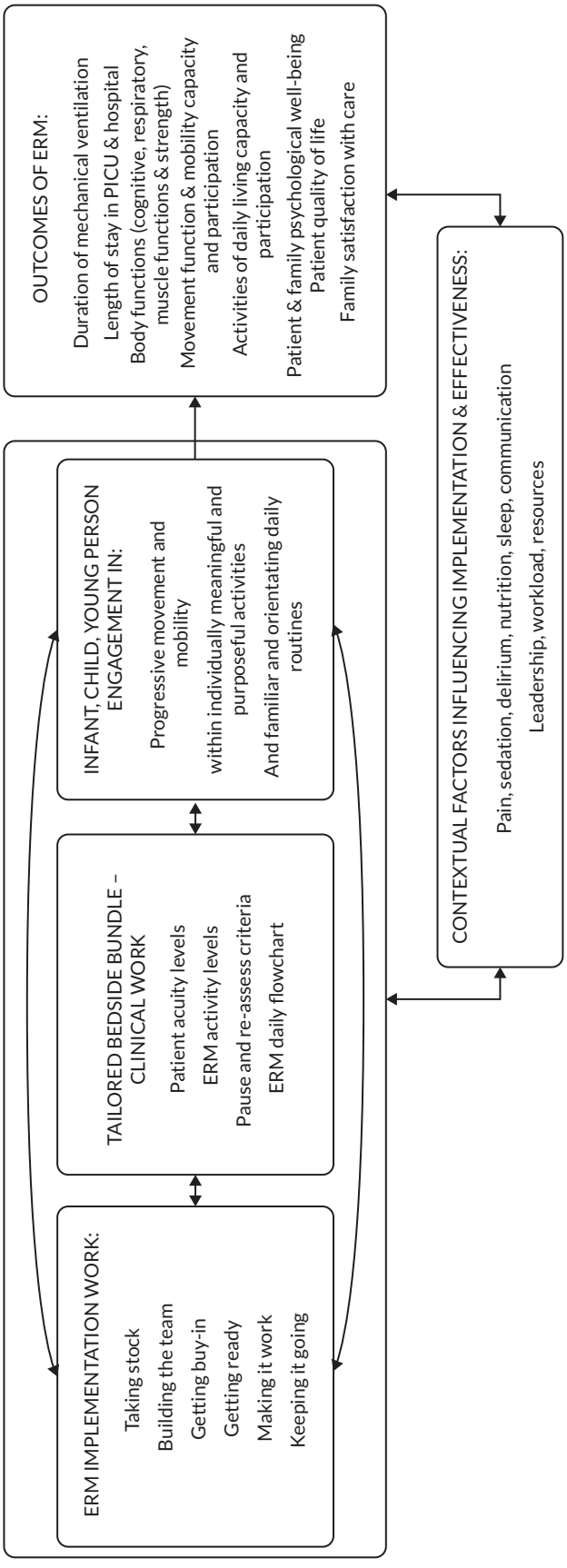

FIGURE 13 Logic model of PERMIT.

Summary of findings to inform the PERMIT study

We know that ERM is currently defined and enacted in multiple ways and that people see the potential value for the diverse patient populations within PICU and are willing to support the (safe) delivery of ERM but are uncertain how best to deliver it.

- We developed core guiding principles around the potential shape and content of the intervention. For example, everyone in PICU, including but not limited to doctors, nurses, physiotherapists and parents, are all essential for ERM delivery – everyone should take some ownership. Also, ERM needs to be as inclusive as possible, with a focus on promoting movement and mobility as early as possible and with progressive increases over time.
- We developed a prototype ERM manual that is focused on both the (safe) delivery of ERM for each patient as well as the introduction and embedding of an ERM approach within a PICU. Centrally, the proposed PERMIT ERM manual is informed by current evidence, experience and theory. It offers a flexible, progressive, approach to the delivery of ERM, with resources including essential clinical materials – the 'bedside bundle' – that consist of patient acuity levels, ERM activity levels, pause and re-assess criteria, and an ERM daily flowchart. It also includes a step-by-step guide to putting ERM into practice – the 'implementation toolkit' – that focuses on building ERM leadership, generating staff buy-in, making ERM workable and keeping it going over time.

Chapter 5 Phase 3: paediatric early rehabilitation and mobilisation during intensive care feasibility study – part 1 study feasibility

Introduction

Following the development of the PERMIT ERM intervention manual in Phase 2 we designed and delivered a pilot feasibility study which would allow both the assessment of the implementation of the intervention in the NHS setting and also the trial feasibility of screening, recruitment and enrolment of CYP into a study that would deliver our manualised ERM intervention. In this chapter, we present the quantitative results of the feasibility of delivering the ERM intervention to CYP. In *Chapter 6* we described in detail the process evaluation of the implementation, feasibility and delivery of the ERM manual within three NHS PICUs.

Study management

The work package was co-led by BRS, JMen and FK. The study management group provided input into protocol, ethics application design and data interpretation. Sati Sahota was trial co-ordinator. JYT designed, adapted and managed REDCAP database. Statistical analysis performed by BRS, RF and James Martin.

Aim

To explore the feasibility and acceptability of implementing the intervention manual in three PICUs.

Objectives

- Determine enrolment, recruitment and delivery of the PERMIT intervention.
- Monitor the safety of the PERMIT intervention and related AEs.
- Establish whether clinically important outcomes can be measured following delivery of the PERMIT intervention.

Methods

Design

A non-randomised unblinded intervention feasibility study with embedded process evaluation.

Intervention

The PERMIT intervention, as described in *Chapter 4*, was defined as a PICU-wide, healthcare professional-delivered intervention, aiming to promote opportunities for the delivery of ERM. The intervention included strategies to develop an organisational environment that supported the delivery of ERM, as well as ERM activities that could be tailored for each individual patient. Each PICU received the PERMIT intervention manual (see *Table 12*). The manual defined two key steps: preparing for the PERMIT intervention; and recruiting patients and delivering the ERM intervention. Within these two steps there were six key phases (*Figure 14*).

Step 1 - PICU preparation: to prepare the PICU for implementing the PERMIT intervention, a group of PERMIT champions (lead multidisciplinary healthcare professionals and managers) was formed

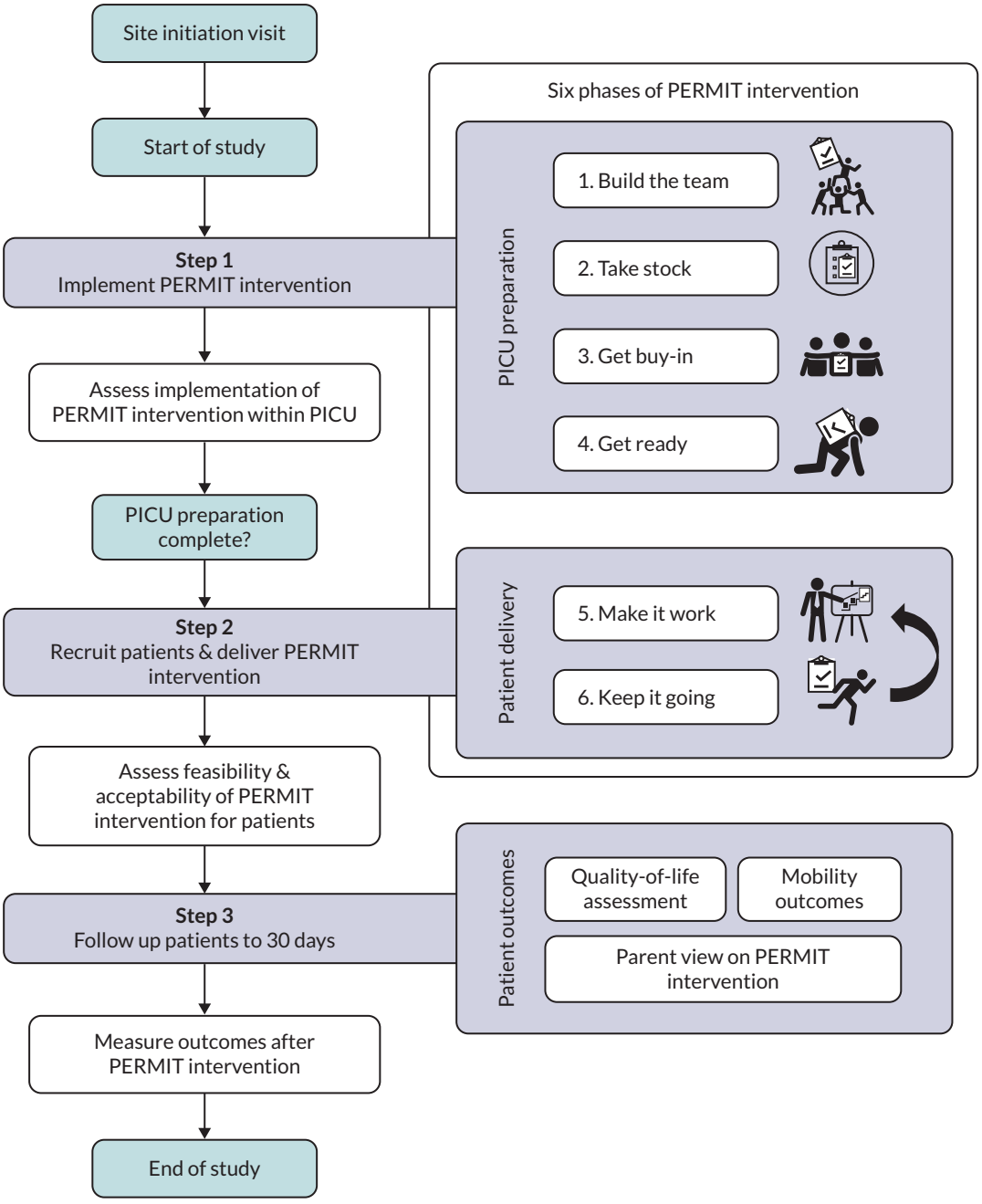

FIGURE 14 Phase 3 feasibility study overview.

(Phase 1 'build the team'). The team then led a rapid self-assessment of their PICU's readiness to implement ERM (Phase 2 'take stock'). Relevant stakeholders were then brought together to participate in local discussions about ERM (Phase 3 'get buy-in'). The local PERMIT team reviewed, adapted and tailored the PERMIT intervention manual to suit the unique circumstances of their PICU and planned how best to incorporate ERM into local work routines (Phase 4, 'get ready').

Step 2 - Patient delivery: once the PICU self-assessed themselves as ready to start to deliver the PERMIT intervention to CYP, the site then progressed into Step 2. At this point, the local PERMIT team started to recruit patients to the trial, receiving ERM as defined by the manual (Phase 5 'make it work'). The study team reviewed the implementation process and worked with the local clinical teams to support ongoing education and training, adjust elements of the process as needed and plan for sustaining the programme beyond the end of the study (Phase 6 'keep it going').

Setting

The study is based in PICUs within three NHS organisations: Birmingham Women and Children's NHS Foundation Trust (Birmingham), King's College Hospital NHS Foundation Trust (London) and University Hospital Southampton NHS Foundation Trust (Southampton). The PICUs were selected because of their diversity in (1) clinical expertise and the patient populations they serve (e.g. two PICUs were both cardiac and specialist PICUs, one non-cardiac but a large neurocritical care and liver transplantation programme), (2) the types of resources and staff groups they have available (e.g. allied health professionals, play specialists, rehabilitation equipment) and (3) ERM experience to date of implementing ERM within usual care (e.g. two units with minimal experience of implementing ERM and one with nationally recognised expertise in ERM).

Sampling and recruitment

Since this study was focused on feasibility and acceptability, an a priori sample size estimation was not required. Instead, our sample size was sufficient for capturing data across the diverse patient groups receiving ERM and the multidisciplinary healthcare professionals involved in implementing ERM.

Children and young people

We aimed to recruit 30 CYP (10 per unit) to receive ERM. All CYP were screened daily against the following eligibility criteria: aged 0–<16 years at the point of admission, admitted to PICU for any reason and likely to remain in the PICU on day 3 post admission. We excluded individuals where, for any reason, the local clinical team did not feel it was appropriate to include them in the study and we recorded the reasons. The majority of CYP were unable to provide informed consent or participate in an assent process (e.g. because of their very young age, levels of sedation medication). We therefore relied primarily on consent from parents/legal guardians (see below). However, where possible and appropriate, we attempted to take steps to involve CYP in decision-making and inform them about the study to the fullest level of their understanding.

Parents/legal guardians

To gain consent for delivering ERM, we approached parents/legal guardians of eligible CYP on day 1 or 2 of admission. As a minimum, they could choose to consent only to their child receiving ERM and to the accompanying data collection (i.e. clinical data about their child and intervention data about the delivery of ERM). This placed no direct burden of data collection on the parents/legal guardians themselves, offering option of participation, without any additional demands during the PICU admission. If parents declined the study then the child received 'standard care' in accordance with the local PICU policy. In addition, parents/legal guardians could choose to consent to completing outcome measures at two different time points – during their child's stay in intensive care and around the time of discharge or shortly afterwards. They could agree to this when they were first approached on day 1 or 2 of admission or at a later stage during their child's PICU stay. We also invited parents/legal guardians to take part in qualitative interviews (see *Chapter 6: Process evaluation*).

Data collection

We collected data about the CYP receiving ERM, the delivery of ERM to patients and the health-related outcomes of relevance to ERM. In this chapter, we report CYP clinical data, PERMIT intervention delivery data and parent/guardian outcome measurement data (*Table 14*). *Chapter 6: Process evaluation* contains details about the data collection of debrief conversations with PICU champions, interviews and survey with health professionals and interviews with parents/legal guardians.

Children and young people receiving ERM: currently, all CYP admitted to PICU have clinical data routinely recorded via the Paediatric Intensive Care Audit Network (PICANet).[67] We identified PERMIT study participants on the PICANet web-based system and conducted a data download of a pseudo-anonymised comprehensive data set pertaining to each individual CYP enrolled into the PERMIT study.

TABLE 14 Overview of PERMIT study data collection

Target population	Measure	Data collection	Items/time required	PERMIT study step	Frequency	Pre-PICU baseline	During PICU	PICU Discharge or 30 days
CYP	Various	Local PERMIT Research Team	Various	2	Various		X	
CYP	Height and weight *Z*-score (admission and discharge)	Local PERMIT Research Team		2	Twice per participant		X	
	Pain visual analogue scale (admission and discharge)		1 item/1 minute	2	Twice per participant		X	
	PELOD-2 score	Local PERMIT Research Team	2 minutes	2	Daily		X	
	cCPAx		5 minutes	2	Daily	X	X	X
	BRADEN-QD		7 items/5 minutes	2	Daily		X	
	CAPD		8 items/4 minutes	2	Daily		X	
	COMFORT Behavioral Score		8 items/3 minutes	2	Daily		X	
	POPC and PCPC		2 items/6 minutes	2	Twice per participant	X[a]	X	
PERMIT intervention data	Patient acuity level	Local PERMIT Research Team		2	Daily		X	
	Prescribed ERM activity level and specific ERM activities			2	Daily		X	
	Delivered ERM activity levels and specific ERM activities (including timing, duration, number and type of staff or family member assisting)			2	Daily		X	
	Reasons for deviating from the prescription, where relevant			2	Daily		X	
	Use of pause and reassess criteria			2	Daily		X	
	Safety and AEs			2	Daily		X	
	Any intervention/manual tailoring proposed or undertaken within the site			2	Daily		X	
CYP	PedsQL™ Infant Scales Version 4.0 – Acute (aged: 1–23 months) OR PedsQL™ Generic Core Scales Version 4.0 – Acute (aged: 2 years+)	Local PERMIT Research Team collect the data from parents/ legal guardians	36 items/<7 minutes 45 items/<10 minutes 21/23 items/<5 minutes	3	Twice per participant	X[a]		X
	PedsQL™ Multi-dimensional Fatigue Scale Version 3.0 – Acute		18 items/5 minutes	3	Twice per participant	X[a]		X

TABLE 14 Overview of PERMIT study data collection (*continued*)

Target population	Measure	Data collection	Items/time required	PERMIT study step	Frequency	Pre-PICU baseline	During PICU	PICU Discharge or 30 days
Parent/legal guardian	Parent Stressor Scale: PICU	Local PERMIT Research Team	30 items/10 minutes	3	Once per participant		X	
	EMPATHIC-30		30 items/<15 minutes	3	Once per participant		X	
	PedsQL™ Family Impact Module Version 2.0		36 items/5 minutes	3	Twice per participant	X[a]		X
	PHQ-4		4 items/2 minutes	3	Once per participant			X
Process evaluation data collection								
PERMIT champions	Weekly debrief discussion	Central PERMIT Research Team	30 minutes	1,2,3	Weekly	n/a		
PICU healthcare professionals	Online survey		15 minutes	1,2,3	Three times per participant	n/a	Online survey	Central PERMIT Research Team
	Interviews		≤60 minutes	1, 2 or 3	Once per participant	n/a	Interviews	Central PERMIT Research Team
Parent/legal guardian (interview)	Interview		≤60 minutes	3	Once per participant			X

a Baseline pre-PICU score will be calculated retrospectively.

The data download included the PICANet minimum data set for each individual participant. This included demographic and socioeconomic data (participant's date of birth, sex, ethnicity); pre-PICU health status (past medical history including underlying conditions and comorbidities); acute illness data [PIM3 (model of PIM that assesses the risk of mortality among children admitted to a PICU)]; PICU admission and discharge diagnoses; comorbidities; operations and invasive procedures performed; type of admission; PICU and hospital LOS, duration of MV, high-frequency oscillatory ventilation, ECMO, renal replacement therapy and vasopressor/inotropic support; sedative medications and days of exposure.

We also collected additional clinical data. The majority of data were collected daily from time of enrolment into the study until PICU discharge (see *Table 14*) and included:

- Level of organ dysfunction: PELOD-2 score.
- Level of physical activity: Children's Chelsea Critical Care Physical Assessment Tool (cCPAx).
- Skin integrity: Braden QD was completed to assess skin integrity and risk of pressure damage/injury.
- Presence of delirium: Cornell Assessment of Pediatric Delirium (CAPD).
- Level of sedation: The COMFORT behaviour scale (COMFORT-B scale) sedation assessment score.
- POPC and PCPC (these were collected at admission to reflect the child's pre-admission status and PICU discharge only).

Data were recorded on individual patient CRFs and transferred for analysis into the REDCap database for the PERMIT study.

Paediatric early rehabilitation and mobilisation during intensive care intervention data: the Local PERMIT Research Team conducted daily screening of CYP on PICU, to calculate the number of patients fulfilling inclusion eligibility and number of patients approached, consented/declined for the study.

Once parents/legal guardians (and CYP where appropriate) had consented, the patients received the PERMIT intervention until PICU discharge. The Local PERMIT Research Team used the PERMIT CRF for each individual CYP to collect the following data about the PERMIT intervention at ward rounds, ERM intervention sessions and through discussion with local clinicians:

- patient acuity level;
- prescribed ERM activity level and specific ERM activities;
- delivered ERM activity levels and specific ERM activities (including timing, duration, number and type of staff or family member assisting);
- reasons for deviating from the prescription, where relevant;
- use of pause and reassess criteria;
- safety and AEs;
- any intervention/manual tailoring proposed or undertaken within the site.

Outcome measurement tools: the Local PERMIT Research Team distributed outcome measurement tools (questionnaires) to parents/legal guardians at two time points: during their child's PICU admission and at the point of PICU discharge or within 30 days after PICU discharge, whichever occurred first. The outcome measurement tools were administered initially as paper questionnaires then by additional methods at parents'/legal guardians' preference. The information was entered into the PERMIT study REDCap database.

During PICU admission: parents/legal guardians provided a retrospective report based on their child's pre-admission status (2 weeks before) by completing a QoL and a fatigue measure (1 and 2) and an assessment of the family pre-admission status (3) from the Pediatric Quality of Life Inventory (PedsQL)™ family of questionnaires:

(1) PedsQL™ Infant Scales Version 4.0 – Acute (Aged: 1–23 months) OR PedsQL™ Generic Core Scales Version 4.0 – Acute (Aged: 2 years+);
(2) PedsQL™ Multi-dimensional Fatigue Scale Version 3.0 – Acute;
(3) The PedsQL™ Family Impact Module Version 2.0 (parent report).

At point of PICU discharge or within 30 days post admission to PICU: parents/legal guardians completed questionnaires based on their child's current health status (1–3) and the family status (4–7):

(1) PedsQL™ Infant Scales Version 4.0 – Acute (Aged: 1–23 months) OR PedsQL™ Generic Core Scales Version 4.0 – Acute (aged: 2 years+);
(2) PedsQL™ Multi-dimensional Fatigue Scale Version 3.0 – Acute;
(3) the PedsQL™ Family Impact Module Version 2.0 (parent assessment);
(4) parent Stressor Scale;
(5) the EMpowerment of PArents in The Intensive Care – 30 Item Version (EMPATHIC-30);
(6) Patient Health Questionnaire-4 (PHQ-4).

Feasibility and acceptability of the questionnaires were captured through monitoring completion rates and feedback from the parent/carer interviews. This is reported in *Chapter 6: Process evaluation*.

Data analysis

We reviewed data for errors, missing data, duplicated records and outliers. Extreme values were set to missing if they were deemed impossible, based on their validity range. Continuous variables were reported as mean and SD or median and IQR based on data distribution. Categorical variables were described in numbers and/or percentages.

Descriptive statistics were used to summarise the PERMIT intervention data, including: success of implementation, recruitment, proportion of consented patients triaged from the acuity table, proportion of consented patients allocated an ERM intervention from the manual appropriate to their acuity level, proportion of consented patients receiving the prescribed ERM, number of AEs and proportion of patients experiencing AEs. Results are presented in text and tables with a narrative summary of findings. Stata v16 was used for all statistical analyses.

Patient and public involvement and engagement

For an overview of the approach to PPIE adopted throughout the study, please see *Chapter 8*. PPIE in this phase of the study focused on exploring the appropriate model of consent, refining participant-facing documents and establishing the overall acceptability of the study. We had planned to speak to parents with direct experience of involvement in research studies, but the research suspension imposed in response to directives to prioritise COVID-related research made this challenging.[100] We spoke to parents of four children (aged 1 month to 16 years) who had experienced one or more PICU admission(s) at BCH and Kings College London. One parent had experience of their child being recruited to a number of non-PICU research studies.

The concept of a staged approach to consent to help reduce the burden about deciding on all aspects of the study at once was liked by the parents (*Table 15*). The challenge of speaking to families so early on in the child's PICU stay was recognised. One parent described the overwhelming emotions and the importance of reducing the demands being placed upon them:

> *There's also the challenge of emotional engagement. When * first came in, there was an overwhelming, primeval pain. This developed into a rollercoaster of positive and negative emotions which over-rided my ability to absorb information ….*
>
> *(PPIE parent)*

Being able to stagger the informed-consent process until a parent was better placed to consider what was being asked of them was endorsed. Other factors that helped were having these messages clearly conveyed in the PIS and ensuring that this process was supported by someone who could provide clarification and answer questions. Parents noted that the material was written at the right level for them; however, concerns reflected the volume of information – 'It's like a book!' – to read and digest. All commented on the value of figures or illustrations to help visualise the sort of interventions that would be involved.

We had also hoped to explore outcome measures and the interview schedules (for consenting parents and declining parents) but this was not possible. All four patients were inpatients on either PICU or had just been discharged to the ward. The parents we worked with were the only parents allowed with their child, so they had a lot of competing demands. It was not felt to be appropriate to provide them with multiple outcome measure questionnaires or interview schedules to review; in fact, this was not allowed in some ward areas due to COVID. The study team therefore drew on our PPIE work from other recent PICU studies that were involved in selecting questionnaires (the OCEANIC study[101]) and qualitative interviews (BRICC trial[102]) to shape the decision-making.

The study received Health Research Authority approval (ref 21/SC/0127), and was registered at https://clinicaltrials.gov/ct2/show/NCT04909762.

TABLE 15 Summary of PPIE feedback and impact on feasibility study

Aspect	PPIE feedback	Impact/changes made
Consent model		
Observational data	Where you are collecting data on what is already taking place – emphasise this. Keep consent simple. If too much is asked at this stage there is a risk people will decline as they are overwhelmed.	Two-stage consent process planned and endorsed: Level A consent: consent for the CYP to receive the PERMIT intervention, with observation and safety monitoring by the team. No additional requirements placed upon parents/CYP. This offers an option for families who want to participate in research, but feel they cannot deal with any additional requirements.
Level B consent: additional questionnaires and interview	Some people might feel able to consider this at the same time as Level A; some families will not. Having the option to defer decision-making about these additional aspects will help some people.	Level B consent: offers parents/legal guardians the opportunity to provide feedback on the experience of receiving the PERMIT ERM intervention through questionnaires and an optional interview post discharge. Parents/legal guardians could consent at the same time as Level A if they felt able to, or at a later stage in PICU stay. Provides choice.
Perspective of those who decline	Good idea, but unsure if people will agree to consent when they've already declined research.	Option of an interview for those who decline to participate.
Patient-facing documents		
Length of the PIS	All four parents commented the document was long and too 'wordy'.	Paragraphs shortened. More subheadings to break up blocks of text. Illustrations added.
Understanding of what ERM interventions could entail or look like	Three parents thought useful to have illustrations/pictures to help visualise the type of interventions involved. Uncertain about use of photos but possibly might be useful for children to help them relate.	Illustrations added, developed by the research team. Illustrations depicted a CYP receiving ERM activities e.g. sitting up in bed or mobilising. In younger child version photos of a child were used (aged 4). These were of D, daughter of our PPIE co-applicant with her consent.
Key information	Minimise information within PIS to 'key information'. Avoid too much focus on data management, this is not a concern. Add this information at the end of the PIS rather than near the start (as less important from parent perspective).	Data-management section kept as brief as possible and added at the end of the PIS.
Infographic	Appropriate and helpful to add clarity to the text.	Infographic used in the PIS to help outline the key steps of the study and to help explain the differences between the levels of consent.
Acceptability of ERM research		
Acceptability of PERMIT phase 3 trial	Trial is important and acceptable based on the information provided in the PIS. Concerns about how this works for children with a pre-existing plan.	Endorsed the study and the current design. PIS emphasises that the alternative (if they decline) is 'standard care' for that PICU to help clarify there is a choice. Site initiation visit (SIV) material prepped to include training on how to discuss this with parents/legal guardians.

Results

Site implementation and recruitment to PERMIT study

Overall, three PICUs participated in the PERMIT feasibility study. The PICUs were chosen as a pragmatic sample with variation in average annual admissions, number of overall PICU staff, types of paediatric specialties and stand-alone children's hospital, co-located adult/paediatric centre.

Sites 1 and 2 started Step 1 of the PERMIT implementation programme in early June 2021. Site 3 was delayed due to contract issues until 2 August 2021 (*Figure 15*). All three sites (100%) achieved the primary outcome and progressed through phases 1–4 of Step 1 (PICU preparation phase) of the PERMIT manual. Time to complete Step 1 and progress to Step 2; site 1: 12.9 weeks, site 2: 15.0 weeks, site 3: 8.4 weeks. *Table 16* reports key feasibility outcomes.

All three sites (100%) recruited their target of 10 patients within Step 2. Site 2 over-recruited (n = 11) as one patient was discharged from PICU a few hours after signing consent and was excluded from reporting below. Full recruitment was completed within 53, 23 and 57 days from the start of Step 2. Overall, 31/35 (89%) of eligible patients were successfully recruited. Only four families declined consent to PERMIT.

Sites completed follow-up to discharge or 30 days (whichever was sooner) of all recruited patients by 91, 32 and 57 days respectively of commencing Step 2.

Of the 31 patients who agreed to consent A (participation in data collection and to receive ERM interventions), 21/31 (68%) also consented to consent B (follow-up assessment tool collection and to be approached about an interview). One patient was discharged from PICU very soon after consent so no data were collected. Therefore, 30 patients were included in ERM assessment data.

Outcome assessment tool completion

Assessment tools were completed at baseline, during daily clinical status assessments and at follow-up (discharge or 30 days after PICU admission) (*Table 17*).

Baseline assessment tools for PCPC and POPC were recorded in 30/30 (100%) of cases. Additional baseline forms were scored for the families consenting to consent B (n = 20). Of these, 19/20 (95%) completed the Family Impact Scale and PedsQL parental core reports, with 7/7 (100%) of those eligible completing the PedsQL Multi-dimensional Fatigue Scale.

The daily patient assessment scores and organ dysfunction scores (PELOD-2 and cCPAX) were collected in nearly all cases (see *Table 17*). In more than 91% of available PICU study days the CAPD, Braden QD and Comfort B scores were collected. Missing data were related to unavailability of research staff to calculate scores contemporaneously, indicating that these were not routinely collected clinical scores by bedside staff.

Follow-up outcome assessment score completion rate was much lower (12/20; 60% of patients), although these were all fully filled in. The protocol defined follow-up time occurring at point of PICU discharge or within 30 days post admission to PICU with flexibility for research staff to assess feasibility. Time from PICU admission to follow-up assessment completion was a median (IQR) of 31.5 (30–40) days. The length of time from discharge of PICU to follow up was median (IQR) 26 (13–36) days.

Demographics

The median age of the 30 patients recruited was 1.8 years (IQR 0.4–5.4) with around a third (9/30; 30%) <12 months (*Table 18*). The most common primary admission diagnosis was a respiratory illness (40%) and 8/30 (27%) were admitted following surgery. Prior to admission, 16/30 (53%) had a normal (PCPC 1) cerebral performance score, and 11/30 (37%) a normal (POPC 1) overall performance score with

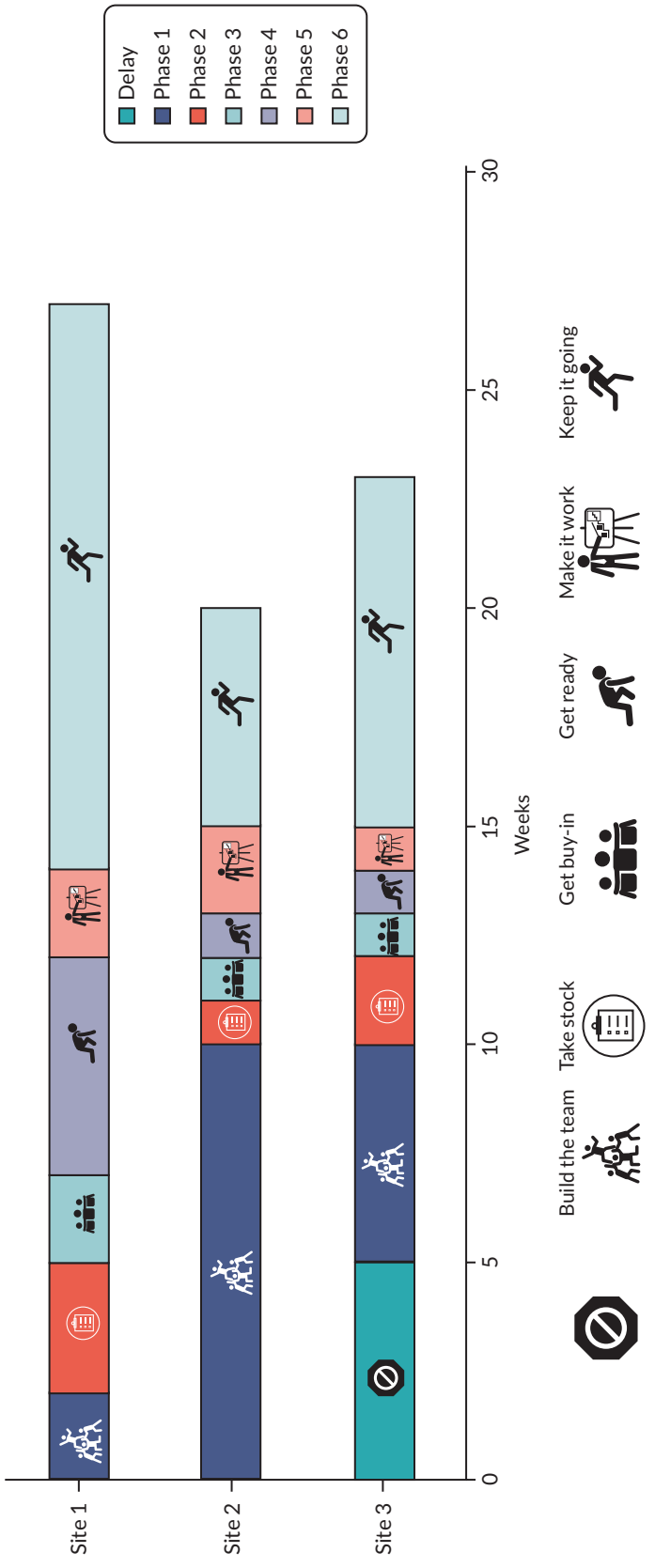

FIGURE 15 Progress of sites through Phase 3 feasibility study.

TABLE 16 Feasibility outcomes for Phase 3 study

	Site 1	Site 2	Site 3	All sites
Implementation steps				
Date study opened	8 June 2021	9 June 2021	2 August 2021	
Date achieved step 1	6 September 2021	22 September 2021	30 September 2021	Range 59–64 days
Days from study open	90 days	105 days	59 days	
Date achieved Step 2 target recruitment	29 October 2021	15 October 2021	26 November 2021	Range 23–55 days
Days from start step 2	53 days	23 days	57 days	
Date of discharge of final recruitment	6 December 2021	24 October 2021	26 November 2021	Range 32–91 days
Days from start step 2	91 days	32 days	57 days	
Recruitment of CYP (and families)				
Eligible CYP patients during Step 2 period	11	14	10	35
Recruited CYP patients during Step 2 (% eligible) (consent A)	10 (91%)	11 (79%)	10 (100%)	31 (89%)
Number of families of CYP agreeing to consent B (% of total recruited)	9/10 (90%)	9/11 (90%)	3/10 (30%)	21/31 (68%) 20/30[a]
Number of families of CYP not consenting to the study but agreeing to interview (consent C)	0/1	0/3	0/0	0/4
Days from PIC admission to study consent med (IQR)	2.5 (2–4)	2 (2–2)	3 (2–4)	2 (2–4)
Days from PIC admission to 1st study day median(IQR)	3 (2–5)	3 (2.5–3)	4 (3–5)	3 (3–5)

a Final number for consent B after one patient discharge.

TABLE 17 Feasibility study outcome assessment tool completion rates

Clinical status scores	Expected (*n*)	Actual (*n*)	Patients (*n*)	Comments
Baseline assessment				
POPC	30	30 (100)	30	Scored for all patients
PCPC	30	30 (100)	30	Scored for all patients
PedsQL Family Impact	20	19 (95)	20	Only consent B
PedsQL Core 4.0 (total)	20	19 (95)	20	Only consent B
Parent report for infants (ages 1–12 months)	7	7		
Parent report for infants (ages 13–24 months)	6	6		
Parent report for toddlers (ages 2–4)	0	0		
Parent report for young children (ages 5–7)	3	3		
Parent report for children (ages 8–12)	0	0		
Parent report for teenagers (ages 13–18)	3	3		
Young child report (ages 5–7)	0	0		
Child report (ages 8–12)	0	0		
Teenager report (ages 13–18)	3	0		

continued

TABLE 17 Feasibility study outcome assessment tool completion rates (*continued*)

Clinical status scores	Expected (*n*)	Actual (*n*)	Patients (*n*)	Comments
PedsQL Multi-dimensional (total)	7	7 (100)	7	Only consent B and patients >2 years
Fatigue Scale 2–4 years	3	3	3	
Fatigue Scale 5–7 years	1	1	1	
Fatigue Scale 8–12 years	3	3	3	
Fatigue Scale 13–18 years	n/a	n/a	0	
Daily clinical status scores				
Level of organ dysfunction: PELOD-2 score	191	189 (99)	30	All patients daily
Level of physical activity: cCPAx.	191	189 (99)	30	All patients daily
Skin integrity: Braden QD will be assessed to assess skin integrity and risk of pressure damage/ injury	191	175 (92)	30	Daily. 15 missed no research nurse
Presence of delirium: CAPD	191	175 (92)	30	Daily. 15 missed no research nurse
Level of sedation: the COMFORT-B scale sedation assessment score	173	157 (91)	30	Daily. 5 on neuromuscular blocking drugs. 15 not able to assess
Pain score	191	184 (96)	30	
Follow-up PICU discharge or 30 days assessment				
PedsQL Multi-dimensional	7	4 (57)	7	
Fatigue Scale 2–4 years	3	2		
Fatigue Scale 5–7 years	1	1		
Fatigue Scale 8–12 years	3	1		
Fatigue Scale 13–18 years	n/a	n/a		
PedsQL Family Impact	20	12 (60)		
PedsQL Core 4.0	20	12 (60)	20	
Parent report for infants (ages 1–12 months)	7	4		
Parent report for infants (ages 13–24 months)	6	3		
Parent report for toddlers (ages 2–4)	0	0		
Parent report for young children (ages 5–7)	3	2		
Parent report for children (ages 8–12)	0	1		
Parent report for teenagers (ages 13–18)	3	1		
Young child report (ages 5–7)	0	0		
Child report (ages 8–12)	0	0		
Teenager report (ages 13–18)	3	1		
PSS PICU	20	12 (60)	20	
Empathic 30	20	12 (60)	20	
PHQ-4: Questionnaire for anxiety and depression	20	12 (60)	20	

Note
Data expressed as numbers (%).

TABLE 18 Demographics: baseline

Group	Med (IQR), *n* (%) *n* = 30
Age (days) median (IQR)	651.5 (128–1968)
Patient age group	
<1 month	1 (3)
1–3 months	6 (20)
4–6 months	2 (7)
7–11 months	2 (7)
1–4 years	10 (33)
5–8 years	3 (10)
9–13 years	2 (7)
13–17.9 years	4 (13)
Sex (female)	14 (47)
Ethnicity	
White	23 (77)
Asian	2 (7)
Black	3 (10)
Not stated	2 (7)
Source of admission	
Same hospital	18 (60)
Reason for admission	
Respiratory	12 (40)
Post general surgery	5 (17)
Cardiac (non-surgery)	2 (7)
Infectious/inflammatory	2 (7)
Neurology	2 (7)
Trauma	2 (7)
Post cardiac surgery	2 (7)
Post neurosurgery	1 (3)
Other medical	2 (3)
Baseline PCPC	
1. Normal	16 (53)
2. Mild disability	10 (33)
3. Moderate disability	1 (3)
4. Severe disability	3 (10)

continued

TABLE 18 Demographics: baseline (*continued*)

Group	Med (IQR), *n* (%) *n* = 30
Baseline POPC	
1. Good	11 (37)
2. Mild disability	13 (43)
3. Moderate disability	3 (10)
4. Severe disability	3 (10)
Ambulatory prior to PICU admission	19 (63)
Crawling/bum shuffling	1 (3)
Standing with support	2 (7)
Assisted walking	1 (3)
Independent walking	14 (47)
Patient weight (kg), median (IQR)	12.2 (4.7–21.6)
Patient height (cm), median (IQR)	85 (58–94.3)
Surgery since PICU admission before start of study	5 (17)

Note
Data expressed as median (IQR), numbers (%).

19/30 (63%) ambulatory. This population was similar to the general population observed in Phase 1c observational study (see *Chapter 3*).

On day 1 of the study (day 3 PICU stay), the median PELOD 2 score was 4 (IQR 3–6). Nearly all were on assisted ventilatory support; 23/30 (77%) invasive MV and 5/30 (10%) on non-invasive support [bilevel positive airway pressure (BIPAP), continuous positive airway pressure (CPAP) or high flow nasal cannula], 6/30 (20%) were on vasoactive infusions and 2/30 (7%) were on neuromuscular blocking drugs (*Table 19*).

Prior to the first study day, four patients had screened positive for delirium. On the first study day the median CAPD score was 14.5 (IQR 9–19). The standard cut-off CAPD score indicating delirium is a score of >12. Therefore, a high proportion (16/30; 59%) screened positive for delirium.

Patients' total LOS on PICU from admission was a median (IQR) of 5 (1–13) days. Following recruitment to PERMIT, the number of study days per study participant was median (IQR) 2 (1–7) days and patients were potentially available to receive ERM on 191 study days. Site 1 had the largest number of ERM study days (*n* = 108) compared to site 2 (*n* = 42) and site 3 (*n* = 41) as a result of a longer LOS for patients at site 1 (*Table 20*).

Number of early rehabilitation and mobilisation activities prescribed per children and young people following patient acuity screening

Of the 191 available study days, 174 (91%) had a morning ward round observed. During the ward round the patient acuity was recorded on 161/174 (93%) occasions. The median (IQR) acuity level (level 1, most unwell to level 4 least, unwell) for study patients was 3 (3–4); only 23/161 (14%) were level 1 or 2 (i.e. most sick). A corresponding ERM activity level for the patient was documented for 159/174 (91%) and an ERM activity prescribed on 137/174 (79%) occasions. PERMIT local researchers were present at the time of the ward round on over half of occasions (58%), providing a range of levels of support (from 17% 'lots of support' to 29% 'no support') to the ward round clinical team.

TABLE 19 Clinical status – day 1 of study

Category	Median (IQR), *n* (%) *n* = 30
PELOD 2 score	4 (3–6)
Airway	
Intubation status	
ETT	22 (73)
Oral	16 (57)
Nasal	6 (20)
Tracheostomy	1 (3)
No airway	7 (23)
Difficult intubation	0
Breathing	
Ventilation status	
No oxygen support	1 (3)
High-frequency oscillator	0
Conventional ventilation	23 (77)
Non-invasive (CPAP/BiPAP)	3 (10)
High-flow oxygen	2 (7)
Supplemental oxygen only	1 (3)
Fraction inspired O_2 [median (IQR)]	0.3 (0.25–0.45) (*n* = 28)
Circulation	
Blood pressure	72 (59–80) (*n* = 30)
Blood lactate	0.75 (0.6–1) (*n* = 22)
Vasoactive drugs (excluding milrinone)	6 (20)
Milrinone	7 (3)
ECMO	0
Open chest/abdomen post surgery	1 (3)
Neurology	
Neuromuscular blocking drugs	2 (7)
Previous delirium screening	9 (30)
Previous positive for delirium	4 (13)
CAPD score	14.5 (9–19) (*n* = 26)
Current CAPD 'positive' for delirium	16 (59)
Glasgow Coma Score	10 (8–13) (*n* = 30)
Drain (chest/wound/other)	5 (17)

continued

TABLE 19 Clinical status – day 1 of study (*continued*)

Category	Median (IQR), *n* (%) *n* = 30
Lines and catheters	
Cannular	23 (77)
Arterial line	16 (53)
Central venous catheter	16 (53)
Haemodialysis catheter	3 (10)
Nasogastric tube	23 (77)
Cerebral function monitoring	1 (3)
Cardiac pacing wires	1 (3)
Drain (chest/wound/other)	5 (17)

Note
Data expressed as median (IQR), numbers (%).

TABLE 20 ERM acuity level, prescription and activities by site

	Site 1	Site 2	Site 3	All
Number of patients recruited	10	10	11	31
Number of patients included in analysis	10	10	10	30
Total ERM patient days	108	42	41	191
ERM patient days per patient (Med IQR)	5 (1–13)	1.5 (0.5–4.5)	2.5 (2–5)	2 (1–7)
Total days received any ERM	89/108 (82)	21/42 (50)	30 (73)	140/191 (73)
Total ERM episodes	234	64	30	328
Total ERM activities	609	96	120	825
Number of ward rounds observed (% ERM days)	106 (98)	27 (68)	41 (100)	174 (91)
Number (%) of ward rounds acuity scored	100/106 (94)	25/27 (93)	36/41 (88)	161/174 (93)
Acuity level at time of scoring (of *n* = 161 scored)				
1 (Most sick)	2	8	2	12
2	2	1	8	11
3	39	13	15	67
4 (Least sick)	57	3	11	71
Acuity level of patients (Med IQR) *n* = 161	4 (3–4)	3 (1–3)	3 (2–4)	3 (3–4)
ERM activity level documented	100/106 (94)	23/27 (85)	36/41 (88)	159/174 (91)
ERM activity planned	80/106 (75)	21/27 (78)	36/41 (88)	137/174 (79)
Total ERM prescriptions	111	22	36	169
ERM prescriptions per patient per day	6 (4–7)	2(1–3)	5 (4–6)	5 (3–7) range 0–16
Documented in ERM prescription booklet	77 (76)	21/21 (100)	36/36 (100)	133/137 (97)
Document in medical records/daily activities	93 (89)	11/27 (41)	38/41 (93)	146/173
Researcher present on ward round	54 (51)	11 (41)	26 (66)	91/156 (58)

TABLE 20 ERM acuity level, prescription and activities by site (*continued*)

	Site 1	Site 2	Site 3	All
Level of support from research team				(*n* = 159)
No prompt/support needed	19	24	3	46 (29)
Prompt/encouragement given	37	0	13	50 (31)
Prompt and explanation needed	22	0	14	36 (23)
Lots of support/education needed	22	0	5	27 (17)
Risk assessment needed	50/107 (47)	11/21 (52)	14/33 (42)	75/161 (47)
Parents present for ERM episodes	200/234 (85)	37/64 (58)	26/30 (87)	263/328 (80)
Parents/staff involved in ERM episodes				
Parents	173	33	26	232 (71)
Nurses	185	22	28	235 (72)
Physios	10	14	17	41 (13)
OT	0	9	0	9 (3)
Speech and language	0	2	0	2 (6)
Others	0	3	0	3 (1)
Medics	0	0	0	0

Note
Data expressed as median (IQR), numbers (%).

In total, 825 ERM activities were delivered within 328 ERM episodes on 140/191 (73%) of patient study days across the three study sites.

Type of early rehabilitation and mobilisation

On study day 1, 26/30 (87%) patients had an ERM activity prescribed and 22/30 (73%) had an ERM episode delivered. Of the eight patients who did not receive ERM, five had an ERM prescription for an activity. One of the four patients not prescribed ERM received an ERM activity on study day 1. Across the first 7 days of the study (*Figure 16*), the rate of receiving a mobility ERM was similar to receiving any ERM. The proportion of patients receiving out-of-bed mobility gradually increased across the study period. For illustration, *Appendix 2*[8] shows the range of ERM activities prescribed and the corresponding proportion that were delivered on study day 1. All sites prescribed a wide range of ERM with a good conversion rate from prescribed to delivered for passive, enrichment and active mobility ERM activities.

Duration of early rehabilitation and mobilisation

Times were recorded at the start and end of ERM episodes. Recording was variable in the database, with some documented episodes as a single ERM activity, others recorded as multiple ERM activities, or continuous delivery of ERM making interpretation difficult.

Appendix 2[9] shows the distribution of recorded durations of ERM: 36/266 (14%) recorded times were <15 minutes duration and 61/266 (23%) 15–29 minutes. The median duration was 30 (IQR 15–75) minutes, which was longer that the median time observed in the Phase 1c observational study of 15 minutes.

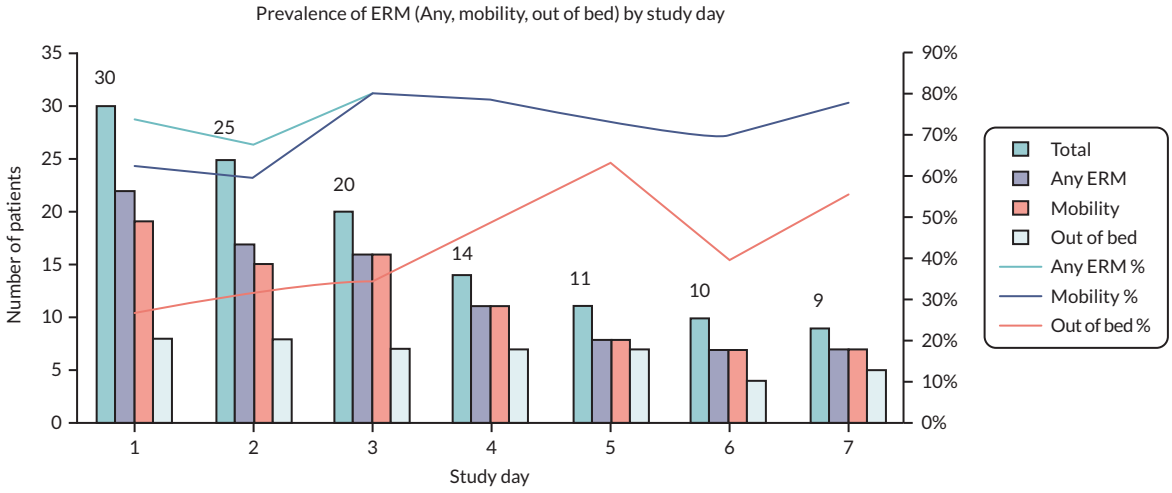

FIGURE 16 Prevalence of ERM delivered on study day 1 by any, mobility and out-of-bed categories.

Safety and adverse event rates during an early rehabilitation and mobilisation activity

The 'pause and assess' criteria embedded within the ERM manual for safe deliver and re-assessment of patients before and during an ERM activity were used in 21/330 (6%) of ERM episodes across 13/30 (43%) patients (*Table 21*). The most frequent categories were desaturation limit exceeded (5/21; 24%) and agitation, anxiety and distress (4/21; 19%).

Only 2/328 (0.6%) of ERM activities in two patients were associated with an AE as specified in the study protocol (*Table 22*). The first was a nasogastric tube dislodged during an ERM episode, but not related to the activity and with mild severity impact on the patient. The second was a blood-pressure change, possibly related to ERM activity, with mild impact on the patient.

Summary of findings to inform the PERMIT study

Overall we successfully and safely introduced a multidisciplinary delivered, PICU wide, early rehabilitation programme using the PERMIT manual to three UK PICUs. All sites implemented the PERMIT programme as described in the PERMIT manual requirement within 8–15 weeks to reach Step 2 to allow patient recruitment.

- A diverse group of PICU patients were recruited on day 3 of PICU admission which represented the wider population of patients identified in Phase 1 observational study.
- All sites successfully recruited the 10-patient target.
- All patients had an acuity level scored and these were repeated on 84% of ward rounds. The acuity level was correctly linked to ERM activity prescription and then subsequently to ERM activity delivered. The level of activity was broadly representative of the acuity level. However, the manual description of progression of activity levels over time was difficult to translate to bedside clinical decision-making and data-recording (e.g. demonstration of increased dose of standing, or mat play).
- All sites modified a local 'menu' of ERM activities specific for each acuity level to allow wider choice of ERM prescriptions.
- A large number of potentially clinically relevant patient outcomes were measured and recorded successfully through validated tools. Baseline and daily tools were recorded over 90% by research and bedside clinical staff and the REDCap database.
- Clinical trial data integration with PICANet existing audit network data collection was successful and allowed reduction in trial data collection.
- All patients received ERM activities safely using the pause and assess criteria with only two trial reported AEs and no severe AEs. The rate of physiological deterioration (e.g. desaturation limit

TABLE 21 Pause and assess criteria

Category	Proportion of ERM episodes *n* (%) *n* = 330
Desaturation limits exceeded	5 (2)
Agitation, anxiety or distress	4 (1)
Pain or discomfort	3 (1)
Parent, care or patient refusal	3 (1)
Heart rate deviation	2 (1)
Blood-pressure deviation	1 (1)
Increase work of breathing	1 (1)
Concerns for airway integrity	1 (1)
Concern for lines	1 (1)
ICP/CPP targets exceeded	0
New arrhythmia	0
Increased respiratory support	0
Ventilator asynchrony (mild)	0
Concern for wound or skin	0
Fall	0
Total	21/330 (6)[a]

CPP, cerebral perfusion pressure.
a Episodes occurred in 13 patients.

Note
Data expressed as number (%).

TABLE 22 Adverse event by site

AE category	Site 1	Site 2	Site 3	All sites
Safety and AEs by site				
Total AEs	0	1	1	2
Total severe AEs	0	0	0	0
Severe AEs per CYP	n/a	n/a	n/a	n/a

n/a, not applicable.

exceeded) was lower than the self-reported AEs in the Phase 1 observational study. None adversely affect the patient, as assessed by the bedside clinical team.

- Although the feasibility study did not aim to do a pre-post implementation assessment on ERM delivery, we did identify that ERM episode durations overall were longer, increasing from a median of 15 minutes in Phase 1 to 30 minutes in Phase 3. In addition, a higher proportion of ERM activities were 'active' compared to 'passive' or 'enrichment' and PT delivered ERM increased from 59% of patients in phase 1 to 93% of patients in Phase 3.

A future trial of ERM therefore appears to be feasible; however, there are a number of recommendations (see *Tables 27*, *28* and *29*). Key messages include:

- A future trial would need to plan for at least a 12-week (3-month) implementation training programme to work through the key components of implementing the PERMIT manual.
- The provision of adequate resources for research data entry and research co-ordinator and regular research team presence on ward rounds appear important to retain the quality and accuracy of data collection.
- Automated integration with existing PICU clinical information systems and workflows would allow additional improvement to data collection.
- We also identified a high rate of delirium when research staff completed the CAPD screening. Previously, PICUs did not screen for delirium automatically (0% of the 15 PICUs in Phase 1c observational study). Delirium screening is a key component of the wider ABCDEF intensive care unit (ICU) liberation bundle.[103] Training and implementation of delirium screening and further investigation of modifiable factors and potential treatments should remain a priority for NIHR funders. Future PERMIT trials should include delirium screening as a key component of the PERMIT manual.

Chapter 6 Phase 3: paediatric early rehabilitation and mobilisation during intensive care feasibility study – part 2 process evaluation

Introduction

Alongside the PERMIT non-randomised implementation feasibility study, we undertook a process evaluation focused on the feasibility and acceptability of ERM and study processes. The implementation evaluation was informed by NPT. NPT identifies factors that promote and inhibit the routine incorporation of complex interventions into everyday practice. It also explains how these interventions work, looking not only at early implementation, but beyond this to the point where an intervention becomes so embedded into routine practice that it 'disappears' from view (i.e. it is normalised). (Text adapted from 'Normalisation process theory: a framework for developing, evaluating and implementing complex interventions' by Murray *et al.*, under CC BY 4.0 licence http://creativecommons.org/licenses/by/4.0/).[87]

Study management

The work package was co-led by BRS, JMen and FK. The study management group provided input into protocol, ethics application design and data interpretation. Sati Sahota was trial co-ordinator. JMen led the process evaluation, with methodological expertise by TR. Qualitative analysis was performed by JMen, TR and Natalie Read.

Methods

We undertook a mixed-methods process evaluation across the three PICU sites. Evaluation of the implementation process was conducted through five key components:

(1) The weekly **debriefs** with PERMIT champions from each of the three PICUs.
(2) Survey of wider PICU healthcare professionals conducted at three time points at each of the three sites throughout the 5-month study period [**normalisation measure development (NoMAD) survey** – implementation evaluation tool[104]].
(3) Qualitative feedback from **interviews with healthcare professionals** from all three PICUs.
(4) Qualitative feedback **from interviews with parents** from all three PICUs.
(5) **Completion rates** of the parent-completed questionnaires (to review feasibility and acceptability).

Sampling and recruitment

We invited two groups of health professionals to take part in feasibility and acceptability work: firstly, ERM champions, those people identified, as part of the PERMIT intervention, as leading the implementation of ERM in the unit and secondly PICU multidisciplinary health professionals involved in any aspect of preparing for or delivering ERM across the unit. Each site aimed to recruit 2–5 ERM champions to take part in weekly debrief conversations (20 debriefs per site; n = 60 total). PICU health professionals were invited to take part in a survey at three time points, aiming for 30 in total per site (n = 90) and consenting staff could also volunteer for a qualitative interview aiming for four or five participants per site (n = 12–15). Parents/legal guardians of CYP recruited to receive the PERMIT intervention were also asked about completing optional outcome measurement tools and an interview. This included those who consented for their child to participate in the PERMIT study (aiming for a sample size of 12–15) and those who declined their child's participation (aiming for one participant per site, n = 3). The study received Health Research Authority approval (ref 21/SC/0127).

Data collection

Weekly debriefs were conducted with ERM champions from each site, either in person or remotely (telephone/video conference). They were recorded in contemporaneous fieldnotes. Qualitative interviews with PICU health professionals and parents were conducted in person or remotely (telephone/video conference/face to face) and were audio-recorded, intelligently transcribed.[105] and edited to ensure respondents' anonymity. Finally, PICU health professionals also completed a brief online survey at three time points (beginning, middle and end of study period).

Debrief conversations, interviews and survey with health professionals focused on exploring implementation progress, determinants and key learning; this happened throughout the study period. Interviews with parents focused on exploring acceptability and feasibility of PERMIT intervention and study processes; this happened towards the end of PICU admission or following PICU discharge (up to 30 days post admission to PICU).

Initial topic guides for debrief and health professionals and parent interviews were designed, drawing on prior literature, experience, NPT[71,72] and TFA.[73] They evolved during the course of data collection, allowing for tailoring and gradual integration of a variety of follow-up issues and topics. The survey was based on the NoMAD Questionnaire, a 20-item self-report instrument[104] (see *Appendix 3*, *Table 41 for NoMAD survey*). The survey was distributed by the local PERMIT champion team through internal e-mail lists, and survey participants had the option to consent to be contacted about an interview with a member of the central PERMIT study team. To ensure both the surveys and interviews captured diverse views across the three units, local teams were encouraged to promote the survey widely to promote different professional groups to engage and participate (criterion-based recruitment).[106] Although data saturation is aspired to within qualitative research, that is when no new themes are emerging,[107] we recognised this would not be achievable within the time scales of this feasibility study.

Data analysis

Notes from the debriefs were imported into NVivo 12 and deductively coded and analysed using a qualitative content analysis approach of systematic coding and categorising.[58] Two researchers (JM, NR) independently familiarised themselves with the data and conducted open-coding, utilising NVIVO™ software for data management. Codes were then discussed and organised into higher-order subcategories and categories.[59,60] In relevant sections of the paper free-text quotes from respondents are reported to add clarity, staying close to the original meanings and context.[61]

The interviews were analysed using a thematic analysis approach. This approach was taken because thematic analysis allows for the identification of common threads that extend across an entire interview or set of interviews.[108] It also values the detailed and nuanced account of data, particularly emphasising the context.[60] Analysis was informed by the work of Braun and Clarke,[109] with NVivo™ software used to assist in the organisation and coding of data. The Framework approach was then used to facilitate systematic, rigorous and transparent data management.[110,111]

The survey data were analysed descriptively. Three questions explored: (1) how familiar ERM felt, (2) if ERM was a 'normal' part of work and (3) if it will become a normal part of work – responses were on a scale of 0–10 (e.g. 0 very new up to 10 completely familiar). The remaining 20 questions required a Likert-scale response (strongly disagree, disagree, neutral, agree, strongly disagree). Responses were allocated a score −2 (strongly disagree) to +2 (strongly agree) for interpretation; median scores for each question are presented.

Results

Study participants

We undertook 48 debrief sessions with ERM champions (*Table 23*). Despite recruiting well to the champion role at each site, the debrief calls were attended consistently by the same people. Debrief

attendees included nurses (*n* = 2), medical representatives (*n* = 3), physiotherapists (*n* = 2), OT (*n* = 1) and clinical research nurses (*n* = 3).

We received survey responses from 118 health professionals across the MDT. The largest response group (66/118; 56%) were registered nurses and overall most had been in PICU 3 years or longer (88/118; 75%) (*Table 24*).

We interviewed 13 health professionals, including medical representatives (*n* = 4), PICU physiotherapists (*n* = 3) and one physiotherapist from a different team (provided on-call cover), advanced nurse practitioners (ANP) (*n* = 2), one OT, one bedside registered nurse and one team leader registered nurse.

In total, 21 parents consented to participate with the optional questionnaires and the interview, with 15 parents interviewed. Of the six who did not participate, two subsequently declined the interview when contacted, one was only in the study for a few hours so did not feel they could offer any insight and the second child had been re-admitted to hospital so parents did not feel able to participate at the time. One child died before discharge from hospital and three parents did not respond when contacted, after a median of three attempts to contact them. One parent was interviewed but then withdrew therefore interviews from 14 parents were included in the analysis. Interviews took place between November and December 2021 and were conducted in a variety of ways, subject to parental preference. Two were conducted face to face at BCH, five took place on Zoom and seven took place over the telephone. The final analysis included mothers (*n* = 12) and fathers (*n* = 2). All of the parents had experience of their child having been intubated and mechanically ventilated during their admission to PICU, and 12 were parents of a child admitted as an unplanned admission.

Pre-paediatric early rehabilitation and mobilisation during intensive care context – questions of capacity

The PERMIT study was introduced into three PICU sites. Across all the sites, potential issues around capacity, especially in relation to levels of MDT staffing, as well as priorities, in relation to place of ERM in ongoing care, were present (*Table 25*). All sites reflected that although ERM was part of care, they 'didn't do it actively or in a structured way' (*Site Two: Medic interview*). Patients with defined pathways – neurology patients, those classified as 'long stay', infants and patients who were elective and had a more predictable recovery – were more likely to receive ERM. Delivery did not often occur 'early' and was undertaken inconsistently:

> *quite limited in terms of what was being done on the unit. There were elements of, I guess, what you could classify as ERM starting to emerge, but I think the timing was definitely at a later point of the child's stay.*
> *(Site Three: Physio interview)*

TABLE 23 Recruitment for the process evaluation study by site and method of data collection

		Site 1	Site 2	Site 3	Total
ERM champion debriefs	No. champions	22	11	12	45
	Attended debriefs	20/20	17/20	11/11[a]	48
	Attendees at debrief (Mean)	3.7	2	1	2.2
Participant interviews	Health professionals	7	4	2	13
	Parents	7	6	1	14
PICU health professionals survey	Health professionals	47	34	37	118

a Only 11 debriefs due to contract delaying start date and therefore reduced study duration.

TABLE 24 NoMAD survey respondent demographics

Category	Site 1 *N* = 47	Site 2 *N* = 37	Site 3 *N* = 34	Total *N* = 118
Profession				
Nurse	27	23	16	66
Medic	14	4	5	23
Physiotherapist	3	5	7	15
Advanced nurse practitioner	0	4	0	4
OT	1	0	3	4
SLT	0	0	2	2
Clinical skills worker	1	0	0	1
Pharmacist	1	0	0	1
Research nurse	0	1	0	1
Speech therapist	0	0	1	1
Years of experience in PICU				
>1 year	3	1	3	7
1–2 years	11	3	9	23
3–5 years	10	7	9	26
6–10 years	4	9	7	20
11–15 years	5	9	3	17
>15 years	14	8	3	25

TABLE 25 Conditions within PICU prior to the study introduction

Workforce contexts	Organisational contexts
Bedside nurses • Provide 1 : 1 care • Focused on 'essential' life-saving/ sustaining work • ERM not seen as part of this currently	Unit bed capacity • Dependent on securing sufficient nurses on shift to shift basis • At times no choice to decline patients so a unit can be at >100% capacity
Nursing workforce • Many staff vacancies • On shift-to-shift basis may have reduced staffing and poor skill mix	Patient acuity • May have appropriate staff:patient ratios for 1 : 1 care, but the patients on the unit are 'sick' and have high level of need • Staff may have to forgo activities seen as 'desirable' to support other staff members
Specialist services (such as SLT, OT) • Large waiting lists, long waiting times (even for inpatient on PICU)	Culture surrounding ERM • ERM often not conducted 'early' • Often seen as physio domain • Lack of ownership within nursing particularly
MDT • Limited resources for full MDT involvement with every PICU patient	ERM programmes • Presence of an ERM programme does not equate to ERM conduct • Absence of an ERM programme does not equate to no ERM • Both situations can find a lack of standardisation
	ERM funding • No funding available for 'extra' work required for ERM currently
	Additional challenges of 2021 • COVID, staff illness, staff isolation • Reduced parental visiting, no extended family visitors

In addition, it was more likely to occur on weekdays, in office hours, and interventions were likely to be 'low level' and often movement-focused. In Site 1, an ERM programme had been launched in 2019, with good leadership and good staff engagement. However, the programme had floundered – with maternity leave, staff turnover and service pressures – and in 2021 there was little awareness of the programme. The champions felt that the feasibility study would be an opportunity to reinvigorate an ERM programme and secure staff buy-in. Neither of the other two sites had a pre-existing ERM programme, although they both reported being very enthusiastic about the idea of commencing one.

Introducing PERMIT – (re)organising the work

Throughout the whole study period all three units experienced huge service demand, running significantly over capacity with reduced staffing. In addition, alongside the impact of COVID-19, there were unanticipated challenges or competing demands. At Site 1 this included the move of the whole PICU to a temporary location. The sites progressed through the first four phases at different paces (see *Figure 15*). Due to the prior history of an ERM programme, Site 1 progressed through initial phases quickly, with more time spent on Phase 3 – supporting staff engagement and training – and Phase 4 – adapting the manual and planning how to effectively deliver the ERM intervention and the trial at their site. Site 2, in contrast, spent more time on Phases 1 and 2. There was less focus on education and training and the specifics of where and how discussions about ERM took place, and more on the logistical factors associated with running the research study and capturing the data. Site 3 experienced a significant delay (9 weeks) in commencing the study, due to local site approval issues. This delay was not only frustrating for a site enthusiastic to start staff training and education, but also added pressure about the feasibility of recruiting 10 patients within an 11-week period. As a result, the site spent relatively little time in each of the phases, with the site starting to screen and recruit by week 16, only 1 week after Site 2 and only 3 weeks after Site 1.

To embed ERM, all sites realised – often more strongly in retrospect – the fundamental importance of 'education, education, education! … I think that's the key thing I think to try and make it work' (*Site One: Physio interview*). Staff training and education were central to conveying information to all staff on the PICU, supporting them to understand the key principles of the ERM programme and build experience and confidence in delivering ERM. Ongoing education and teaching within formal contexts (e.g. organised study days), alongside informal, ad hoc moments (e.g. at bedside) and being 'more opportunistic with teaching when clinical' (*Site Two: Debrief*) were needed to support delivery of ERM. A refined, considered, educational strategy was introduced in Site 1:

> *Clear education plan, trainers are being trained and there is a training log planned to keep track of who has had what training.*
>
> *(Site One: Debrief)*

This strategy focused on identifying what key information staff needed to understand, how many people needed training and a plan for how to train them.

There were challenges to providing the education and training sites that were felt to be required to achieve adequate staff commitment, confidence and skills. A core factor was the short trial period – 20 weeks from start to finish, less for Site 3, due to delays. At Site 2, someone commented that 'the speed at which we had to put it in place and the speed at which we had to then recruit I don't think gave us time to grow the roots enough' (*Site Two: ANP interview*). At this site an additional challenge emerged, with educational resources having to be directed towards getting staff trained as quickly as possible on a new ventilator. Sites felt that the absence of any pre-prepared education and training materials accompanying the manual had been a challenge throughout the 5-month study period. As a result, Site 1 shared training material (which was then localised and rebranded) as well as access to a core trainer to support training and education at the other sites.

Delivering PERMIT – integrating early rehabilitation and mobilisation

Despite all the challenges associated with education and the speed with which the study was rolled out, PERMIT was seen by health professionals and parents as worthwhile (*Table 26*). All three sites reported positively about how the ERM programme cultivated multidisciplinary working, helped with clarification of roles and helped with elements about leadership and staff buy-in around ERM. MDT work was recognised as being central to delivering the desired level of ERM. This meant embracing multidisciplinary working to optimise service provision:

> *There are not enough hours in the day for a therapist to deliver the amount of ERM they'd like to be seeing going on. … It needs to become an MDT-based focus … everybody's role. Therapists can't be the only ones delivering this.*
>
> *(Site Three: Physio interview)*

In particular, the role of the bedside nurse was recognised as vital to support delivery. The challenge was about raising the profile of ERM as a priority in nurses' daily work so ERM was no longer seen as just a desirable component, but an essential aspect of care provision. At moments, people struggled with whether to prioritise supporting colleagues:

> *Nursing staff report feeling guilty that they're doing nice things with patients – play, music etc. when the rest of the staff are very busy and struggling with unit demands.*
>
> *(Site One: Debrief)*

However, exposure to ERM over time, especially seeing ERM in action on a unit, could help in the process of it becoming embedded as 'standard care'.

Exposure was, in part, challenging, however, because there were differences across sites to the extent that PERMIT was rolled out. At Site 1, ERM following the PERMIT manual – that is assessment of acuity, activity planning, risk assessments and family involvement – was regarded as the standard for all patients. At the other sites, only patients recruited to PERMIT received ERM as per the manual. Although there was variety in the use of the bedside bundle, there was recognition of the value to support ERM delivery and a shift in the traditional mind-set of a patient needing to be stable to be eligible to receive ERM. In practice, exposure emerged in a variety of ways, be that through strategies in place to promote staff buy-in and enhance involvement over time:

> *there's posters going up, conversation in the coffee room taking place. Physio colleagues are more active in reminding clinicians at the bed space, or at least reminding the nurses to ask doctors doing the ward rounds … lots of general awareness that early rehab and mobilisation is actually important for the patients.*
>
> *(Site One: Medic interview)*

In and through taking part in PERMIT, staff exposure to ERM increased over the study period. Ward rounds also offered a space in which to undertake ERM discussions, at the very least in relation to whether a patient may be eligible for the study, as well identifying activities of rehabilitation for those recruited, if not for others outside PERMIT. Additionally, positive family feedback about involvement with ERM, when shared with staff, increased exposure and understanding of potential impact.

Over time, health professionals understood that ERM was important for the physical and psychological recovery of the CYP, as well as the psychological well-being of parents/carers supporting their involvement in their child's care. For example, one site noted that:

> *Parents are engaged and involved, really keen on the ERM process. Parents are filling out the activity booklet and adding lots of detail. Seems to give them a focus and a process to be involved in.*
>
> *(Site Three: Debrief)*

TABLE 26 The four constructs of NPT mapped against the three PERMIT study sites

NPT construct	Site 1	Site 2	Site 3
Coherence: do people make sense of ERM?			
Understanding of the purpose of ERM	Good. Expanded beyond 'movement' to become more holistic	Unclear within the study team. Unclear about wider PICU. Clear for parents	Good within site champions. Unclear about wider PICU. Clear for parents
Understanding of the roles of staff in relation to ERM delivery	Developed over the study. Some differences in views of what was ERM vs. 'good nursing care'. Some concerns about professional boundaries emerged	Staff clear about roles. Also, clear no capacity to do 'extra'	Staff clear about roles, but lack of engagement from nursing. Also, clear no capacity to do 'extra'
Understanding of the study within clinical team	Moderate, but supported by research team	Limited, but supported by research team where possible	Unclear, limited (research team) resources to support
Understanding of the study within parents	Generally good on purpose and possible impact	Generally, on purpose and possible impact	Generally good on purpose and possible impact
Understanding of the impact of ERM on staff's work	Good, but felt already at capacity	Good, but felt already at capacity	Good, but felt already at capacity
Potential value and worth of ERM programme	Good and worthwhile. Staff some concerns about sustainability without additional resources	Good and worthwhile. Staff concerned not possible to continue without additional resources once study ends.	Potentially good and worthwhile. Champions aware not possible to continue without additional resources once study ends.
Cognitive participation: do people get involved with providing ERM and stay committed?			
Were there key people driving ERM forward?	Good leadership, MDT involvement and good attendance at debrief	Physio and research nurses predominantly. Debrief attendance minimal	Good leadership from physio but limited other engagement. Debrief attendance minimal
Is ERM seen as a legitimate part of staff role?	Yes: research team Yes: clinical nurses/physios Uncertainty for medical staff about exact role Yes: parents	Yes: research team (funded) Yes: physios Uncertainty from some other staff Yes: parents	No: research team (none available) Yes: physios Uncertainty from some other staff Yes: parents
Did staff get involved and incorporate ERM into practice?	ERM rolled out to all patients as standard care. ERM delivery reported (mostly low level)	Only patients recruited to PERMIT received ERM. Unclear extent ERM delivered	Only patients recruited to PERMIT received ERM. Unclear extent ERM delivered
Are the team motivated to support ERM over time?	Yes, but concerned as already experienced one failed attempt to embed an ERM programme	Yes, but will not take a programme any further until further resources funded	Yes, but recognise they need time and resources to re-launch a programme
Are parents motivated to support ERM over time?	With support parents are willing and motivated to work with healthcare professionals to deliver	With support parents are willing and motivated to work with healthcare professionals to deliver	With support parents are willing and motivated to work with healthcare professionals to deliver

continued

TABLE 26 The four constructs of NPT mapped against the three PERMIT study sites (*continued*)

NPT construct	Site 1	Site 2	Site 3
Collective action: do people make ERM work in practice?			
Did participation with the study require additional staff training?	Yes, underestimated. Tried initially to train all staff, then scaled back	Yes, targeted to staff caring for study participants	Yes, targeted to staff caring for study participants
Was ERM operationalisable?	Yes	Unclear	Yes
• Ward round	Change difficult, but ↑	Unclear	Unclear
• Daily acuity assessment	↑ with time	Unclear	Unclear
• Activity selection	↑ with time	Unclear	Unclear
• Risk assessment	↑, but not fully conducted	Unclear	↑, but not fully conducted
• Parental involvement	Supported and encouraged	Supported and encouraged	Supported and encouraged
• Trial-related documentation	Completed by bedside staff and research nurses	Completed by research nurses. Bedside staff struggled with paper documents	Completed by PI/champion – found very challenging. No research nurse support
Reflexive monitoring: do people evaluate ERM and PERMIT as worthwhile?			
Was ERM evaluated as worthwhile?	Yes: feel ERM shifted to being seen as part of routine care. Positive impact for child and family	Yes: not sustainable without additional resources and nursing leadership. Positive impact for child and family	Yes: considering innovative methods to sustain. Positive impact for child and family
Acceptability of PERMIT study data collection?	Yes: because there was research nurse support	No: too much burden on clinical staff because it did not integrate with IT system	No: too much burden on PI/champion. No research nurse support
Acceptability of PERMIT outcome measurement tools for staff?	Yes: number of questionnaires a concern but they were short	Some concerns: re time points and length for families	Yes: but fewer families consented (3/10)
Acceptability of PERMIT outcome measurement tools for parents?	Yes: but not always perceived as relevant to their child	Yes: but not always perceived as relevant to their child	Yes: but not always perceived as relevant to their child
Overall acceptability of the study for staff	Good	Mixed – good	Good
Overall acceptability of the study for parents	Good: increased parents' confidence, sense of purpose and satisfaction. Some saw direct benefit for child. Saw positive impact on staff behaviour and prioritisation	Good: increased parents' confidence, sense of purpose and satisfaction. Some saw direct benefit for child. Saw positive impact on staff behaviour and prioritisation	Good: increased parents' confidence, sense of purpose and satisfaction. Some saw direct benefit for child. Saw positive impact on staff behaviour and prioritisation
Is a future study viewed as worthwhile by staff?	Yes: staff concerns reflect workload and resources	Yes: staff feel need to address nursing and medical leadership, workload and resources	Yes: staff feel need to address leadership, workload and resources
Is a future study viewed as worthwhile by parents?	Yes: further research is important	Yes: further research is important	Yes: further research is important

All the sites reported that PERMIT has supported parental involvement. Feedback from parents was reported as 'overwhelmingly positive and everyone's saying how important it was within their journey' (*Site Three: Physio interview*). All parents commented that there had been benefits to participating. This seemed to span from the emphasis the programme placed on parental involvement to the purpose that the programme provided. However, parental involvement in activity selection varied, with some referring to paperwork to help guide choices, while for others it appeared to be more led by the health-care professionals, whereas other parents reported not seeing a list or feeling actively involved in activity selection. Engagement in process was clearly enabling for parents:

> *It was quite nice to know, "Oh we can move onto the next stage" or you know, "Oh look there's a new activity on the list, oh I hadn't thought about doing that activity with him". Or realising that sitting in the bed is a milestone almost. You know, it's a new activity. As a parent you can see that as a milestone of their recovery.*
>
> *(Site Two: Parent interview)*

Overall, most of the activities were undertaken while their child was 'in bed'. The most commonly reported activities were cuddles, reading, singing, talking, touch or massage and stretches, which matched recorded activities completed by the bedside staff. The impression was that most parents felt the activities were tailored and appropriate for the stage the child was at.

Many parents reported feeling more confident in becoming involved in supporting ERM, that for them 'I think it was so empowering' (*Site One: Parent interview*). Parents reflected on how sick their child had seemed to them initially, but once they were familiar with what ERM involved and how they could be involved it gave them a sense of purpose:

> *But it also gives us something to do to feel useful because you're in a situation where it's one to one care. They know exactly what they're doing, we've got no idea. We can't help do anything in ICU, but you're just looking at your child and you can't do anything. But being able to have a structure as to what we can do to help, all of the activities that we could do … it meant that we could do something to actively help his recovery.*
>
> *(Site Two: Parent interview)*

Parents perceived that being recruited to the study provided guidance to staff about activity assessment and selection and also encouraged them to consider the child holistically. They also felt more confident leaving their child to have a much-needed break because they trusted that staff would also follow the programme. Some saw a direct benefit to their child. Others were less sure or queried whether it was fully relevant to their child because they were an infant, but still saw the study as worthwhile. For many the main positive impact for their child was the contact the programme encouraged with parents. This spanned all aspects of care, particularly cuddles. Parents recognised how central they were to their child and their presence was therefore important to help support their child. However, outside the context of PICU delivery, support and guidance for delivering ERM were lacking. Several families reported that leaving PICU is only the first stage in recovery and more needed to be done to support them with ERM beyond PICU discharge.

Delivering PERMIT – integrating trial processes

Having access to research delivery support was central to supporting recruitment, data collection and data entry. This reduced demand on bedside staff as well as freeing up the site team for education and ERM delivery. Sites 1 and 2 worked with research nurses – with Site 1 having access to a clinical research nurse from Stage 4 – whereas at Site 3 did not. At Site 3 the lead champion took on all the workload associated with implementing the study and evaluating ERM delivery and they noted that:

> *The research side is very time consuming. The data collection and research collection are the biggest barrier to doing the ERM, the data collection, the consent process, the questionnaires – it's all so time-consuming.*
>
> *(Site Three: Debrief)*

All three sites commented on the large volume of work associated with conducting the PERMIT study. A research team presence, ideally to cover all days and times of the week, was seen as essential. All parents also provided positive feedback about the role and presence of the research team during recruitment: their professionalism, the sensitivity with the timing of discussions and their ability to respond to questions.

Overall, the families were positive about the study recruitment process. Two parents referred to the challenge of written leaflets for parents with additional needs. As ERM was rendered as the 'usual' standard of care within the units – by the PIS and research team – many parents had low expectations about the potential risk of participation:

> *My main question was about if there was anything extra that was going to be done, anything invasive, and if it wasn't then I didn't see any reason why I wouldn't consent to it.*
>
> *(Site One: Parent interview)*

For the majority the perception of 'minimal' to 'no' risk meant that they found this a relatively simple decision. The choice of a staged consent model was significantly influenced by other studies within the PICU environment[66,102] and the PPIE work conducted within the PERMIT study (see *Chapter 8*). Of the 30 children recruited to the trial, 21 of the parents/legal guardians consented to participate in the 'additional' aspects of the PERMIT study (70% consent rate). Seven families (33%) consented in a staged approach, with 14 (67%) happy to consent to all parts in one go. Some parents felt signing up in stages had been really helpful for them, not overloading them at a difficult time. There was also a sense from some families that because ERM was standard practice on a PICU that an opt-out consent approach where families did not have to actively consent or could be asked at a later stage could be acceptable.

Introducing and embedding the study paperwork was challenging at times. This was only produced as physical documents and Site 2 did not have time or capacity to adapt it to their electronic patient management system, so

> *[h]aving the documentation all on paper created resistance from staff, they like everything to be done on the computer. This was perceived as a lot more work to have to do.*
>
> *(Site Two)*

Easy access to documents at the bedside helped support and sustain study work. Sites also had some concerns about the outcome measurement tools provided to families, in part tied to the logistics of managing the process – with uncertainty about the time points required and the challenge of getting these completed. They also were uncertain about the volume of questionnaires to be provided to families. However, on the whole the questionnaires were viewed as acceptable by parents. Negative comments reflected that some questions were inappropriate for their child in terms of their ability to do the developmental outcomes (mostly for the parents of neonates), length and the slightly repetitive nature of some questions.

Embedding ERM post-PERMIT and PERMIT trial – (continuing) questions of capacity

As part of Phase 4 work, a debrief was held 2 months after the study had closed to recruitment. Despite huge enthusiasm about the potential for ERM to continue after PERMIT closed, all ERM activity related to the programme had stopped at Sites 2 and 3. However, at Site 1, even in the contexts of increased PICU workloads and COVID creating challenges for staffing, they still felt that ERM had shifted to being seen as part of routine care. They noted how 'the research has increased frequency and awareness of ERM' (*Site One: Debrief*), with most patients now having their acuity assessed daily and staff considering what ERM could be conducted, even if it was not always possible to undertake the planned activities.

Bedside nurses appeared to have increased confidence in initiating and conducting ERM, with increased awareness of what each MDT member could contribute to ERM.

Core issues to embedding ERM after PERMIT remained, with Site 3 reflecting that

> *the challenges have taught us so much! … Need increased presence and visibility of an ICU specific therapy team to fully integrate into ICU. We learned also that therapy doesn't need to be so structured and planned, we can do it in so many ways.*
>
> *(Site Three: Debrief)*

They felt they would 'review, revamp and re-launch!' with more time factored in for the programme to embed, and that the 'minimum time to make this really embed would be 12 months' (*Site Three: Debrief*). All three sites felt that additional resources were required to support (ongoing) staff education and training; that visibility, experience and (positive) feedback around multidisciplinary ERM working was key, as well nursing staff taking ownership being central to embedding.

The NoMAD survey results align with the way that sites, over time, began to realise the complexity of the work of introducing and embedding an ERM programme. Between time point one and two there was an increase in ERM familiarity through initial engagement, with a realisation that ERM was currently part of normal practice and would become part of normal practice (see *Appendix 3*, *Figure 20*). However, by the final and third survey the level decreased back to baseline.

A similar temporal pattern was seen in four NPT items: around questions of the legitimacy of ERM being a part of their role (Q15); being open to working with colleagues in new ways to use ERM (Q16); and notably, continuing to support ERM (Q17) and that sufficient resources are available to support ERM (Q23) (see *Appendix 3*, *Figure 21*). However, across all time points there was strong (and stable) agreement about seeing the potential value of ERM in their work (Q13) and strong (and stable) disagreement across all time points that ERM disrupts working relationship (Q19).

Summary of findings to inform PERMIT study

Although there were many challenges to implementation of the PERMIT intervention within the context of busy PICUs during a global pandemic, there was significant multidisciplinary input and support from parents/carers for ERM to be standardised within clinical practice. A future trial was therefore viewed as acceptable and we identified a number of recommendations for a future trial (*Tables 27*, *28* and *29*). Key messages include:

- Within a future trial, ERM needs to be embedded as standard routine practice for all CYP within the PICU. This would also enable an opt-out informed consent to be utilised and potentially reduce some of the challenges that parents outlined in relation to consent processes.
- Research delivery support is vital to successfully complete the trial processes, but the research team cannot lead the implementation of a programme or it will not fully embed.
- Bedside nurses are ideally placed to help deliver ERM but this workforce is already stretched. Currently ERM is not in their priorities and is seen as desirable, rather than essential. Adequately resourced PICU therapists will be required to support implementation and delivery.
- There is no spare capacity to deliver 'extra' ERM within current resources.
- ERM is seen as important for the physical and psychological recovery of the CYP, but is also important for the psychological well-being of parents/carers supporting their involvement in their child's care.
- Being involved with ERM is seen as hugely important for parents/carers. Further consideration of how we provide training and support for parents to facilitate this involvement is needed.

TABLE 27 Summary of recommendations about trial design for a future PERMIT trial

	Source of information	Debrief	Staff int.	Parent int.	Trial data
ERM	• ERM needs to be the standard of care on the unit for all CYP	✓	✓	✓	
	• All staff need to be prepared and knowledgeable about planning and delivering ERM	✓	✓	✓	
Population	• ERM can be delivered to a broad, diverse population of critically unwell or injured children				✓
	• Focusing resources to provide ERM to patients in PICU on day 3 and longer is acceptable	✓	✓		✓
	• Most PICU patients are on assisted respiratory support; use of duration of organ support may be a viable primary outcome for a future trial				✓
Parental consent	• If ERM becomes the standard of care then an opt-out consent model is acceptable			✓	✓
	• Consent in the first few days of a PICU admission is possible, but challenging for parents			✓	✓
	• If informed consent is required on a per patient basis then consider a staged approach to parents/legal guardians to reduce burden of decision-making			✓	
	• Interviews with parents who consent to research is an acceptable additional request. Need to offer flexibility in their conduct			✓	
Parent information	• Avoid making the PIS too long			✓	
	• Consider additional methods to help share information – parent stories, short online (e.g. YouTube) videos			✓	
	• Consider preparation and/or raising awareness for elective patients			✓	
Study outcome measures	• Collect as few data as possible (including questionnaires) to minimise burden	✓	✓	✓	✓
	• Appropriately fund research delivery time to provide support to facilitate completion and data entry	✓	✓		
	• Adapt method of data collection about ERM delivery to local site preference (and support integration of CRFs into electronic patient management systems where applicable)	✓	✓		✓
	• Provide clarity about the time points questionnaires (if required) need to be distributed	✓			
	• Conduct questionnaires at as few time points as possible (as repetition challenging, time-consuming)			✓	✓
	• Consider ways to facilitate completion for parents with additional needs			✓	

TABLE 28 Summary of recommendations about trial ERM intervention and tools for a future PERMIT trial

	Source of information	Debrief	Staff int.	Parent int.	Trial data
ERM launch	• Sites need to provide clarity about study purpose, roles and expectations, differences from standard practice and clear messages about what the study will involve	✓	✓		
	• Use multiple methods to communicate and support launch – informal (bedside) and more formal (study days, training material)	✓	✓		
ERM staff education and training	• Sites must develop education strategy for all staff (identifying what training is required, to whom, by whom and to how many people)	✓	✓		
	• Need dedicated staff to support education and training roll out (centrally or locally provided) and ongoing support (locally provided)	✓			
	• Training to include practical advice on how to conduct ERM (not just concepts of ERM) and variety of teaching methods (face to face, bedside, on-line)		✓		
	• Study team need to provide sites with all education and training material and resources (which can be localised and branded) that are simple and easy to use as possible	✓	✓		
	• Acuity level closely associated with ERM delivery, dose and activity				✓
Acuity assessment	• Develop clear acuity-assessment tool (consider logo and identity concept)	✓		✓	✓
	• Consider visibility and accessibility of tool to staff and parents at bedside (parents like to see any progression)	✓	✓	✓	
	• Refer to acuity tool in ward round and daily planning		✓		✓
	• Champion and research team presence on ward round promotes acuity-tool use	✓		✓	✓
Activity-selection tool	• Accessible activity-selection tool for staff and parents to aid activity selection (enhances parental involvement)	✓	✓	✓	✓
	• Encourage shared use of the tool	✓	✓	✓	
	• Provide documentation of 'ERM Prescription' to support ERM delivery	✓	✓	✓	✓
	• MDT help to select most appropriate patients		✓		✓
	• Ease of access – tool available at the bedside		✓	✓	✓
Risk-assessment tools	• Provide guidance on documents to assess risk	✓			
	• Clear guidance on safety and AEs to ensure accurate capture	✓	✓		
	• Pause and assess criteria can be used alongside AE reporting in ERM trials				✓
	• Delirium monitoring is essential in PICU; previously under-monitored and identification may improve care				✓

continued

TABLE 28 Summary of recommendations about trial ERM intervention and tools for a future PERMIT trial (*continued*)

	Source of information	Debrief	Staff int.	Parent int.	Trial data
ERM delivery	• Provide guidance on the roles and responsibilities of all staff	✓	✓		
	• Consider definitions of ERM and provide guidance on the ERM interventions (where needed)	✓	✓		
	• The bedside nurse is vital to deliver ERM	✓	✓	✓	✓
	• Additional funding for multidisciplinary staff time is required to support ERM delivery above current practice	✓	✓	✓	✓
	• Additional funding for additional equipment to support ERM interventions (e.g. chairs)	✓	✓	✓	
	• Consider parental involvement in ERM delivery	✓	✓	✓	✓
	• Need to consider documentation/recording of activities to ensure captured, accurate dosing assessment (consider shared documentation staff and parents, especially duration of activity and level of intervention)	✓			✓

TABLE 29 Summary of recommendations about trial monitoring and feedback for a future PERMIT trial

	Source of information	Debrief	Staff int.	Parent int.	Trial data
Safety	• Review any safety concerns/AEs in timely manner and address locally	✓	✓		✓
	• Sites need to have ongoing mechanism for local safety feedback and review, in addition to trial monitoring requirements	✓			✓
	• Safety and AE reporting can align with pause and assess criteria within ERM intervention				✓
Staff feedback and comments	• Important to seek staff concerns and feedback about the trial	✓	✓		
	• Local site to consider methods for staff engagement and communication – newsletter, e-mails, social media use	✓			
	• Need to address in timely manner or risk staff becoming disengaged	✓	✓		
CYP and parent/carer feedback	• Important to capture CYP/parent/carer feedback about their experience within the trial	✓	✓		
	• Sharing messages about trial participation with sites to increase the visibility of the study and to share positive messages	✓	✓		

Chapter 7 Phase 4: consensus and future recommendations

Introduction

To inform the design of a definitive trial of ERM intervention within UK PICUs we consolidated the Phase 1–3 PERMIT study findings and presented them to key stakeholders. In addition, we developed a preliminary proposal for the design of a definitive effectiveness trial, incorporating the key feasibility points from Phase 3.

Study management

The work package was led by BRS. JMen led the PPIE component. Rebecca Wooley and Karla Hemmings (BCTU trial statisticians) performed sample size calculation. RF co-ordinated PICANet data analysis. The study management group participated in consensus conference and reviewed the future trial proposal.

Aims

This study aimed to:

(1) provide parent perspectives on the results to ensure clarity in the summary of results for health-care professionals;
(2) provide parent perspectives on the summary of results for parents of children who were PERMIT trial participants;
(3) refine messages to share with parents/legal guardians who were not study participants;
(4) obtain feedback on the importance of a future trial of ERM and the outcome measures we should include in a future trial;
(5) propose a preliminary design of a future trial.

Method

This study consisted of three parts: (1) parent consensus meeting; (2) HCP meeting; and (3) study management group trial design.

Parent consensus meeting

We invited all parent/family member participants (n = 17) who consented and provided contact e-mail address details in Phase 3 to a virtual meeting (via Zoom) in January 2022. Invitations were sent in December 2021 and a reminder invitation in January 2022. The meeting included a presentation by BS (study design, rationale and key quantitative results), Natalie Read (results from site debriefs) and JMen (key results from healthcare professional and parent interviews).

The video presentation (30 minutes duration) was recorded, uploaded to a private web-based video-housing channel and a summarised leaflet with key study findings (pdf format) was created.

Following the meeting all parents/family members were sent the slides and video link with a short online questionnaire relating to feasibility and acceptability. No sensitive or identifiable information was collected. Implied consent was indicated on completion and submission of the online questionnaire.

The questionnaire asked:

(1) whether they found it useful to see the study results;
(2) appropriateness of an opt-out consent in future study;
(3) which outcome measures should be included in a future study (ranked according to importance);
    (a) the amount of ERM a child received (dose);
    (b) the type of ERM activities a child received;
    (c) the length of time spent on PICU;
    (d) the length of time on a ventilator;
    (e) the LOS in hospital;
    (f) physical measure such as muscle strength;
    (g) an outcome reflecting longer recovery (e.g. return to nursery/school);
(4) other suggestions of what should be measured (free-text response);
(5) whether a future trial of ERM was required.

Healthcare practitioner consensus meeting

We planned to hold an online HCP consensus meeting to discuss a proposed future trial design. However, additional COVID pandemic restrictions and NHS workforce pressures in January 2022 resulted in the cancellation of this meeting, with a plan to reschedule in May 2022 during the national PCCS-SG annual investigators meeting.

Study management group trial design

The study management group met on three occasions to review the findings of the Phase 3 feasibility study and discuss the design and structure of the future trial. Additional methodological expertise was obtained from Birmingham Clinical Trials Unit statisticians and study team at PICANet. Meetings were conducted over Zoom and, following the verbal consent of all attendees, recorded for comprehensive notes to be made to inform trial development.

Results

Parent consensus meeting

An invitation to attend the parent consensus meeting was sent to 17 participants in the Phase 3 feasibility study with the recorded materials. No parents/legal guardians (n = 0/17, 0%) attended the live virtual meeting. However, four parents/legal guardians responded to the online survey. All respondents (n = 4) found it useful to see the key study findings and agreed that an opt-out model of consent was appropriate for a future study.

The outcome measures were rated as follows.

All four respondents rated as very important:

(1) the amount of ERM a child received (dose).

In addition, they ranked from highest to lowest the following outcomes:

(2) the type of ERM activities a child received (highest ranked);
(3) the length of time spent on PICU;
(4) the length of time on a ventilator;
(5) the LOS in hospital;
(6) physical measure such as muscle strength;
(7) an outcome reflecting longer recovery, e.g. return to nursery/school (lowest ranked).

Other measures suggested in free-text response included:

> *For younger children/babies perhaps a measure of stress/anxiety – do erm activities such as reading help with sat* [oxygen saturation] *stability or overall sats* [oxygen saturation] *vs. children who do not receive ERM. E.g.: we continued to read night-time stories to try and maintain a degree of normality as well as comfort.*
>
> *(Parent C)*

Two parents replied Yes: further research on ERM was required and two said No: reasons being that they felt the evidence was conclusive:

> *Probably not, the benefits are obvious and the feedback is conclusive I would say.* (Parent D)
> *I guess to get this to be a standard of care you will need more evidence it works. But with the positive feedback from parents I personally think enough research has been done – it provides a positive environment for all.*
>
> *(Parent C)*

Impact for future paediatric early rehabilitation and mobilisation during intensive care trial

Parent satisfaction is extremely high surrounding ERM and contributed to two parents feeling that from their perspective further research was not required. However, there was recognition that for this to become a standard of care for all patients this would require more evidence, with further work focusing on identification of outcome measures relevant to patients and parents/legal guardians.

Study management group trial design proposal

The study management group, with trial methodologist input, met, reviewed all the PERMIT study findings and discussed an overall proposal for a future trial design.

Importance of research question and professional support for early rehabilitation and mobilisation

There remains a clear need to improve the morbidity and mortality of children requiring care within PICU after PICU critical surgery, illness or injury. We identified evidence from our scoping review that ERM is safe, feasible and, in combination with the adult literature, has the potential to be effective at improving patients' recovery from critical illness; however, further trials are needed. We identified significant HCP enthusiasm, across the multidisciplinary groups within PICU, regarding the role and potential of ERM intervention. The Phase 1b survey demonstrated wide community buy-in for future studies, the Phase 1c observational study had a high level of interest, investment of time and participation by bedside nursing staff and therapists, and the speed and number of PERMIT champions recruited in Phase 3 was very reassuring. Establishing ERM as a credible PICU intervention through a future definitive study is clearly a high priority with NHS staff.

Intervention

The development of the PERMIT manual and the successful, safe, implementation of the manual within the PERMIT Phase 3 feasibility study has confirmed that a complex, multidisciplinary, PICU-wide ERM intervention can be evaluated. The PERMIT manual includes a six-step implementation guide, learning and training resources, and ongoing site support from ERM experts. It incorporates daily acuity scoring, activity-level guidance and a pause and assess safety structure, which are modified to local resources, environment and staffing structure. Through research staff investment, debriefs and local site involvement, we have established the initial implementation of the manual takes approximately 12 weeks. This time period should be integrated into any implementation training phase in a trial.

Trial design and consent model

As with other trials in PICUs, the most powerful trial would use a stepped-wedged cluster design. Not only would this increase the power of the trial, it would also mean that all PICUs involved would benefit from training in the intervention. This design has worked well in PICU previously; the HTA-funded SANDWICH trial[66] of a sedation and ventilator liberation protocol intervention recruited 8843 patients across 18 UK PICUs over 18 months.

Opt-out consent is the preferred model of consent. This was successful in the Phase 1 observational study and strongly recommend in the Phase 3 process evaluation, interviews and PPIE work. This consent model would work within a cluster RCT design and implementation of the PERMIT manual and ERM delivery across the whole PICU.

Population

The PERMIT programme of research has clearly shown that elements of ERM are delivered in some form to nearly all patients in PICU, including the sickest patients on maximal organ support. Therefore, the whole diverse spectrum of PICU patients should have the opportunity to benefit from ERM early in their PICU care pathway and for as long as is required. However, for ERM to impact a measurable patient-related outcome it would be logical that a period of exposure to the ERM intervention is required. Therefore, patients with short stays in PICU (e.g. <48 hours) are unlikely to gain measurable benefit. Our approach of including patients on day 3 of PICU in the Phase 1c observational study and Phase 3 feasibility study allowed identification of this patient group. Trial inclusion criteria should allow selection of these patients for assessment of efficacy of ERM, although the ERM intervention could and ideally should be delivered to every patient within the PICU to ensure maximal embedding of the ERM manual and processes with staff. We therefore recommend that a future trial population includes critically ill/injured patients of all ages (0–<18 years) admitted to PICU. They would be identified and enrolled in the study early in their PICU stay (e.g. within 72 hours after PICU admission). This would allow the interventions in the PERMIT manual to be commenced in patients who could receive an adequate amount of ERM, which may lead to measurable benefit. Patients would be excluded by parents/guardians opting out, or clinicians' decision that ERM or trial inclusion is inappropriate (e.g. anticipated death in PICU, or planned palliative care and withdrawal of life-sustaining therapies). We recognise that ERM activities may be important and recommended end-of-life interventions in this population (e.g. part of pain relief, enrichment to surroundings patient and family PICU experience); however, these would require different patient-reported outcomes or to be delivered outside of a trial setting.

Comparison

The comparison (control arm) would be standard of care before implementation of the PERMIT manual. We have established that even PICUs with an existing ERM programme can benefit and improve with the PERMIT manual and programme (e.g. Site 1 in the Phase 3 feasibility study). The ability for the PERMIT manual to work alongside and enhance, refine and develop existing programmes would allow increased recruitment of PICU sites to a future study. The research programme and process evaluation are also attractive to PICU sites as additional resources would be available.

Outcomes

Through PPIE and parent/family feedback, the amount and dose of ERM were identified as the most important outcome measure. However, we identified in Phases 1 and 3 that it is very difficult to quantify ERM dose due to (1) a heterogeneous patient population (e.g. 0–<18 years of age, developmental stages, size, ambulatory status), and (2) diverse types of ERM activities delivered. Inclusion of health-related QoL outcome measures is recommended in PICU studies[47] and is felt important by healthcare professionals and parents/carers; however, the burden on families to complete these tools was clear in Phase 3. Therefore, a pragmatic measure of improvement in critical illness or injury recovery would be required, with accompanying intervention fidelity assessment (i.e. measurement of increased ERM dose delivery at the site and patient levels). Potentially suitable outcomes include length of MV and LOS in PICU (or days free of ventilation/PICU). The advantages to length of MV as an outcome is that it has a

clearly defined beginning and end point (e.g. successful extubation without the need for re-intubation). It is also the primary outcome measure in the ongoing pilot, stepped-wedge trial of ERM in the USA PICU UP! study, which would allow direct comparison.[112] The disadvantage is that this will exclude up to 35% of PICU patients with critical illness not requiring ventilation. LOS, as an outcome measure, would allow all patients admitted to PICU to be included in a trial. However, the disadvantage is that the end point is less precise. Discharge from PICU can be to any of step-down to high-dependency unit, ward location, other hospital PICU, neonatal intensive care, home, palliative care facility. The timing of this discharge can be affected by additional factors external to improvement in critical illness and injury (e.g. bed availability on the ward) and is therefore subject to measurement inaccuracy, which may affect trial findings.

With no definitive primary outcome choice, we present a draft proposal based on LOS and length of ventilation (LOV). We need to explore this area further.

Sample size

Approximately 20,000 patients are admitted to PICU each year, of whom around 65% receive invasive MV at admission. The eligible population, using LOV as an outcome, would come from the patients who are on MV on day 3 and stay in ICU for an additional 4 days (this gives us the population who are both most likely to benefit and can receive at least a minimal amount of ERM). The UK national PICANET data report that approximately 19% of patients admitted fulfil these criteria, so 2470 patients will be eligible per year.[67] Allowing for ~5% attrition, 2350 patients will be available for analysis. This equates to approximately seven eligible participants per 1-month period per cluster.

There is a total of 26 suitable PICUs across the UK. Provisional interest in participation in a full PERMIT study is high, and it is reasonable to assume that 21 PICUs would want to participate, which could also include the three sites in the feasibility study. This trial design requires that all participating PICUs begin the control phase of the trial when the data-collection period begins. Further analysis will be required to accurately estimate required parameters for a stepped-wedge cluster randomised trial including the intracluster coefficient (ICC) and cluster autocorrelation coefficient (CAC). Provisional data from BCU PICU provided a mean length of time on MV as 19.3 days for those in PICU more than 7 days, with a SD of 28.4. A reduction of 1.5 days on MV is considered to be meaningful to patients and parents. The SANDWICH trial[66] estimated the ICC to be 0.005. Personal correspondence from the USA PICU Up! trial and SANDWICH trial[66] leaders suggests that the CAC may be close to 1.

Our proposed design is in shown in *Figure 17*. Similar to the SANDWICH trial protocol (adapted under CC BY 4.0 license http://creativecommons.org/licenses/by/4.0/),[113] there will be an initial 3-month period of baseline data collection during which the PICU will not be exposed to the intervention. Following this, every 3 months, three sites will be randomly selected to transition to the intervention. This will start a 3-month training period of the intervention. As we cannot assume that the PICUs are exposed or not exposed to the intervention during the training, no patients will be recruited through this 3-month period. Once a PICU crosses over to the intervention, it will remain exposed to the intervention for the remaining duration of the study. There will be a final 12-month period during which all PICUs will be fully exposed after the last PICU has transitioned to the intervention. This 12-month period is to ensure that the ERM programme is fully embedded following implementation, which is a key requirement expressed by clinicians to be part of PERMIT and was not achieved in the feasibility study. Assuming an average of seven patients per 1-month period, and total follow-up period of 36 months, 80% power would be achieved. This would equate to a sample size of 4851 participants.

If LOS is used as primary outcome this increases the eligible population to 3800 (19% of 20,000) (*Table 30*). Allowing for 5% attrition provides a population size of approximately 3600 patients and approximately 11 participants per 1-month period per cluster. The same data from BCH PICU provide a mean estimate of LOS to be 23.7 with a SD of 31.0. Using the same design matrix as for length of time

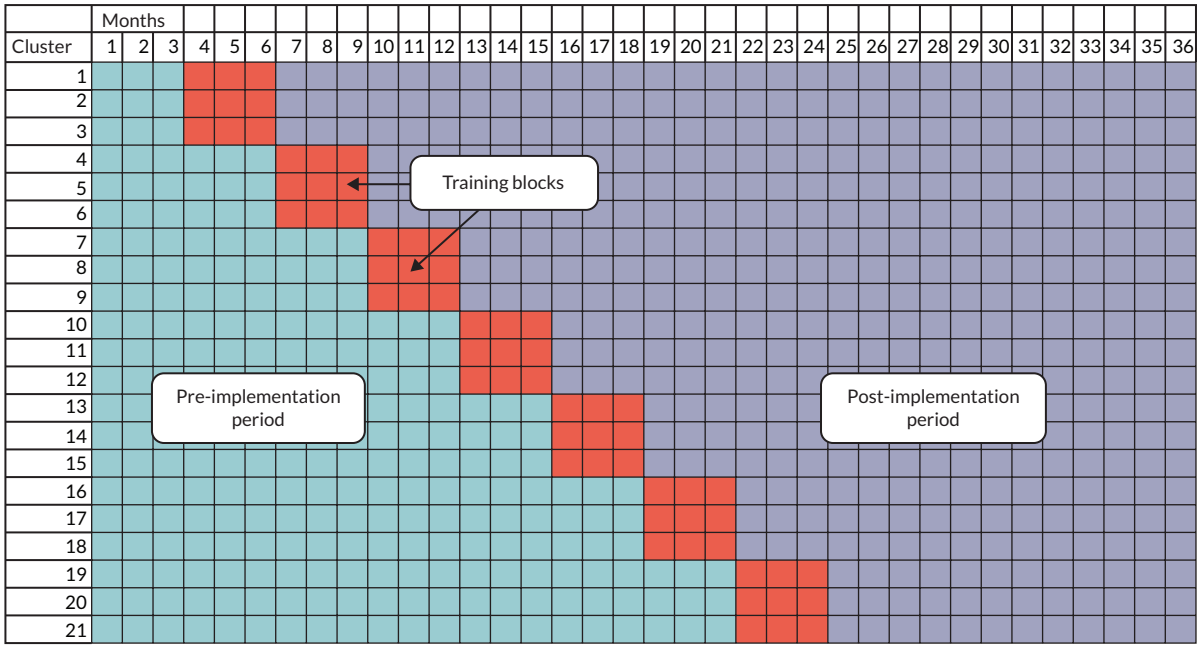

FIGURE 17 PERMIT trial design cluster, stepped-wedge.

TABLE 30 PICANet yearly total for variable LOS in PICU

Year	Total admission	LOS 3–<7 days	LOS 7+	All patient LOS 3+
2017	19,869	4673 (23.5%)	3842 (19.3%)	8515 (42.9%)
2018	20,172	4825 (23.9%)	3977 (19.7%)	8792 (43.6%)
2019	20,383	4855 (23.8%)	3878 (19.0%)	8733 (42.9%)

on MV, and an ICC of 0.02 estimated from the PICANet data, the sample size of 7623 would provide over 80% power to detect a 1.5 reduction in LOS.

There will be an initial 3-month pre-implementation block for 21 clusters (e.g. PICUs), stepping into a 3-month training block (staggered for 3 clusters at a time) with 12 months or more post-implementation period.

A further sample size calculation will be performed using the whole PICANET data set with LOV outcome for UK population. At the time of report submission these data were not available because of a cyber-incident on the Leeds University server.

Additional consideration

Chapter 7 concludes with a list of trial elements which will be important to incorporate into a future trial design (see *Tables 27*, *28* and *29*).

In addition, further evaluation of the sample size and primary outcome will be required to justify the size and scale of a definitive trial. We acknowledge that plausible effect size for the primary outcome will also need to be estimated in an internal or external pilot phase of a future study.

Important considerations are needed on the potential confounders which may occur in a large pragmatic trial. The risk of education contamination bias, for example retaining separation between arms of the trial, is important. The huge investment of staff time, resources and effort that we identified during the

Phase 3 feasibility study would be replicated in a definitive trial in each PICU. The risk of this occurring outside of the conduct of the trial and at the correct step in the design we believe is low. However, we acknowledge that PICUs in the UK have implemented ERM programmes in various forms, but we also recognise that those PICUs have struggled with maintaining programmes, without well-theorised implementation programmes like PERMIT (e.g. Birmingham and the MOVE4WARD programme).

Finally, the PERMIT feasibility study was conducted with a limited budget and although we provided research support staff funding for data collection and trial conduct at each site, we did not provide resources for any additional ERM delivery by therapists or nursing staff. In addition, we did not undertake an economic evaluation or involve a health economist in the PERMIT feasibility study as per the original commissioning brief. In a future trial, additional NHS support costs will be needed for adequate staff support of both the implementation and the delivery of ERM within clinical care, as identified in *Chapter 6: Process evaluation*.

Summary of findings to inform paediatric early rehabilitation and mobilisation during intensive care study

- The PERMIT manual is a complex intervention and is best assessed through a clustered stepped-wedge RCT in PICU.
- Following consultation, a draft proposal for the clustered stepped-wedge RCT in PICU is proposed.
- There is strong support for a definitive efficacy trial of ERM from HCPs. Feedback from participants for the PERMIT study, although limited in number, also supports a future trial and suggests important design and measurement elements.
- The primary outcome of LOV is a pragmatic compromise on measurable PICU outcome and likely accurate measure of improvement in critical illness recovery. Further consensus work in developing the primary outcome will be required with the UK PCCS-SG and trialist prior to a definitive study proposal.

Chapter 8 Paediatric early rehabilitation and mobilisation during intensive care study approach to patient and public involvement and engagement

Introduction

Designing and conducting research within the PICU context are recognised to be extremely challenging.[114] The PERMIT study team therefore set out from the outset to ensure the study was designed in collaboration with parents of a child who has experienced a PICU admission. We needed co-applicants who really understood the perspective of what it was like to have a child admitted to PICU and the role rehabilitation and mobilisation could play in recovery. SL and her daughter Darcy (D) agreed to join the team. They have direct experience of PICU and with JMen (our PPIE lead) can ensure PPIE has been woven through the study, building on information gained through each phase.

Study management

The PPIE work throughout Phases 1, 2, 3 and 4 was led by JMen and SL (our PPIE co-applicant). The study management group inputted into protocol designs, ethics application scope and drafting of the PPIE report.

Overview of patient and public involvement and engagement work

- In Phase 1 our PPIE co-applicant endorsed the importance of understanding current practice surrounding ERM through a survey of practice with healthcare professionals and understanding the published literature. The area that was felt to require focus was PPIE work to support the design and conduct of the observational study.
- In Phase 2 the focus was on the development of an Early Rehabilitation and Mobilisation Manual: the intervention for the Phase 3 feasibility study. PPIE activity was envisaged to be about co-designing the manual and identifying relevant trial outcome measures. PPIE work was conducted to inform the Research Ethics Submission. Unfortunately, following ethics review and approval, all non-COVID-related research was suspended. Following discussion with the NIHR HTA funder, it was agreed that some elements of Phase 2 would not be conducted and modifications to the Phase 3 feasibility study design were made to include some components of the aims and objectives from Phase 2 as well as related PPIE activity.
- In Phase 3 PPIE work was therefore essential to ensure the trial was feasible and acceptable. Activities focused on the trial design, conduct and duration and the appropriate model for informed consent, as well as all the study-related patient-facing material.
- In Phase 4 the purpose is to draw together all the key messages from the three phases and develop consensus about a future ERM RCT. PPIE elements to this are to ensure that the key messages from the Phase 3 work are correct and endorsed by parents/legal guardians.

Objectives for each phase are outlined in *Table 31*.

TABLE 31 Summary of PPIE objectives for each phase of the PERMIT study

Phase 1: to understand current practice surrounding ERM	Phase 2: to develop an ERM manual in conjunction with CYP and parents	Phase 3: to develop a feasibility trial of ERM	Phase 4: consensus work
• Obtain PICU parents' views on the design of the observational study • Obtain views on the appropriate model of consent for the study	• Discuss the trial design, conduct and duration • Discuss outcome measures for trial	• Obtain parents' views on the appropriate model of consent for the study • Discuss the trial design, conduct and duration	• Provide parent perspectives on the results to ensure clarity in the summary of results for healthcare professionals
• Review participant-facing materials for acceptability and clarity • Review outcome measures		• Review participant-facing materials for acceptability and clarity • Review and develop the interview schedule for qualitative work with parent participants	• Provide parent perspectives on the summary of results for parents of children who were PERMIT trial participants
• Discuss potential barriers or opportunities to recruitment and successful data collection		• Review outcome measures for the trial • Discuss potential barriers or opportunities to recruitment and successful data collection	• Refine messages to share with parents/legal guardians who were not study participants • Obtain feedback on the importance of a future trial of ERM and the outcome measures we should include in a future trial

Our approach to patient and public involvement and engagement

There are three key domains to conducting patient and public involvement (PPIE) work – planning, supporting and recording and evaluating.[115]

Planning patient and public involvement and engagement – developing a plan for patient participation, involvement and engagement in a trial

The study team adopted an approach based on consultation, where people are asked for their views, which are then used to inform decision-making.[116] Although this is regarded as the lowest rung of the patient form of involvement[117] this was felt to be appropriate given the nature of the research context and the specific remit of the NIHR funding. The team were keen to contribute to the knowledge base surrounding PPIE within the PICU context[118] and highlight the impact of PPIE at each stage. A plan was therefore made, although this had to be adapted significantly due to COVID.

Planning patient and public involvement and engagement – identifying parent contributors

Researchers are advised to approach patients and public through formal patient groups, charities, community groups, national directories such as 'People in Research' or Health and Social Care patient advisory panels.[119] Partnership with parents who are in a similar situation to potential study participants is vital to ensure that important aspects of the research question have been considered.[120] However, there is recognition that there can be challenges with identifying appropriate contributors.[121,122] The concept of 'similar situation' is challenging in the PICU context as the service provision is for all CYP aged 0–<18 years and there is a broad case mix of underlying diseases and diagnosis.[123] In addition, the PERMIT team faced a challenge in accessing a formal established group. There were no pre-established groups in existence within the Clinical Research Network (CRN), the affiliated Trusts for the research (Birmingham Women's and Children's NHS Foundation Trust and Southampton Children's Hospital), and none within the two sites' PICUs. There were also no national groups of parents with experience of PICU established,[118,124] a situation which continues to the current day. In these circumstances identifying

people through personal contact or recommendation is therefore acceptable.[119] Our PPIE co-applicant SL and her daughter both felt that it was important that we made efforts to engage with parents who had experience of a child being admitted to PICU. Families without this experience might not understand the extreme emotions parents experience during the first few days of a PICU admission. This approach is supported by other national PICU studies.[120,125–127]

Planning patient and public involvement and engagement – impact of COVID

The plan to recruit to a PERMIT-specific parent advisory group made up of parents who had experience of their child being in a PICU was then compounded by COVID. The PERMIT team were re-deployed to clinical work, contact with families was hindered through the wearing of personal protective equipment (PPE) impairing communication and there were the additional challenges of restricted visiting and parental exclusion if parents were symptomatic.[128]

In addition, there was an added challenge to speaking to parents with experience of deciding about research participation in PICU because of research suspension. Despite fewer children with COVID-19 admitted to hospital and even fewer admitted to ICUs, PICUs experienced the same disruption to clinical research as adult ICUs. Seventy-five per cent of PICU/ICUs internationally suspended recruitment to some if not all research during 2020.[100] Suspension of research recruitment reduced the number of studies which were open and recruiting and reduced researchers contact with families. This created additional challenges for the PPIE lead to speak to parents with experience of being recruited to research.

There were therefore challenges to the number of parents we could engage with for PPIE. INVOLVE (2012)[129] recommend a minimum of two PPIE participants and there is growing recognition that the available number of participants with the relevant experience may be low.[119] We therefore did not set a specific number of PPIE participants, but aimed to involve parents with as varied experience as possible.

Planning patient and public involvement and engagement – children and young people

Conducting PPIE work with CYP was also challenging. A previous review had identified that few PICU studies had managed to conduct PPIE work with CYP with experience of PICU.[118] Although there are excellent Young People's Advisory Groups available through the NIHR[130] and locally[131] their membership at the time included no CYP with experience of a PICU admission. Previous studies have consulted with siblings of CYP who have had experience of PICU[132,133] However, COVID meant there were no sibling visitors allowed on site within the hospital (still the situation currently) and the YPAG groups were suspended for a period of time.

The decision was therefore made to conduct 'standalone' PPIE – identifying and liaising with parents/carers as required for each of the phases. The team also had extensive wider PPIE and qualitative research experience from related studies which were drawn on. Pre-COVID efforts were made to engage with CYP and siblings where possible but this was not possible from 2020 onwards.

One of the concerns of the study, especially pertinent given the additional challenges of COVID, was to ensure that we facilitated parents/legal guardians to have the opportunity to shape and influence research. In a study which was designed to be relevant to all patients admitted to PICU it was vital that we considered equality, diversity and inclusivity in our PPIE. Study materials were specifically developed with graphics to help those for whom English was not their first language, those with dyslexia and those with lower literacy levels. PPIE was also conducted across more than one site to ensure there was representation of parents from a wide geographical area as well as families who lived locally in Birmingham and London. A variety of methods were used to assist with families' engagement. Face-to-face introductions helped to explain that this was to inform research design, rather than to participate in research. Short information leaflets were provided about what was required. Parents could provide feedback face to face with the PPIE lead or a member of the local research team or by writing responses

and returning them in a stamped addressed envelope. PPIE activity could happen within the hospital or within the home environment (if it coincided with other research activity).

Planning patient and public involvement and engagement – allocating appropriate costs

Historically PPIE participants have not always received any payment for their time and involvement; however, this payment is now recognised as good practice.[134] All PPIE activities were costed in line with NIHR (2018) guidance on reward and recognition for public contributors and participants appropriately rewarded.[135]

Planning patient and public involvement and engagement – managing the expectations of public contributors

The PERMIT PPIE co-applicant and the parent representative on the Trial Steering Committee were prepared for their roles with clear guidance on the role and what was required. PPIE participants were provided with information about the consultation work by the staff member approaching them. The expectations of their role were identified and as they were involved with 'standalone' PPIE there was no ongoing commitment.

Supporting patient participation, involvement and engagement

For patients new to a PPIE role, support to develop their abilities and confidence to express their views and question researchers may be relevant. In order to support our parent co-applicant and the parent representative recruited to the Study Oversight Group both were offered access to appropriate training via a number of resources. Materials supplied included guidance on involvement in PPIE,[136] links to local resources within the West Midlands CRN and on-line training available through NIHR.[137] In addition, SL attended a national one-day UK symposium about PICU outcomes and rehabilitation (2017) with members of the PERMIT team in order to help her understand the wider perspective.

There are many PPIE tasks where training is not necessary, where a different perspective or experience of a healthcare condition is the required expertise.[119,134] In line with this PPIE participants within PERMIT did not receive any formal training.

Recording and evaluating patient participation, involvement and engagement

While there is consensus that PPIE has considerable potential to benefit clinical trials, there has been little formal evaluation of its impact.[115] None of the PICU studies in a UK review provided an objective measurement of the impact of PPIE.[118] The PERMIT team were therefore keen to create a clear picture of when and where PPIE happened, what impact this had on the trial, the nature of PPIE activities and the impact of the activity on the trial design and conduct.[138] This is captured in the report above, with specific examples of what changed as a result of consultation detailed below.

Impact of patient and public involvement and engagement: the PERMIT team collaborators

Researchers who conduct PPIE often report on the experiential learning and positive impact it has for them as a researcher.[139] As a research team we would therefore like to report the positive impact PPIE had for us as a team. Despite all the challenges encountered, particularly due to COVID, we felt that that we were able to engage with parents and obtain meaningful insights which made an impact on the design and conduct of the study; particularly the models of consent utilised in Phases 1 and 3. We would also like to acknowledge the impact for SL and D, our co-applicants. They have linked up with PICU, BCH, to help with all things ERM (outside of the PERMIT study). From featuring on posters promoting ERM on the unit, to pictures on online training material, to reviewing local documents such as an information leaflet about ERM for elective surgical patients, they have both taken an active role. D is now in secondary school. She recently contacted the PPIE lead to provide some feedback about the

leaflet and expressed how she was wondering if there was anything else she could do to help promote rehabilitation and help other children:

> *Being as I had some experience with the same things other may go through, I was talking to my mum about maybe coming to PICU to help others, if its allowed? I'd really like to help other children.*
>
> *(D)*

We are now working with SL and D to develop videos and guides to help guide children, parents and family members about ERM activities. In addition, D has joined the local Young Person's Advisory Group (YPAG) and is contributing to their wider work within the Trust.

Chapter 9 Equality, diversity and inclusivity

Background

The NIHR strategy Best Research for Best Health (2021) highlights inclusion within the five key operating principles, from ensuring there is opportunity for everyone to participate in research through to providing opportunity for researchers from different disciplines, specialisms, geographies and backgrounds to develop and progress a career in research. Within this chapter we will demonstrate how the study team considered equality, diversity and inclusion within the PERMIT study team, PPIE participants and PERMIT study participants, both patients and parents.

PERMIT study team

The PERMIT study team was assembled to reflect expertise on the subject of rehabilitation and mobilisation and paediatric intensive care. The study team was composed of eight females, eight males. Ten of the study team were affiliated to eight NHS organisations, in a range of different geographical areas. These organisations had a wide variety of service users from a wide range of socioeconomic backgrounds. Early rehabilitation and mobilisation is an intervention which requires MDT involvement and the study team represented this with three paediatric intensivists (BS/KM/NP), two consultant paediatric neurologists (FK/RF), two physiotherapists (JT/MG), two registered nurses (JMan/JMen), an OT (JMc) and a psychologist (GC). From 2018 when the PERMIT study funding was awarded more junior members of the PERMIT team were supported with their career progression and development opportunities. JT was successfully appointed to a PhD, University of Birmingham (2020). JMc completed her PhD and was successfully appointed to Lecturer at the University of Salford. JMen was initially responsible for PPIE but went on to become second author on the national survey paper and was supported to lead the process evaluation within Phase 3.

Patient and public involvement and engagement

In *Chapter 7* we report in full on our approach to PPIE. In total our PPIE participants included mothers (n = 6), fathers (n = 4), and one sibling of infants and children who had experienced an admission to PICU and young people naive to PICU (n = 2). The current age of the child admitted to PICU (n = 9) ranged from 1 month to <16 years of age and the reason for admission ranged from single organ failure (respiratory) in children who had been previously fit and well, through to children with multiple health conditions and rare diseases. All the families we engaged with could speak and read English and felt able to contribute to PPIE activities, although it was not the first language for at least three parents. Three participants identified as Asian and one parent as black, although parental ethnicity of PPIE participants was not fully reported. Parents of children admitted to two NHS organisations – Kings College Hospital, London, and Birmingham Women's and Children's NHS Foundation Trust – were approached about PPIE engagement. Both organisations have a local population, as well as families referred to the centre due to specialist services. Both perspectives were represented by participants with our PPIE work.

PERMIT study participants

Question 1: who should my trial results apply to?

Children and young people

Early rehabilitation and mobilisation is an intervention which is believed to be useful for all patients admitted to PICU. It was therefore important for the feasibility study to be as inclusive as possible, including infants and children of all ages 0–<16 years, admitted for PICU care either electively or as an emergency. The only exclusion criteria were if the parents/legal guardians chose to opt out (Phase 1) or declined consent (Phase 3) or if there was a local decision by the clinical team/principal investigator not to include the patient. CYP are recognised to be an under-served group with respect to research opportunities[140] and recruitment of critically ill CYP to research is low.[141] Fewer than 1 in 100 admissions to PICU globally are recruited to a clinical trial, compared to 1 in 10 adults in adult ICU,[142] and a recent review identified that <1% of patients undergoing cardiac surgery are currently recruited to research.[143] The PERMIT study therefore set out to be inclusive, opening the observational study in 50% of all UK PICUs (*n* = 15) to ensure participants from across the UK had the opportunity to participate. All CYP admitted to participating PICUs for over 48 hours were then eligible for inclusion. This ensured that some of the most vulnerable patients, for example CYP with cognitive impairments, learning and physical disabilities and multiple health conditions, were eligible for participation.

We recruited 169 participants in the Phase 1 observational study and 30 participants were recruited to the Phase 3 study. The ethnicities of CYP recruited across the two phases of the study were: white 116 (79%), Asian 20 (14%), black 15 (10%), mixed 4 (3%), other 2, not stated 20 (14%). When this is compared to the data collected by one study[67] of patients admitted to PICU (2018–20) we can see that the ethnic diversity of the study participants' is representative of the ethnicity of all UK/Republic of Ireland PICU admissions: white: 75%, Asian 12.5%, black 5.4%, mixed 3.6%, other 3.5%. Overall there were no differences in our planned trial population and those who successfully participated.

Parents

All parents of children admitted to PICU and approached for the feasibility study (Phase 3) were also offered the opportunity to be study participants and provide feedback about their child and family experience through questionnaires (21/30) and an additional optional interview (*n* = 14 participated). There were no exclusion criteria, although we were unable to provide translated versions of the validated questionnaires and we did not have the option to interview participants in any language other than English. In addition, we sought to hear the voice of parents who declined their child's participation in the study. This perspective is seldom heard and the four families which this applied to were all offered the opportunity. Unfortunately, this was declined by all four families.

Are the groups identified in Question 1 likely to respond to the treatment in different ways?

A number of previous ERM studies have excluded patients <3 years of age,[20,15] even though 60% of UK PICU admissions are <36 months.[62] The PERMIT Phase 3 study team was therefore keen to ensure that families of infants were offered the opportunity of participation. This was successfully achieved across the three study sites with 9/30 (30%) participants under 12 months of age. We were also concerned to ensure that the study captured patients at risk of or experiencing multiple organ failure. Twenty-seven per cent (*n* = 8) of patients were admitted following surgery, including two patients who had undergone cardiac surgery. Other admission reasons included trauma (*n* = 2), infectious/inflammatory (*n* = 2) and neurosurgery (*n* = 1). In addition, 63% of recruited patients had an underlying disability (mild-severe) as indicated by a baseline POPC score. We therefore feel that opportunities to participate in PERMIT were offered equitably and ensured that under-served CYP and families had an opportunity to participate in research.

Will my trial intervention and/or comparator make it harder for any of the groups identified in Question 1 to engage with the intervention and/or comparator?

Evidence has shown that admission to PICU is extremely stressful for parents and many find it difficult to consider research during the initial few days.[141] Our concern was that this would then serve as a barrier to families who were approached about the study for a full informed consent. Our PPIE work indicated that an opt-out consent approach would be appropriate in Phase 1 (observational only), which was confirmed by 100% (*n* = 169) of parents choosing for their child's data to be included in the study. In Phase 3 an informed consent approach was required; however, steps were taken to help parents to understand each step of the study and reduce the stress associated with participation. Study participants endorsed this approach and, importantly, helped provide vital insight into the low perception of risk associated with a future trial. A future trial could therefore proceed with an opt-out consent, which helps facilitate research engagement for a wider range of patients and families.

Will the way I have planned and designed my trial make it harder for any of the groups identified in Question 1 to consider taking part?

We worked hard with our PPIE participants to design the trial and the patient-facing information as clearly as possible given the challenging situation eligible families were in. We also provided thorough training within the site initiation visit (SIV) with sites to discuss the importance of a sensitive approach to families and the value of the staged informed consent approach. We view the relatively low decline rate of 4/34 (12%) as testament to the clear participant information sheets and support of the research delivery teams. One aspect where we were mindful of ensuring choice was in the method of completing outcome measures. We did not want to digitally discriminate or disadvantage families so offered outcome measures in a number of different formats, including paper, online and completed with a researcher by phone.

Reflections and areas for improvement

One of the challenges for future research is about developing study information to help make research more accessible. Families suggested access to information leaflets on YouTube and opportunities to learn more about research in advance of a PICU admission when there is more time to consider what is involved. We also recognise that CYP want to be more involved with decision-making about research, but with the complications of assent while intubated and sedated we need to do more work to consider how we can better prepare those coming for an elective admission.

Upon reflection we realise that to demonstrate evidence about addressing equality, diversity and inclusion, we need to identify and measure relevant metrics. In our PPIE work we were cautious about collecting 'unnecessary data' and did not record or ask parents for information such as their ethnicity, age, employment status, number of other children and their own health status, all of which help to demonstrate that under-served communities are being included. In the future we will adopt a more standardised way of capturing these data so we can ensure a wider variety of perspectives are captured.

Chapter 10 Discussion and conclusions

Summary of main findings

Phase 1a: scoping review

In our scoping review of paediatric ERM literature, we identified that optimal aspects of ERM intervention delivery, timing, content, active ingredients, dose–response relationships, progression and implementation strategies have yet to be established. Multicomponent 'non-mobility' and 'mobility' ERM interventions were feasible and safe and most involved physical therapy, OT and SLT.

Children under 3 years old were more likely to receive interventions such as cuddles or in-bed mobilisation, whereas non-ventilated children or those aged 3 years and older were more likely to receive mobility interventions involving physical therapy or OT. Importantly, family involvement appeared crucial, and the lack of a well-defined ERM protocol was a significant barrier to ERM implementation. With no clear evidence on the impact of bundles of care or behavioural interventions incorporated within ERM, further research in this area is essential.

Phase 1b: survey of current practice

This national survey of HCPs from UK PICUs identified the importance of ERM as an intervention which participants believe can improve the physical, psychological and cognitive recovery of critically ill or injured infants and children across all ages. Our findings indicated support for ERM, but highlight uncertainty with suitability, variability with the definition of this complex intervention, variation in timing of initiating and which patient groups should receive ERM. Similar to our scoping review, the reported lack of ERM protocols in most (21/26) UK PICUs reinforced a strong requirement for evidence-based standardised protocols with optimal timing, intensity, frequency and duration of ERM. There is a need for flexible protocols to allow for tailoring rather than prescription. Key barriers to ERM delivery were identified (e.g. funding and staffing) and potential clinical (e.g. improved psychological outcomes) and economic (e.g. reduced PICU LOS) benefits to patients and PICUs.

Phase 1c: observational study of early rehabilitation and mobilisation practice

We observed ERM practice in 169 patients across 15 PICUs who reached 9 a.m. on day 3 after PICU admission in our 14-day observation period. Ninety per cent of eligible patients were enrolled using an opt-out consent model. On the first study day (day 3 after PICU admission) 162/169 (96%) of patients received an ERM activity; 87% involved a mobility and 38% an out-of-bed mobility. The rate of ERM activities for patients remained constant across the subsequent 7 days of their PICU admission (or until PICU discharge).

Over the observation period, 3696 ERM episodes delivered 4978 ERM activities across all PICUs. Most were delivered by a registered nurse or parent/family member. Positioning with and without mobility elements accounted for nearly half of all ERM activities. A wide range of ERM activities were reported, but were more likely to be passive or enrichment activities rather than active ERM. 'Cuddles' by a family member/nursing staff was the most frequent out-of-bed activity. We identified that family presence significantly increased out-of-bed ERM, although MV, presence of a urinary catheter and pre-existing severe developmental delay were associated with not receiving out-of-bed ERM. Presence of an ERM protocol did not impact the chance of out-of-bed mobility. However, ERM was delivered to nearly all patients, including those of all ages, admission diagnosis and with the highest level of organ dysfunction or organ support.

ERM was delivered safely with a low (<3%) reported rate of AEs per ERM activity. Most AEs did not require any corrective intervention. Of concern was that delirium screening was universally absent in study-participating PICUs and this requires attention. Nursing staff and parents delivered the majority of

ERM activities throughout the 24 hours period. Physiotherapists only delivered 10% of ERM although 59% of patients received at least one PT-delivered ERM episode at some point. There was minimal input from other medical, therapy, or support staff reported. Any ERM manual or intervention plan will need to be designed to utilise available staff or require significant increased resources to support them.

Phase 2: paediatric early rehabilitation and mobilisation during intensive care manual development

Our synthesis of the key messages, assumptions and uncertainties that emerged from our prior Phase 1 work showed that ERM is currently defined and enacted in multiple ways. Importantly, people see the potential value for the diverse patient populations within PICU and are willing to support the safe delivery of ERM but are uncertain how best to deliver it. Our three face-to-face workshops with NHS HCPs (n = 18) and one online workshop with international experts (n = 3) helped generate some core guiding principles around the potential shape and content of the intervention. For example, everyone in PICU (doctors, nurses, physiotherapists, and parents) is essential for ERM delivery – everyone should take some ownership. Also, ERM needs to be as inclusive as possible, with a focus on promoting movement and mobility as early as possible and with progressive increases over time. Our review of existing ERM protocols and discussions with healthcare professionals enabled us to develop a prototype ERM manual that was focused both on the safe delivery of ERM for each patient, and on the introduction and embedding of an ERM approach within a PICU. The manual was informed by current evidence, experience, and theory. It offered a flexible, progressive, approach to the delivery of ERM, with resources including essential clinical materials – the 'bedside bundle' – that consist of an ERM daily flowchart, patient acuity levels, ERM activity levels, and pause and re-assess criteria. It also included a step-by-step guide to putting ERM into practice – the 'implementation toolkit' – that focused on building ERM leadership, generating staff buy-in, making ERM workable, and keeping it going over time.

Phase 3: feasibility trial and implementing evaluation of non-randomised early rehabilitation and mobilisation intervention

All three sites implemented the PERMIT programme as described in the manual. The families were positive about the study recruitment process and all sites successfully recruited the 10-patient target. To achieve ERM delivery, all patients (1) had an acuity level scored (and repeated on 84% of ward rounds) and (2) had an acuity level correctly linked to an ERM activity prescription and then subsequently to a delivered ERM activity. The level of activity was broadly representative of the acuity level.

Other key findings were that a large number of clinically relevant patient outcomes were measured through validated tools and all patients received ERM activities safely using the pause and assess criteria with only two trial reported AEs and no severe AEs. ERM was important for the physical and psychological recovery of the CYP, as well as the psychological well-being of parents/carers supporting their involvement in their child's care. PERMIT was seen by health professionals and parents as worthwhile, feasible and acceptable. Finally, having access to research delivery support was central to support recruitment, data collection and data entry.

Phase 4: consensus study and trial design

With input from PPIE, parent/family members and multidisciplinary members of the study management group we reviewed and refined the findings from Phases 1, 2 and 3 of PERMIT. We confirmed that a future PERMIT ERM clinical trial was necessary and likely to be feasible with consideration of additional trial design elements. The most suitable trial design for the complex intervention is a clustered stepped-wedge randomised control trial within PICUs across the NHS. The primary outcome requires further consideration. LOV (or days free from ventilation) is a pragmatic compromise on measurable PICU outcome and a likely accurate measure of improvement in critical illness recovery. It would also allow comparison of the PERMIT manual and intervention with the only other similar PICU-wide ERM intervention study, the PICU UP! programme, ongoing in the USA.[112] Further consensus work in developing the primary outcome will be required with the UK PCCS-SG and trialists prior to a definitive study proposal. Any future trial will require health economic evaluation in addition to assessment of patient-related outcomes.

Strengths and limitations

Phase 1a: scoping review

We conducted a comprehensive search using broad inclusion criteria, but the risk of publication bias remains. We also acknowledge the inherent limitations of vote-counting used to determine effective ERM interventions since RCTs included in this review were not adequately powered, and findings may not be clinically relevant.

The majority of studies included in this review had design flaws, and varied in the consistency and reporting of interventions or outcomes evaluated. No between-group mean/SDs or effect with precision intervals were ever reported. These outcomes might have different implications on the strength of the evidence when the cost effectiveness of ERM is considered. Lastly, most studies did not provide information about intervention delivery to understand active drivers of successful implementation. Consequently, inferences drawn are based solely on explanatory findings.

Phase 1b: survey

The strength of this survey was an inclusive representation of 90% of UK PICUs and views from the wider MDT. A limitation was the use of a non-validated questionnaire. None or partial responses may indicate poor engagement in the ERM topic, and as with all self-reported surveys, responses indicate reported rather than necessarily actual clinical practice. Finally, the findings represent the views of UK NHS staff and may not be generalisable to other healthcare settings.

Phase 1c: observational study

We observed over half of all UK PICUs, geographically diverse, with varying population characteristics, PICU size, case mix and staffing structures during the two observation periods. However, the types of PICUs may not be generalisable to other UK or non-UK PICUs. To focus observations on early ERM, but to avoid very short-stay PICU patients (e.g. <48 hours), we started observation at 9 a.m. on the third day after PICU admission. ERM practice and delivery to patients in the first 72 hours of PICU stay may also be important in guaranteeing dose and efficacy of intervention. In addition, we stopped observation after 7 days of study observation (day 10 of PICU) or at discharge. Thirty-two per cent (54/169) of our cohort continued to stay in PICU and longer-term PICU care and use of ERM may also be important. Also, ERM may have a role in step-down high-dependency care or ward areas.

We acknowledge the potential risk of observer bias and Hawthorne effect in our study design. ERM activities were listed on the bedside activities document to allow ease of recording. Presence of the documentation or the known process of observation may have affected the amount of ERM delivered to patients during the observation period (e.g. increased number, duration or variety of ERM activities, stimulated by the bedside information).

ERM activities were recorded in the medical records by bedside clinical staff. Research staff extracted this information for our PERMIT CRFs. AEs were self-reported by the clinical team without independent confirmation and therefore may have under- or overestimated the frequency of events or relatedness to the ERM activity; however, the rates identified closely matched those extracted in the scoping review.

We identified a very high rate of ERM activity on study day 1 using the inclusive definition of any ERM. This limited any ability to perform the planned logistic regression modelling to explore patient-, site- or ERM-related factors. In our out-of-bed logistic regression model, due to the small number of patients per site, we were unable to use site as a random effect. Further exploratory analysis of factors affecting different subtypes of ERM are planned and may highlight wider variation in practice across sites.

Phase 2: manual development

A strength of this study was the multiple sources of evidence we used to develop the ERM intervention manual: evidence from a wide range of existing studies, concepts, tools and resources, as well as the

experience of diverse practitioners and topic experts. A further strength was that the manual was informed by a range of theories of implementation. However, given the COVID context during the study, we were unable to conduct workshops and interviews with parents and CYP with PICU experience, so we were not at all successful in using their direct experience to shape the ideas within the manual. The work of learning from parents' experiences was instead undertaken through the process evaluation work in Phase 3.

Phase 3: part 1 feasibility study

A strength of this study was the phased introduction and embedding of a novel intervention (the PERMIT manual) alongside a set of novel trial processes. A further strength was the engagement of staff within and across sites, including those who championed and led the ERM programme, those who delivered ERM, as well as those other staff at the sites not directly involved in bedside ERM delivery. This enabled us to introduce an ERM programme at pace, enrol planned numbers of patients and parents, demonstrate data collection is feasible and the ERM is delivered safely. We were not successful in obtaining timely local site approvals at one site, which meant that the introduction of the ERM programme was delayed. As a result, this site spent relatively little time in each of the phases. Also, when research staff were not available at sites – notably on ward rounds – we did lose some quality and accuracy in some areas of data collection. A health economic evaluation was removed from the feasibility study after the request of the HTA board. Full health economic evaluation and support in a future study are required.

Phase 3: part 2 process evaluation

A strength of our data is the spread of data across methods, as well as across sites and participants. We obtained a comprehensive account of the difficulties of introduction and embedding across the sites. A further strength was the multidisciplinary respondents from each site – including those who championed and led the introduction, those who delivered ERM, as well as those other staff at the sites not directly involved in bedside ERM delivery. This enabled us to document the range of perspectives on problems and tensions around the evolving context and delivery across the sites. Parental accounts were helpful in clarifying trial processes, as well as providing insight into their perspectives of delivering ERM, and were essential to the highlighting of elements to change in future. We were not successful in recruiting parents who had refused consent to the main study for an interview to explore their reasons for declining.

Phase 4: consensus and trial development

The short duration of the Phase 4 study and continued impact of COVID pandemic on PICU health-care staff and parents and families who participated in PERMIT limited the scope of consultation and feedback. Further work with PPIE groups and the PICU clinical community is required to evaluate the definitive primary outcome. This will include additional sample size calculations with more extensive PICANet data after overcoming the cyber-incident at the University of Leeds.

Conclusions and summary of key research recommendations

Early rehabilitation and mobilisation is a complex intervention requiring institutional, departmental and multidisciplinary involvement. We have demonstrated that implementation of the PERMIT manual is acceptable, feasible and can deliver ERM safely to critically unwell and injured infants and CYP within PICUs. Further research in a definitive trial with economic assessment and demonstration of improvement in patient-related outcomes is justified and required.

Implications for healthcare practice

This is a feasibility study and thus has no direct implications for healthcare practice at this stage.

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Below we list key members of those teams.

Contributions of authors

Barnaby R Scholefield (https://orcid.org/0000-0002-6198-4985) (Chief Investigator, NIHR Clinician Scientist and paediatric intensive care (PICU) physician, University of Birmingham) conceived the study, original grant application and protocols and led Phases 1 and 4, and co-led Phase 3 of PERMIT. Wrote the first draft final report, had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

Julie C Menzies (https://orcid.org/0000-0003-2080-3364) (Nurse Researcher, PICU and NIHR 70@70 Senior Nurse Research Leader, Birmingham Women's and Children's NHS Foundation Trust) led the PPIE throughout the study, contributed to the analysis of the Phase 1 survey, contributed to the research delivery of Phase 3 and led the Phase 3 process evaluation. Critically reviewed, analysed and edited full report and was a co-investigator.

Jennifer McAnuff (https://orcid.org/0000-0002-1636-0049) (Research Fellow, Northumbria University and paediatric occupational therapist) co-designed and led the Phase 2 intervention development study, led all Phase 2 data collection and analysis, co-wrote the ethics application for Phase 3, led the write-up of *Chapter 4* and was a co-investigator.

Jacqueline Y Thompson (https://orcid.org/0000-0002-9775-361X) (Research Fellow, University of Birmingham) trial co-ordinator and data manager for PERMIT observational study, designed and led the scoping review, co-ordinated and analysed Phase 1 survey. Database designer and manager Phase 1 observational and Phase 3 feasibility study. Wrote the first drafts of *Chapters 1* and *2*.

Joseph C Manning (https://orcid.org/0000-0002-6077-4169) (NIHR ICA Clinical Lecturer, Clinical Associate Professor in CYP and Families Nursing, University of Nottingham) critically reviewed, analysed and edited full report, member of the Phase 1 and Phase 3 study core-development team and was a co-investigator.

Richard G Feltbower (https://orcid.org/0000-0002-1728-9408) (Principal Investigator for PICANet, Senior Epidemiology, University of Leeds) critically reviewed, analysed and edited full report, statistical expertise and was a co-investigator.

Michelle Geary (https://orcid.org/0000-0002-2092-6113) (Divisional therapy lead and Specialist children's physiotherapist within neurology and neurorehabilitation Southampton children's Hospital) critically reviewed, analysed and edited full report and was a co-investigator.

Sophie Lockley, Patient and Public Involvement and Engagement (PPIE) representative and was a co-applicant.

Kevin P Morris (https://orcid.org/0000-0001-8911-6306) (Consultant in Paediatric Intensive Care, Birmingham Women's and Children's NHS Foundation Trust) critically reviewed, analysed and edited full report and was a co-investigator.

David Moore (https://orcid.org/0000-0002-4163-4080) (Associate Professor of Evidence Synthesis, University of Birmingham) provided methodological guidance and contributed to the literature review and was a co-investigator.

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Fenella Kirkham (https://orcid.org/0000-0002-2443-7958) (Professor of Paediatric Neurology, UCL and Southampton children's Hospital), co-lead for Phase 3, co-wrote the ethics application for Phase 3, critically reviewed, analysed and edited full report and was a co-investigator.

Robert Forsyth (https://orcid.org/0000-0002-5657-4180) (Consultant in Paediatric Neurology, University of Newcastle), co-lead for Phase 2, critically reviewed, analysed and edited full report and was a co-investigator.

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Data-sharing statement

All data requests should be submitted to the corresponding author for consideration. Access to anonymised data may be granted following review.

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Appendix 1

Trial oversight committee

An independent trial oversight committee was appointed by the NIHR in keeping with standard structure and definitions. The Trial Steering Committee was responsible for overall supervision on behalf of the Sponsor and Funder, and ensured that it was conducted in accordance with the rigorous standards set out in the Department of Health's Research Governance Framework for Health and Social Care and the Guidelines for Good Clinical Practice. The Trial Steering Committee comprised the Chief Investigator plus independent members (including independent PPIE representatives).

Dr Shane Tibby (Consultant in PICU), Chair, Clinician, Trialist.

Prof Mark Peters (Professor of Paediatric Intensive Care), Clinician, Trialist.

Dr Kerry Woolfall (Senior Lecturer Health Services Research), Qualitative Researcher.

Ms Suzanne Dottin-Payne (Parent representative), PPIE representative.

Prof Jim Lewsey (Professor of Medical Statistics), Statistician.

Data monitoring and ethics committee (DMEC)

An independent DMEC was appointed by the NIHR in keeping with standard structure and definitions. An independent DMEC monitored recruitment and retention, adherence with the intervention and patient safety.

Prof Bronagh Blackwood (Professor), Chair, Clinician, Trialist.

Dr ClionaMcDowell (Senior Statistician), Statistics.

Dr Siva Oruganti (Consultant in PICU), Clinician.

Appendix 2

Scoping review search strategy

MEDLINE

Database: Ovid MEDLINE(R) and In-Process and Other Non-Indexed Citations < 1946 to 12 December 2019 (repeated 1 November 2021).

(1) exp Pediatrics/or Paediatric.mp. (106506);
(2) Paediatrics.mp. (7305);
(3) Pediatric.mp. (276918);
(4) 1 or 2 or 3 (356323);
(5) Intensive Care Units.mp. or exp Intensive Care Units/(91849);
(6) Critical Illness.mp. or exp Critical Illness/(31374);
(7) Critical Care.mp. or exp Critical Care/(73300);
(8) (critical* adj3 (ill* or care*)).tw. (71316);
(9) intensive care.tw. (132554);
(10) critical care.tw. (25491);
(11) icu.ab,ti. (50876);
(12) 'intensive care'.ab,ti. (132554);
(13) (critical* adj3 (ill* or care)).ab,ti. (70706);
(14) 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 (243400);
(15) 4 and 14 (23482);
(16) Physical Therapy.mp. or exp Physical Therapy/(48742);
(17) Physical Therapy Modalities.mp. or exp Physical Therapy Modalities/(147898);
(18) Exercise Therapy.mp. or exp Exercise Therapy/or Exercise Movement Techniques/(50084);
(19) Occupational Therapy.mp. or exp OT/(16730);
(20) exp Rehabilitation/or rehabilitation.mp. (504279);
(21) physiotherapy.mp. (18150);
(22) Early Ambulation.mp. or exp Early Ambulation/(3460);
(23) Early Mobilization.mp. or Early Mobilisation/(4999);
(24) Chest PT.mp. or exp Chest PT/(802);
(25) (therap* adj3 (physical* or exercise* or occupation* or respiratory or music or animal)).ab,ti. (50992);
(26) ((cycle or bicycle) adj1 ergomet*).ab,ti. (11390);
(27) ((bed or 'daily living') adj3 activity).ab,ti. (2394);
(28) 'physical therapy'.ab,ti. (16266);
(29) 'Physical Therapy Modalities'.ab,ti. (134);
(30) 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25 or 26 or 27 or 28 or 29 (553008);
(31) (Early or earlier or accelerat* or acute or immediate*).mp. (3288276);
(32) 15 and 30 and 31 (228).

TABLE 32 Characteristics of included studies

Author, year, design, centre, country	Population (*n*, inclusion/exclusion criteria);	Intervention (definition of ERM, content)	Primary/co-primary and secondary outcome measures	Other findings
Study design	Timing ≥24 hours of admission			
Choong 2014a[11] Prospective pilot study Single centre Canada	*N* = 33 CYP aged 1–18 years admitted with a minimum of 24-hour PICU stay Exclusion criteria Patients cardiorespiratory instability (e.g. unstable airway, progressive shock), an adequate baseline level of function, imminent death, and contraindication to mobilisation	Single-component intervention In-bed cycling: Ex N'Flex EF-300 for children 3–7 years and MOTOmed Letto2 for patients 8–17 years Day 1: Minimum 10 (safety/tolerance) to 20 minutes Day 2: 20 minutes × 2 days Usual care: Physical therapy Patient intolerance, i.e. pain and/or discomfort, and safety (tube or catheter dislodgement)	Primary/co-primary outcome(s) *Physiological/clinical*: cardiorespiratory response via physiological measurements at baseline, during and after ERM Degree of UL and LL extremity movement using Actigraph GT3X accelerometers attached to the participants' wrists and ankles *Methodological:* feasibility, safety (AEs such as cardiorespiratory instability, tube dislodgment, pain, discomfort or injury) @24-hours	Increase in in-bed cycling (mean ± SD: 266.47 ± 166.12) vs. during non-intervention times (mean ± SD: 20.94 ± 15.26, counts/20 minutes, $p < 0.001$) different to baseline had no impact on UL activity (mean ± SD: 27.3 ± 12.55 vs. 51.32 ± 23.68 counts/20 minutes, $p < 0.05$)
Curry 2021[25] Quality improvement project Quaternary care, paediatric onco-critical care unit, Single centre USA	Pre-implementation period, *N* = 294 Post-implementation period, *N* = 272 Children ages 1 day to 21 years who required ICU or step-down admission were eligible for early mobility. Exclusion criteria included patients with an open chest or abdomen, unstable fractures, or with provider-placed medical orders specifying otherwise. A retrospective review of the medical records for all critical care and step-down admissions from January 2019 through June 2020 was performed; divided into two 9-month periods: pre-BRAVE implementation (January–September 2019) and post-BRAVE implementation (October 2019–June 2020) Early mobility activity was defined as any activity intended to maintain or restore musculoskeletal strength and function performed within 72 h of admission to the ICU	Multicomponent interventions ABCDEF ICU liberation bundle (spontaneous awakening and breathing trials; choice of sedation and analgesia, delirium prevention, surveillance and management; early mobilisation and exercise programmes with or without adjuncts; family engagement and empowerment) Early mobilisation – within 72 hours of admission from baseline of 21% to 80% within 9 months of implementation delirium. A positive delirium screen was defined as a CAPD score ≥9 Activities could be passive or active; included in-bed and out-of-bed interventions given by rehabilitation therapists, nursing staff or family members/caregivers. Level of activity was discussed during daily medical rounds, determined by patient's stability and the amount of medical support required, and documented	Primary/co-primary outcome(s) *Physiological/clinical*: cardiorespiratory response via physiologic measurements at baseline, during and after ERM *Methodological:* proportion of patients with a physician- or AP consult orders for OT and/or PT within 72 hours of admission, who received an early mobility activity provided by rehabilitative services, and the percentage of positive delirium screens after 24 hours of ICU admission Early mobility outcomes were evaluated in patients with LOS >48 hours and all LOS. *Secondary outcome measures:* type of early mobilisation activities performed, perceived and identified barriers to early mobility, deferral and AEs during rehabilitation interventions, and doses of sedative and analgesic infusions	Positive delirium screen in 43% of patients pre-implementation and 37% post-implementation time frame ($p = 0.46$). Patients who received at least one out-of-bed activity with PT/OT within 72 hours of admission increased (16–29%, $p < 0.001$) Number of activities deferred increased because of caregiver refusal, conflict with a diagnostic test or procedure, and staff concern about the patient's clinical status. 47/51 (92%) of staff reported positive impact on their patients and caregivers due to early mobility. 33 (65%) identified a collaborative approach as helpful. 43/51 (84%) reported moderate or full support from PICU during implementation, and 35/51 (69%) felt that they could prioritise and actively incorporate mobility as part of their patients' daily plan

TABLE 32 Characteristics of included studies (*continued*)

Author, year, design, centre, country	Population (*n*, inclusion/exclusion criteria);	Intervention (definition of ERM, content)	Primary/co-primary and secondary outcome measures	Other findings
	≥48 hours PICU admission			
Abdulsatar 2013[7] Prospective single-arm RCT Single centre	*N* = 12 CYP aged 3–18 years admitted minimum 48-hour PICU stay. Exclusion criteria Anticipated death or withholding life-sustaining therapy, physical inability to mobilise, cardio-respiratory instability, language barrier and inability to comprehend instructions or perform the intervention (i.e. deep sedation or severe cognitive) or functional disability, poor POPC and PCPC	Single-component intervention Interactive virtual reality game using Nintendo Wii Boxing for at least 10 minutes twice a day for 2 days Not defined. Probably at 48 hours PICU admission	Primary/co-primary outcome(s) *Methodological:* feasibility and safety over 8 months Secondary outcome(s) *Clinical/PROMs:* vital signs; UL activity measured using Actigraph GT3X accelerometers; Muscle strength using the dynamometer; Caregiver and participant satisfaction using self-administered questionnaire with a 7-point Likert scale	Clinical outcomes were worse (mean ± SD change of 1.08 ± 1.0, p = 0.02) among two-thirds of patients who received ERM, although no activity-related AEs were reported No improvement in grip strength or physiological status, despite increased activity levels (mean ± SD, UL activity pre: 9.36 ± 4.12 vs. post: 57.12 ± 46.60 counts) and higher carer satisfaction
Choong 2017[20] Pilot RCT – randomised 2 : 1 Single centre Canada	*N* = 30 CYP aged 3–17 years, admitted to 12-bed tertiary care, medical-surgical PICU Immobilised at time of screening and predicted at least an additional 48-hour PICU stay Exclusion criteria: • Patients at baseline level of function and mobile within 24 hours • Imminent death (expected within 72 hours) • Physical or anatomical restrictions to fitting cycle ergometer	Single-component intervention In-bed cycling: paediatric cycle ergometers 30 minutes/day, 5×/week + PT until functional independence achieved for at least 2 days or max. of 7 days of cycling Control: Usual care PT or OT in-bed cycling for 30 minutes/day	Primary/co-primary outcome(s) *Physiological/clinical/PROMs*: PICU-acquired morbidities, duration of MV, PICU and hospital LOS, 30-day mortality Functional outcome measured by PEDI-CAT speedy version at baseline, PICU discharge and 1-month post PICU discharge *Methodological:* feasibility (enrolment of 75% of eligible patients, accrual rate of >75% and 30-day follow-up rate of >75%) Safety/AEs related to mobilisation	No difference between arms (0.17, IQR: −0.01–0.36) among 24/30 patients (80%) who developed new functional difficulties in PICU (PEDI-CAT). In the usual-care arm 7/10 (70%) with median of 0.4 (IQR: 0.3–0.6), and 17/20 (85%) in the cycling arm (median: 0.6, IQR: 0.4–0.7) 10% of patients recovered functional ability at 1 month, and mobility was the slowest outcome to return

continued

TABLE 32 Characteristics of included studies (*continued*)

Author, year, design, centre, country	Population (*n*, inclusion/exclusion criteria);	Intervention (definition of ERM, content)	Primary/co-primary and secondary outcome measures	Other findings
Fink 2019[43] RCT Multicentre USA	*N* = 58 CYP aged 3–17 years admitted with acute diagnoses: traumatic brain injury, cardiac arrest, stroke, brain mass (e.g. tumour, arteriovascular malformation), or CNS infection/inflammation Minimum 48-hour PICU stay were enrolled ≤72 hours of admission, English-speaking parents/guardians, expected PICU stay ≥2 days Exclusion criteria Children with a do not resuscitate status, PCPC score 4–5 prior to diagnosis, or imminent death within 24 hours	Multicomponent interventions Early assessment and rehabilitation including PT, OT, SLP or usual care Intervention: PT, OT and SLT consultations placed within 72 hours of PICU admission, *n* = 26 Usual care: PT, OT and/or SLT consultations per the treating team, *n* = 32	Primary outcome(s) *Methodological:* feasibility and safety of PICU-based PT, OT and SLT therapies Secondary outcome(s) *Physiological/clinical/PROMs*: physical, cognitive, emotional, family functioning, QoL, 6-month hospital discharge, PCPC and POPC and FSS, VABS scores *Methodological:* timing of PT initiation, OT, SLT consultation *Process:* Family disposition at hospital discharge and PICU and hospital LOS	PT was delivered 80% of the time in the usual-care arm and 100% of the time among patients receiving early protocolised ERM Patients receiving early protocolised rehabilitation had less post-PICU rehabilitation
Prospective cohorts	≥48 hours of admission			
Choong 2015[19] Prospective observational study Single centre Canada	Age: over 12 months – 17 years. with developing functional skills, presence of at least 1 organ dysfunction on admission, limited mobility or bed rest during the first 48 hours of PICU admission, a minimum 48 hour PICU LOS Exclusion criteria Children directly transferred from a neonatal PICU prior to ever being discharged home, patients already mobilising well or at baseline functional status at the time of screening/or caregivers with an English language barrier and prior enrolment	Single-component intervention In-bed cycling	Primary outcome(s) *Methodological:* feasibility (protocol violation, withdrawal and follow-up rates) Secondary outcome(s) *Clinical*: POPC, PCPC, ventilator-free days, mortality, PICU and hospital LOS, and immobility morbidities (new-onset joint contractures, pressure ulcers and PICU-AW) Functional outcome (FSS), task performance measured by CAS. Factors influencing participation in mobility and self-care tasks in children ≥ 6 months to 7.5 years Age-appropriate exercise tolerance (>4 years) at hospital discharge, 3 and 6 months discharge *Process:* parental or caregiver stress measured via PSI at 3 months post discharge	ERM was feasible. At 3 and 6 months, functional ability measured using PEDI improved among 28% and 42% of the study cohort, respectively. 22% of those with a pre-existing chronic condition and 14% with functional limitations returned to baseline levels at 6 months. 60% of previously healthy children and 58% of children with normal baseline function regained full functional abilities. Moreover, the overall mortality rate was 3/33 (9%), and almost a third of patients (63%) were readmitted within 6 months of PICU discharge

TABLE 32 Characteristics of included studies (*continued*)

Author, year, design, centre, country	Population (*n*, inclusion/exclusion criteria);	Intervention (definition of ERM, content)	Primary/co-primary and secondary outcome measures	Other findings
Prospective cohorts	≥72 hours admission			
Choong 2021[24] cross-sectional, 2-day point prevalence study Multicentre Canada	*N* = 128 patients across 16 PICU's; day 1 *N* = 9 patients across 11 PICU's; day 2 Patients with a PICU LOS (LOS) ≥72 hours as of 7 am on each point prevalence day were included PICUs were eligible to participate if they:	PT and OT documented assessments in 72 hours of PICU admission. Mobility events were collected prospectively: (1) types and timing of mobility; (2) providers or assistance with mobility; (3) barriers to mobilisation	Primary outcome(s) *Process:* prevalence and nature of mobilisation practices in critically ill children while in the PICU Secondary outcome(s)	Highest level of mobility (HLM) achieved in children with ETTs in situ were most commonly not actively mobilised (31/50; 62.0% patient-days) but were mobilised out-of-bed on 18/50 patient-days (36%) Out-of-bed mobility (48/56; 85.7% patient-days) was the most common in non-MV patients Out-of-bed mobility (being held by a parent or PICU staff (37/87; 42.5%)) was the most common activity under 3 years (71/100; 71%), whereas no active mobility predominated in older children (18/37; 48.6% patient-days)
	(1) cared for mechanically ventilated infants and children and (2) were located in a distinct physical space dedicated to paediatric patients. Institutional review board approval was obtained at all sites with a waiver of informed consent for the collection of de-identified data	(4) potential AEs Mobility was defined as any activity involving physical movement of patient, except routine care and was categorised as follows: (1) no active mobility (2) in-bed mobility (3) edge of bed mobility (4) out-of-bed mobility	*Process:* factors associated with out-of-bed mobilisation and rehabilitation therapist-provided mobility, the rate of potential AEs, and perceived barriers to mobilisation Rehabilitation therapists were physiotherapists (PT) or occupational therapists (OT) Therapist-provided mobility was identified when a patient received ≥1 mobility event facilitated by a therapist on the study day	Nurses (286/387; 73.9%) commonly facilitated mobility alone, with family or other PICU staff and family facilitated 188 mobility events (48.6%). Children under 3 years were most commonly held (36/71; 50.7%) or were transferred from bed to chair (22/71; 31.0%). Children ≥3 years participated in transfers (6/16; 37.5%), pre-ambulation (4/16; 25.0%), and ambulation activities (3/16; 18.8%) Barriers were cardiovascular instability (*n* = 18; 14.9%), excessive sedation (*n* = 13; 10.7%), medical contraindication (*n* = 13; 10.7%), postoperative restrictions (*n* = 13; 10.7%) and lack of supportive personnel/equipment (5.0%) and invasive MV (4.1%)

continued

TABLE 32 Characteristics of included studies (*continued*)

Author, year, design, centre, country	Population (*n*, inclusion/exclusion criteria);	Intervention (definition of ERM, content)	Primary/co-primary and secondary outcome measures	Other findings
Cui 2017[14] Prospective study Single centre USA	Children between ages 2 weeks and 18 years, PICU LOS ≥3 days over 3 months	Multicomponent intervention PT, OT screening with the goal of formulating a rehabilitation plan within 72 hours of admission, followed by referral when indicated	Primary outcome(s) *Process:* PICU PT/OT consultation and treatment consultation timing, therapy type and duration and reasons for deferral Secondary outcome(s) *Process:* factors associated with PT/OT and patient outcome	Feasibility and safety of interventions were demonstrated
Ista 2021[42] Multicentre across 15 countries in Europe Netherlands, France, Spain, Germany, Italy, UK	*N* = 722 Two-day cross-sectional point prevalence study (29 May 2018, and 6 November 2018) PICUs from European countries were eligible to participate if they met the following criteria: (1) provide care for mechanically ventilated infants and children and (2) located in a distinct physical space within a paediatric hospital	Records of PT and OT consultation and treatment documentation for the first 72 hours of PICU admission were abstracted Out-of-bed mobility was defined as 'a transfer from bed to chair, held by family or staff, mat play, standing, or walking' Activities such as passive motion, sitting in bed, and bath were defined as in-bed mobility Mobility events were any single activity or clustered activities involving the child's physical movement, except for routine care. Barriers and potential safety events were selected from a pre-specified list	Primary outcome(s) *Process:* 'therapist-provided mobility', defined as at least one mobility event performed by a PT or OT on the study day Secondary outcome(s) *Process:* out-of-bed mobility, barriers to mobilisation and potential safety events	78% of children <3 years received out-of-bed mobility compared to 22% of patient's ≥3 years ($p < 0.001$). Non-MV patients were more likely than MV patients to achieve out-of-bed mobility (70% vs. 30%; $p < 0.001$). MV did not receive more therapist-provided mobility than those who were not (42% vs. 36%; $p = 0.181$) Out-of-bed activity was being held by a parent or a nurse ($n = 519$), bed-to-chair transfer without standing ($n = 120$) and mat play ($n = 51$) Patients ≥3 years received more PT- and/or OT-provided mobility, 50% (68/137) compared with age <3 years, 35% (111/319) ($p = 0.003$) Nurses ($n = 584$, 46%) provided mobilisation alone; with family (17%) or with PT or OT (6%); and family alone (16%)

TABLE 32 Characteristics of included studies (*continued*)

Author, year, design, centre, country	Population (*n*, inclusion/exclusion criteria);	Intervention (definition of ERM, content)	Primary/co-primary and secondary outcome measures	Other findings
				Mobilisation events did not occur on 115/456 patient-days (25%) in MV patients (75 of 115 patient days, 65%). Among MV children, passive range of motion (age <3, 23%; age ≥3, 23%) and being held by family/nurse (age <3, 27%; age ≥3, 22%) were common. Non-MV children held by family/nurse (44%); while bed-to-chair transfer was 17% in ≥2-year-olds Barriers were cardiovascular instability (*n* = 47, 10%), over sedation (*n* = 39, 9%), and medical contraindication (*n* = 37, 8%)
Kudchadkar 2020[18] Cross-sectional point prevalence study Multicentre study USA	*N* = 82 US PICUs on 2 days (the 9 November 2017, and the 12 February 2018) (1) PICU LOS ≥ 72 hours at 7 am on each point prevalence day (2) mechanically ventilated infants and children and (3) located in PICU	Multicomponent interventions PT and OT consultation and treatment documentation for the first 72 hours of PICU admission	Primary outcome(s) *Process:* PT mobility of ≥1 mobility event performed by PT/OT on the study day. Secondary outcome(s) *Process:* mobilisation rates, type and timing of mobility events, barriers and facilitators of mobilisation, AEs	Among children who did not require MV, children <3 years old were frequently cuddled (51%) by family or nurses, while older children were commonly ambulated (29%)
Tsuboi 2017[32] Prospective pre-post study Single centre Japan	*N* = 57 (23 before EM and 34 following EM) CYP ≤16 years who received liver transplantation	Multicomponent interventions MDT approach to PICU ERM: PT; bed mobility activities (e.g. bridging, rolling, lying to sitting) 72 hours after transplantation	Primary outcome(s) *Process:* PT consultations @ 72 hours after transplantation Secondary outcome(s) *Clinical/PROMs*: Functional mobility, intubation length, PICU or hospital LOS, mortality *Methodological:* safety (AEs from ERM)	Increase in frequency of physical therapy, with more patients achieving their rehabilitation goals. Proportion of patients who received physical therapy pre- and post-ERM periods increased, 11 and 33, respectively. More patients achieve post-intervention goals at 72 hours post-surgery (pre-ERM: 0 vs. post-ERM: 22), irrespective of baseline status and pre-operative hospitalisation

continued

TABLE 32 Characteristics of included studies (*continued*)

Author, year, design, centre, country	Population (*n*, inclusion/exclusion criteria);	Intervention (definition of ERM, content)	Primary/co-primary and secondary outcome measures	Other findings
Prospective cohorts	Undefined timing of admission			
Colwell 2018[13] Prospective before-after study Single centre (cardiac and medical-surgical unit) USA	PICU patients on admission, supported by vasoactive infusions, invasive respiratory support and ECMO, and did not exceed practitioner-ordered activity limitations	Multicomponent interventions Goal-directed mobilisation protocol (PT and OT) over 9 months (3 months implementation period and 6 months post implementation)	Primary outcome(s) *Process:* bi-weekly mean mobilisation ratio Secondary outcome(s) *Methodological:* safety (AEs), adherence, protocol deviation *Process:* barriers to mobilisation	Higher adherence among younger patients ($p = 0.04$), with higher baseline severity of illness ($p < 0.001$) when mobilisation sessions were goal-directed ($p < 0.001$) There was no difference in mobilisation rates (pre: $p = 0.86$ vs. post: $p = 0.84$) or AEs (2.5%, $p = 0.18$) between groups
Retrospective cohorts	≥24 hours of admission			
Choong 2012[12] Single centre Observational pre- and post-study Canada	*N* = 91 CYP aged 0–17 years admitted with a minimum 24-hour PICU stay.	Multicomponent interventions PT, OT, SLP	Primary/Co-primary outcome(s) *Process:* proportion and nature of rehabilitation – type, timing and frequency Secondary outcome(s) *Process:* barriers to PT mobilisation, clinical outcomes of non-mobility/PT, morbidities due to immobility AEs due to PT	ERM was frequently delivered when evaluated using PT and OT consultations
Retrospective cohorts	≥48 hours of admission			
Alqaqaa 2017[8] Retrospective study Single centre USA	*N* = 29 CYP 2 months to 18 years, requiring invasive and non-invasive MV regardless of patient interface except for nasal cannula and flow support Exclusion criteria Severe disability, coma or vegetative state and brain death	Multicomponent interventions Algorithm to identify patients suitable for mobilisation (PT, OT, SLP) + training on benefits of mobilisation + education on safety techniques + family advisors' feedback	Primary outcome(s) *Process:* mobilisation rate Secondary outcome(s) *Physiological/clinical/PROMs*: PICU and hospital LOS, FSS *Methodological:* safety (incidence rates of AEs) *Process:* discharge disposition	Higher mobilisation rates among non-ventilated patients (mean difference of about a day) than no change for mechanically ventilated patients No safety concerns or AEs were identified

TABLE 32 Characteristics of included studies (*continued*)

Author, year, design, centre, country	Population (*n*, inclusion/exclusion criteria);	Intervention (definition of ERM, content)	Primary/co-primary and secondary outcome measures	Other findings
Betters 2017[10] Retrospective study Single centre (36-bed medical-surgical PICU) USA	Consecutive review of admission records of patients who receive early mobilisation (EM) in the PICU between December 2013 and October 2016 Screening to formulate rehabilitation plan within 72 hours of admission, with a referral when indicated Exclusion criteria High-frequency oscillator ventilation, critical airway, deep sedation, neuromuscular blockade, unstable traumatic brain injury, reduced inspired oxygen (FiO2), spinal precautions, haemodynamic instability	Multicomponent interventions PT, OT (PT and OT co-ordinate with the patient's nurse, SLP and RT to schedule an optimal time to mobilise the patient) EM sessions last from 10 minutes to an hour	Primary outcome(s) *Process:* ERM consultation Secondary outcome(s) *Methodological:* safety (AEs during EM)	Higher ERM consultations (median duration 30, IQR: 29–45 minutes) with no major AEs
Choong 2014b[21] Multicentre Retrospective study Canada	*N* = 600 CYP aged 0–17 years. Minimum 24-hour PICU stay in tertiary PICUs	Multicomponent interventions PT, OT, SLT. Bed mobility activities (e.g. bridging, rolling, lying to sitting); strengthening exercises	Primary outcome(s) *Process:* nature and timing of PICU rehabilitation practices Secondary outcome(s) *Process:* predictors of mobilisation and time to mobilisation	Children who were older, healthy, admitted during the winter, not mechanically ventilated, receiving neuromuscular blockade or sedatives were more likely to receive mobility therapy
Justice 2019[16] Retrospective pre- and post-study Single centre USA	Comparison of data from January 2015 to December 2016 (pre-WeeMove) to January 2017 to post-WeeMove for all patients admitted to the CTICU for >48 hours ERM defined as activity (active or passive) within 48 hours of critical illness Exclusion criteria: High frequency of activity was contraindicated	Multicomponent interventions PT, OT	Primary outcome(s) *Process:* OT and PT consultations Secondary outcome(s) *Physiological/ clinical/PROMs*: PICU LOS Methodological: safety (AEs) *Process:* staff barriers	Small improvements in PICU length-of-stay (average LOS pre-WeeMove = 6.25 days vs. post-WeeMove LOS = 5.23 days), and time spent intubating patients (pre-WeeMove was 27.86 hours, post-WeeMove = 25.09 hours)

continued

TABLE 32 Characteristics of included studies (*continued*)

Author, year, design, centre, country	Population (*n*, inclusion/exclusion criteria);	Intervention (definition of ERM, content)	Primary/co-primary and secondary outcome measures	Other findings
Retrospective cohorts	≥72 hours of admission			
Wieczorek 2016[17] Observational pre-post study USA	*N* = 200 (100 pre-intervention and 100 post intervention) CYP aged 1 day to 17 years admitted with minimum 72-hour PICU stay Retrospective review: July–August 2014 (pre-implementation phase) and July–August 2015 (post implementation) medical-surgical unit Exclusion criteria: ECMO, open chest or abdomen, unstable fractures, or medical orders specifying alternate activities	Multicomponent interventions Implementation of a tiered early mobilisation programme. Sleep hygiene promotion and routine delirium screening for all children Increasing mobility levels from level 1 (repositioning) to level 3 (sitting, out of bed activities or ambulation)	Primary outcome(s) *Process:* OT/PT consultations; number/types of mobilisation activities on PICU Day 3 Secondary outcome(s) *Methodological:* adherence (number and reasons activities were stopped), safety (mobilisation-related AEs, inadvertent extubation or line removal) *Process:* barriers to activities	Nearly half of the children (48/100) received at least one ERM intervention by day 3 of admission, and the proportion of children receiving at least one in-bed activity increased by 18% ($p < 0.001$) There was no change in passive mobilisation rates, only an increase in active interventions (26% vs. 57%; $p < 0.001$), especially among children ≥3 years. There was also a slight increase in the number of children orally intubated post intervention, facilitating ambulation

CAS, caregiver assistance scale; FSS, functional skills scale; LL, lower limb; PEM, participation and environment measure; PROM, patient-reported outcome measure; VABS, Vineland adaptive behavioural scale.

Note
Primary outcomes or co-primary outcome(s); short term (≤6 months post discharge); intermediate term (≥6 months post discharge) with details about methods and timing of measurement.

TABLE 33 Quality assessment using ROBINS-I and indication of effectiveness for studies (*n* = 18) included in the systematic review

	Studies/signalling questions	1	2	3	4	5	6	7	8	9
1.	Abdulsatar 2013[7]	Serious	Moderate	Moderate	Moderate	Serious	Critical	Low	Moderate	Favours intervention
2.	Alqaqaa 2018[8]	No information	No information	No information	Serious	No information	No information	Serious	Critical	Unpredictable
3.	Betters 2017[10]	No information	Low	Low	Moderate	Low	No information	Moderate	Moderate	Favours intervention
4.	Choong 2017[20]	Moderate	No information	Moderate	Moderate	Moderate	Moderate	Moderate	Moderate	Towards null

TABLE 33 Quality assessment using ROBINS-I and indication of effectiveness for studies (n = 18) included in the systematic review (*continued*)

	Studies/signalling questions	1	2	3	4	5	6	7	8	9
5.	Choong 2015[19]	Moderate	Low	Moderate	Moderate	Moderate	Moderate	Moderate	Moderate	Towards null
6.	Choong 2014a[11]	No information	No information	Serious	Serious	Serious	Serious	Serious	Serious	Away from null
7.	Choong 2014b[21]	Moderate	Moderate	Serious	Moderate	No information	Moderate	Serious	Moderate	Unpredictable
8.	Choong 2012[12]	Moderate	Moderate	Moderate	Serious	Moderate	Moderate	Serious	Moderate	Unpredictable
9.	Choong 2021[24]	Low	Low	Moderate	Low	Low	Low	Low	Low	Unpredictable
10.	Colwell 2018[13]	Serious	Moderate	Moderate	Moderate	No information	Moderate	Moderate	Moderate	Unpredictable
11.	Cui 2017[14]	Serious	Serious	Serious	Serious	No information	Serious	Serious	Moderate	Unpredictable
12.	Curry 2021[25]	Serious	Moderate	Moderate	Low	Low	Low	Low	Moderate	Unpredictable
13.	Fink 2019[43]	Serious	Low	Moderate	Low	Moderate	Moderate	Moderate	Moderate	Unpredictable
14.	Ista 2021[42]	Low	Low	Moderate	Low	Low	Low	Low	Low	Unpredictable
15.	Justice 2019[16]	Serious	Moderate	No information	No information	No information	No information	No information	Serious	Unpredictable
16.	Kudchadkar 2020[18]	Low	Low	Moderate	Low	Low	Low	Low	Low	Unpredictable
17.	Tsuboi 2017[32]	Moderate	Moderate	Moderate	Moderate	Moderate	No information	Moderate	Moderate	Unpredictable
18.	Wieczorek 2016[17]	No information	No information	No information	No information	No information	No information	No information	No information	Unpredictable

Notes
All studies were prospective or retrospective designs except Choong 2017 and Fink 2019 (RCTs).
Signalling questions:
1. Bias due to confounding – were the inclusion/exclusion criteria consistently applied across individuals or comparison groups and important confounding variables considered in the design/analysis? (confounding, i.e. impairment, comorbidity).
2. Bias in selecting participants into the study – was the strategy for recruiting participants into the study the same across individuals or comparison groups? (selection bias, confounding).
3. Bias in the classification of interventions (selection bias, confounding).
4. Bias due to deviations from intended intervention (selection bias, generalisability).
5. Bias due to missing data – were missing data handled appropriately? (Detection bias, attrition bias).
6. Bias in measurement of outcomes – was the length of follow-up the same across study groups and assessors blinded to the outcome or exposure status of the participants? (Attrition bias).
7. Bias in the selection of the reported result – (performance bias, reporting bias).
8. Overall risk of bias judgement.
9. Overall direction of bias.

TABLE 34 Consensus on Exercise Reporting Template (CERT) for included studies

Study	WHAT: materials 1	WHO: provider 2	DELIVERY: 4	DELIVERY: 5	DELIVERY: 6	DELIVERY: 7a	DELIVERY: 7b	DELIVERY: 8	DELIVERY: 10	DELIVERY: 11	DOSAGE: 13	TAILORING: 14a	TAILORING: 14b	TAILORING: 15	HOW WELL: 16a	HOW WELL: 16B
Abdulsatar 2013[7]	Yes	No	Yes	Yes	No	No	No	No	No	Yes	Yes	No	No	Yes	Yes	Yes
Alqaqaa 2018[8]	No	No	No	No	No	No	No	No	No	No	Yes	No	No	No	No	No
Betters 2017[10]	Yes	Yes	Yes	No	Yes	No	No	Yes	Yes	No	Yes	Yes	Yes	Yes	No	Yes
Choong 2017[20]	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	No	Yes	Yes	Yes	No	Yes	Yes	Yes
Choong 2015[19]	No	No	No	No	No	Yes	No	No	No	No	No	No	No	No	Yes	No
Choong 2014a[11]	No	No	No	No	No	Yes	No	No	No	No	No	No	No	No	Yes	No
Choong 2014b[21]	Yes	Yes	No	Yes	No	Yes	No	No	No	No	No	Yes	Yes	No	Yes	No
Choong 2012[12]	No	No	Yes	No	No	No	No	No	No	No	No	No	No	No	No	No
Choong 2021[24]	Yes	Yes	Yes	Yes	No	No	No	Yes	Yes	Yes	Yes	No	No	No	Yes	Yes
Colwell 2018[13]	No	Yes	No	No	No	No	No	No	Yes	No	No	No	No	No	No	No
Cui 2017[14]	No	Yes	Yes	Yes	No	No	No	Yes	No	Yes	No	No	No	No	No	No
Curry 2021[24]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	No	Yes	Yes	Yes
Fink 2019[43]	No	No	No	No	No	Yes	No	No	No	No	No	No	No	No	No	No
Ista 2021[42]	Yes	Yes	Yes	Yes	No	No	No	Yes	Yes	Yes	Yes	No	No	No	Yes	Yes

TABLE 34 Consensus on Exercise Reporting Template (CERT) for included studies (*continued*)

Study	WHAT: materials 1	WHO: provider 2	DELIVERY: 4	DELIVERY: 5	DELIVERY: 6	DELIVERY: 7a	DELIVERY: 7b	DELIVERY: 8	DELIVERY: 10	DELIVERY: 11	DOSAGE: 13	TAILORING: 14a	TAILORING: 14b	TAILORING: 15	HOW WELL: 16a	HOW WELL: 16B
Justice 2019[16]	Yes	No	No	No	No	No	Yes	No	No	No	No	Yes	No	No	Yes	No
Kudchadkar 2020[18]	Yes	Yes	Yes	Yes	No	Yes	No	No	No	Yes	Yes	Yes	Yes	No	No	Yes
Tsuboi 2017[32]	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	No	No	No
Wieczorek 2016[17]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	No	No	No

Appendix 3

Additional tables and figures

TABLE 35 Content of ERM and non-ERM protocols

Items	Within an ERM protocol (*n* = 12 respondents) Yes *n* (%)	Within a non-ERM protocol (*n* = 124 respondents) Yes *n* (%)
Physical therapy requiring additional equipment	9 (75)	18 (15)
OT interventions	9 (75)	18 (15)
Physical therapy not requiring additional equipment	8 (67)	17 (14)
SLT interventions	4 (33)	12 (10)
Psychology interventions	0 (0)	8 (6)
Delirium screening	0 (0)	1 (1)

TABLE 36 Characteristics of survey respondents (*n* = 124 respondents)

Professional group	*n* (%)[a]
Nurse	34 (27)
Physiotherapist	28 (23)
Medical doctor (consultant)	22 (18)
OT	19 (15)
Play therapist	7 (6)
Psychologist	7 (6)
Dietician	6 (5)
SLT	1 (1)
Years of experience	*n* (%)[a]
<1 year	7 (6)
1–<5 years	27 (22)
5–<10 years	30 (24)
10–<15 years	14 (11)
15–<20 years	33 (27)
More than 20 years	15 (12)

a Percentages may not total 100 due to rounding.

TABLE 37 Current views of ERM in PICU (*n* = 121 respondents)

Current view of ERM in PICU	*n* (%)[a]
Crucial, should be the top priority in the care of PICU patients	15 (12)
Very important, should be a priority in the care of PICU patients	67 (55)
Important, should be a priority in the care of PICU patients	35 (29)
Somewhat important, should be considered in the care of PICU patients	4 (3)
Not of great importance, clinicians should bear it in mind in the care of PICU patients	0 (0)
Of minimal importance to the care of PICU patients	0 (0)
Of no importance to the care of the PICU patients	0 (0)

a Percentages may not total 100 due to rounding.

TABLE 38 Which professional or parent group in PICU initiates ERM (*n* = 124 respondents)

Professional or family group	Yes *n* (%)
Physiotherapist	96 (77)
Physicians	92 (74)
Bedside nurse	64 (52)
Senior nurse	58 (47)
Other members of the medical team	55 (44)
OT	37 (30)
Parent or family member	24 (19)

TABLE 39 Types of ERM equipment available in each PICU (*n* = 26 PICUs)

ERM equipment available in each PICU	*n* (%)
Specialist static seating	25 (96)
Portable ventilators	23 (88)
Mobile lifts	22 (85)
Tilt table	22 (85)
Bed with full chair position	18 (69)
Specialist wheelchair	18 (69)
Bed with Trendelenburg features	13 (50)
Patient rolling walker	11 (42)
Bedside cycle or in bed cycle	10 (38)
Ceiling lifts	8 (31)
Speciality bed with continuous side-to-side rotation	8 (31)
Bed with retractable footboard	7 (27)
Bed with chair egress exit out the foot of the bed	5 (19)
Transcutaneous electrical nerve stimulation	3 (12)

TABLE 40 Early rehabilitation activities and category classification

Description	Broad group	Enrichment, passive, active mobility group	Any ERM	Mobility ERM	Out-of-bed mobility ERM	Mobility ranking
1. Cuddles (in bed)/comfort holding	CUDDLES	Enrichment	X	X		4 Held by parent or nurse
2. Cuddles out of bed/kangaroo care	CUDDLES	Enrichment	X	X	X	4 Held by parent or nurse
3. Sibling support, e.g. watching TV/iPad together	FAMILY SUPPORT	Enrichment	X			
4. Reading a story/singing	MUSIC THERAPY	Enrichment	X			
5. Entry in patient diary	PSYCHOLOGICAL SUPPORT	Enrichment	X			
6. Communication using communication tools	PSYCHOLOGICAL SUPPORT	Enrichment	X			
7. Music therapy, e.g. listening to music or singing to a child	MUSIC THERAPY	Enrichment	X			
8. Massage therapy	SENSORY STIMULATION	Enrichment	X			
9. Counselling/psychological support	PSYCHOLOGICAL SUPPORT	Enrichment	X			
10. Pet therapy	PSYCHOLOGICAL SUPPORT	Enrichment	X			
11. Engagement in activities of daily living (age-appropriate)	ENGAGEMENT IN DAILY ACTIVITIES	Active mobility	X			
12. Orientation to self/place/time of day	SENSORY STIMULATION	Enrichment	X			
13. Established daily routine, e.g. timetable	SENSORY STIMULATION	Enrichment	X			
14. Day/night routine encouraged, e.g. eye mask/earplugs/ headphones used to promote sleep at night	SENSORY STIMULATION	Enrichment	X			
15. Positioning for tone	POSITIONING – NM	Passive	X			
16. Neonatal positioning	POSITIONING – NM	Passive	X			
17. Positioning for development or functional benefit	POSITIONING – MOB	Passive	X	X		1 Passive ROM
18, Splints/braces – application of	POSITIONING – NM	Passive	X			
19. Sitting up in bed (30–90°)	SITTING	Active mobility	X	X		2 Sitting and exercises in bed
20. Sitting on the edge of bed	SITTING	Active mobility	X	X		3 Sitting edge of bed

continued

TABLE 40 Early rehabilitation activities and category classification (*continued*)

Description	Broad group	Enrichment, passive, active mobility group	Any ERM	Mobility ERM	Out-of-bed mobility ERM	Mobility ranking
21. Sitting in a chair	SITTING	Active mobility	X	X	X	5 Transfer bed to chair
22. Sliding board transfer	TRANSFERS	Active mobility	X	X		2 Sitting and exercises in bed
23. Sit to stand (bed to chair)	STANDING	Active mobility	X	X	X	5 Transfer bed to chair
24. Step transfer	TRANSFERS	Active mobility	X	X	X	7 Standing
25. Stand transfer	TRANSFERS	Active mobility	X	X	X	7 Standing
26. Lift|57. (1) One person|58. (2) Two-person	TRANSFERS	Active mobility	X	X	X	5 Transfer bed to chair
27. Hoist transfer	TRANSFERS	Active mobility	X	X	X	5 Transfer bed to chair
28. Sensory stimulation via touch/textures/visual	SENSORY STIMULATION	Active mobility	X			
29. Floor/mat play	DEVELOPMENTAL PLAY – MOB	Active mobility	X	X	X	6 Mat play
30. Developmental play: supine, side-lying, prone, sitting	DEVELOPMENTAL PLAY – MOB	Active mobility	X	X	X	6 Mat play
31. Play (e.g. messy play, painting, finger painting, etc.)	DEVELOPMENTAL PLAY – MOB	Active mobility	X	X	0	2 Sitting and exercises in bed
32. Interactive virtual reality, e.g. games, goggles	DEVELOPMENTAL PLAY – NM	Enrichment	X	X		
33. School teacher to bedside	SCHOOL	Enrichment	X			
34. Passive ROM	RANGE OF MOVEMENT	Passive	X	X		1 Passive ROM
35. Active ROM (movement following instructions)	RANGE OF MOVEMENT	Active mobility	X	X		2 Sitting and exercises in bed
36. Active assisted ROM (assisted movement following instructions)	RANGE OF MOVEMENT	Active mobility	X	X		2 Sitting and exercises in bed
37. Rolling – active or facilitated	RANGE OF MOVEMENT	Active mobility	X	X		2 Sitting and exercises in bed
38. Stretching exercises in bed	RANGE OF MOVEMENT	Active mobility	X	X		2 Sitting and exercises in bed

TABLE 40 Early rehabilitation activities and category classification (*continued*)

Description	Broad group	Enrichment, passive, active mobility group	Any ERM	Mobility ERM	Out-of-bed mobility ERM	Mobility ranking
39. Strengthening exercises (age-appropriate bed exercises such as bridging, straight-leg raises, etc.)	EXERCISES IN BED	Active mobility	X	X		2 Sitting and exercises in bed
40. Strengthening exercises – out of bed, e.g. squatting	EXERCISES OUT OF BED	Active mobility	X	X	X	6 Mat play
41. MOTOmed or cycling in bed	IN-BED CYCLING	Active mobility	X	X		2 Sitting and exercises in bed
42. Physio-directed exercise programme (comprehensive)	PHYSIOTHERAPY	Active mobility	X	X		2 Sitting and exercises in bed
43. Standing (next to bed with or without support)	STANDING	Active mobility	X	X	X	7 Standing
44. Standing frame	STANDING	Active mobility	X	X	X	7 Standing
45. (1) Walking with support/aid. (2) Walking unsupported	AMBULATING	Active mobility	X	X	X	8 Walking in room/unit
46. (1) Mobilising (≤1 m) (2). Mobilising (≤5 m). (3) Mobilising (>5 m)	AMBULATING	Active mobility	X	X	X	8 Walking in room/unit
47. Marching on the spot	AMBULATING	Active mobility	X	X	X	8 Walking in room/unit
48. School	SCHOOL	Active mobility	X			
49. Physio. dept. e.g. gym session	PHYSIOTHERAPY	Active mobility	X	X	X	9 Walking off unit
50. Trip/outing, e.g. chapel, canteen/restaurant	AMBULATING	Active mobility	X	X	X	9 Walking off unit
51. Mobilising	AMBULATING	Active mobility	X	X		2 Sitting and exercises in bed
52. Bath/shower/toilet	ENGAGEMENT IN DAILY ACTIVITIES	Active mobility	X	X		U Uncategorised
53. Other exercises out of bed	EXERCISES OUT OF BED	Active mobility	X	X		U Uncategorised
54. SLT (speech & lang. therapy), e.g. tastes, development of communication tools (i.e. using letters/words/typing in tablets) and swallow assessment	SENSORY STIMULATION	Enrichment	X			
55. FES or NMES	SENSORY STIMULATION	Passive	X	X		

FES, functional electrical stimulation; NMES, transcutaneous electrical muscle stimulation.

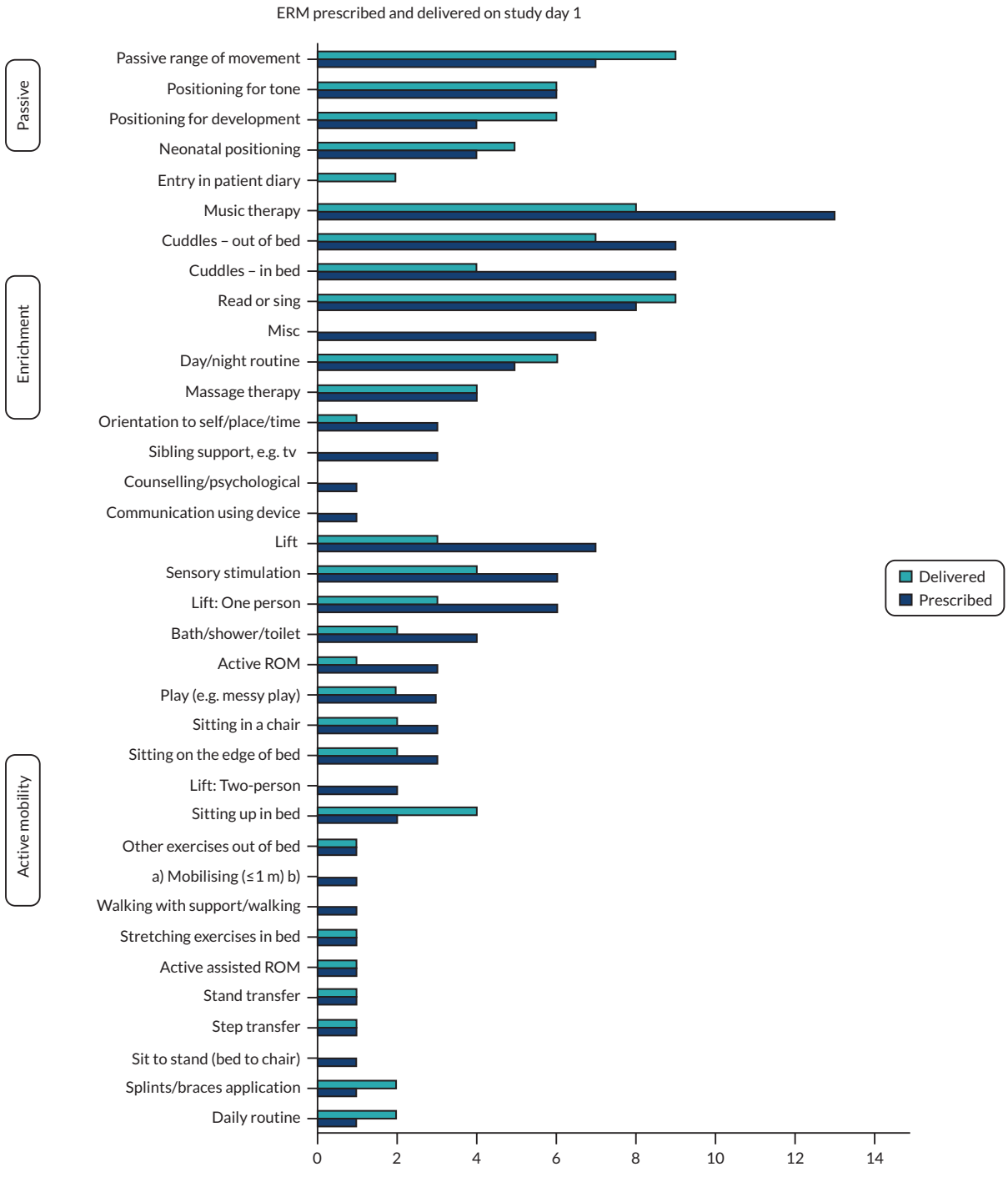

FIGURE 18 ERM prescribed and delivered activities on study day 1.

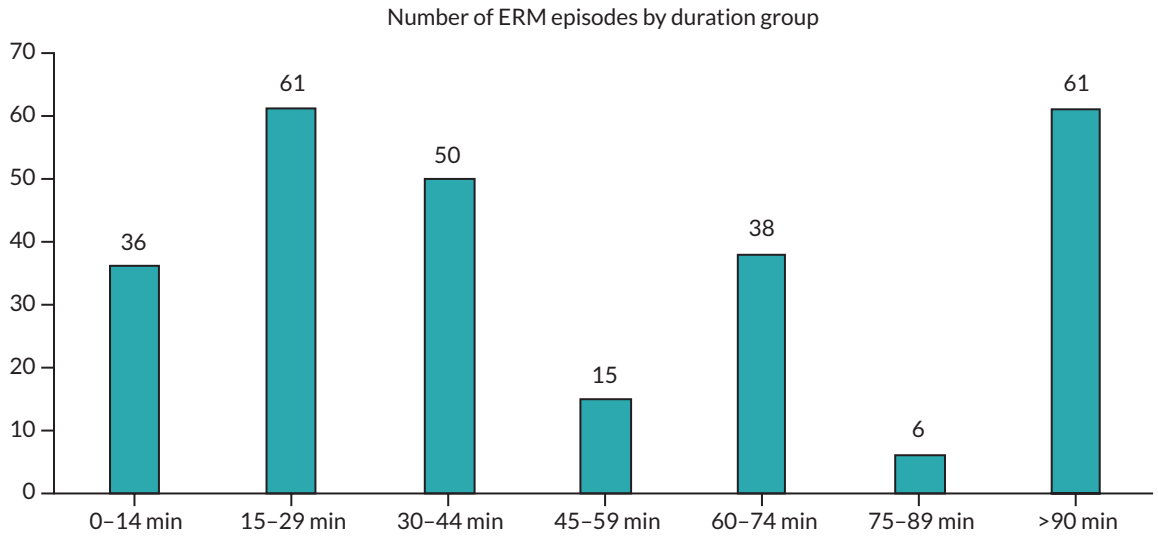

FIGURE 19 Number of ERM episodes by duration.

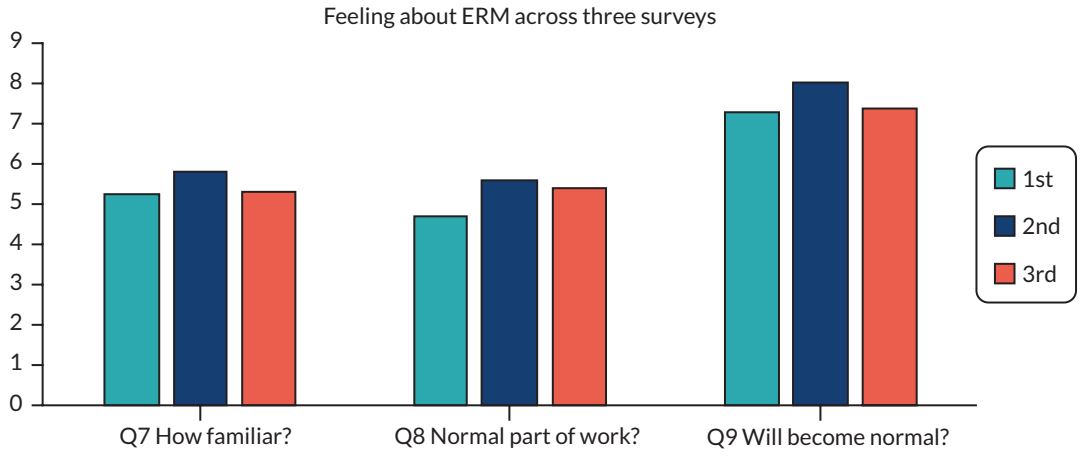

FIGURE 20 NoMAD reports of familiarity and normality of ERM in practice across first, second and third surveys.

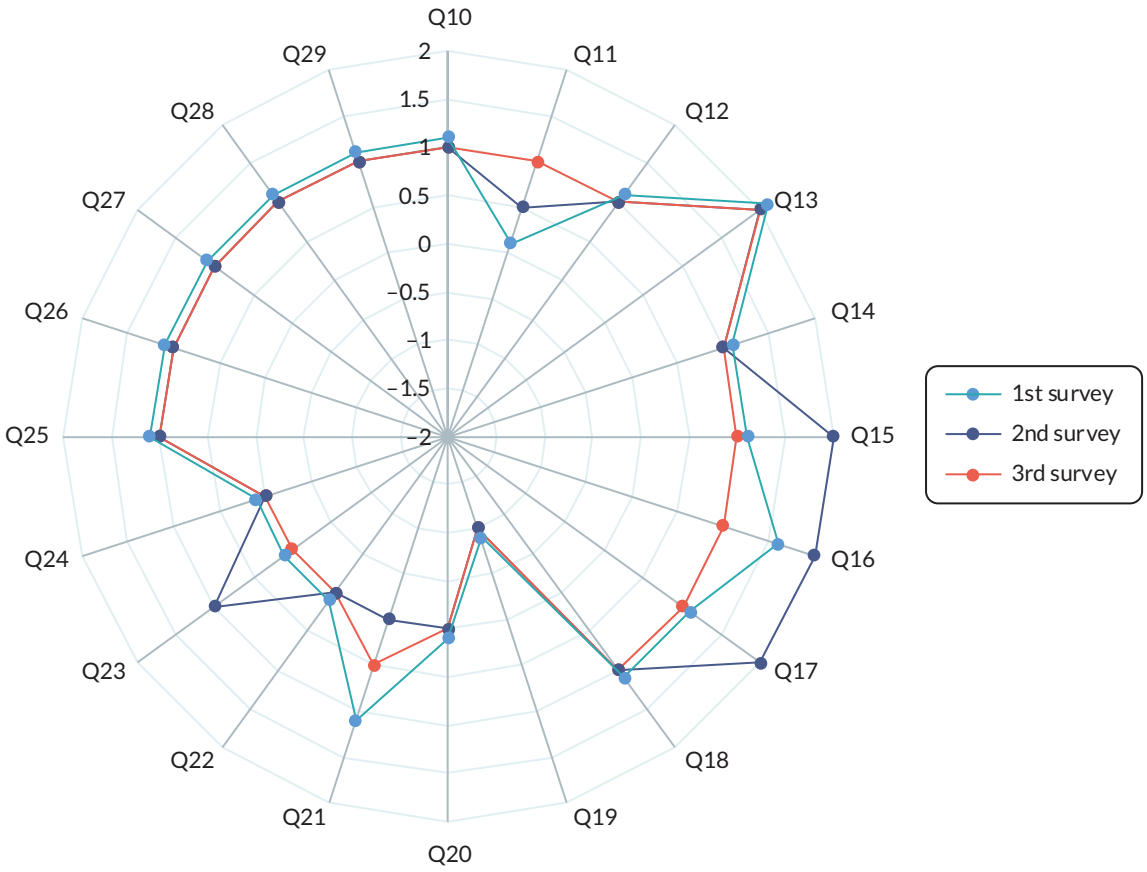

FIGURE 21 Radar plot of overall (median) score for questions (see *Table 41*) for all participants across three survey time points.

TABLE 41 Full-length questions for NoMAD survey

Q7. When you undertake ERM, how familiar does it feel?
Q8. Do you feel ERM is currently a normal part of your work?
Q9. Do you feel ERM will become a normal part of your work?
Q10. I can see how ERM differs from usual ways of working
Q11. Staff in this organisation have a shared understanding of the purpose of ERM
Q12. I understand how ERM affects the nature of my own work
Q13. I can see the potential value of ERM for my work
Q14. There are key people who drive ERM forward and to get others involved
Q15. I believe that participating in ERM is a legitimate part of my role
Q16. I am open to working with colleagues in new ways to use ERM
Q17. I will continue to support ERM
Q18. I can easily integrate ERM into my existing work
Q19. ERM disrupts working relationships
Q20. I have confidence in other people's ability to use ERM
Q21. Work is assigned to those with skills appropriate to ERM
Q22. Sufficient training is provided to enable staff to implement ERM

TABLE 41 Full-length questions for NoMAD survey (*continued*)

Q23. Sufficient resources are available to support ERM
Q24. Management adequately supports ERM
Q25. I am aware of reports about the effects of ERM
Q26. The staff agree ERM is worthwhile
Q27. I value the effects ERM has had on my work
Q28. Feedback about ERM can be used to improve it in the future
Q29. I can modify how I work with ERM

This work is adapted from 'Improving the normalization of complex interventions' by Finch *et al.*,[104] used under CC BY 4.0, http://creativecommons.org/licenses/by/4.0/.

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