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Title: Protocol for a multicentre longitudinal mixed methods study: Feeding and survivorship outcomes in previously healthy young Paediatric IntensivE Care Survivors – The PIES study

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Abstract

Introduction

An admission to Paediatric Intensive Care (PICU) is associated with multiple physical and environmental stressors, often involving many negative and painful oral experiences. Evidence from children with complex medical conditions suggest that feeding difficulties post-PICU stay are common, causing significant parental anxiety. Adult intensive care (ICU) survivor studies suggest feeding issues lasting up to 3 months post discharge from ICU. There is, however, a paucity of evidence regarding feeding outcomes for previously healthy children following a PICU admission and whether painful oral experiences during an admission contribute to feeding difficulties post-discharge, negatively impacting on parental/caregiver anxiety.

Methods and analysis

This longitudinal concurrent mixed method study will explore the impact of feeding difficulties, identifying any clinical risk factors during the first 6 months of PICU-discharge in previously healthy young children (≤ 4 years). Parents/caregivers of children will be asked to complete questionnaires relating to; feeding difficulties, parental/caregiver stress, child and parental/caregivers feeding behaviours, at the point of PICU-discharge, 1, 3 and 6 months post-discharge. Parents/caregivers will be invited to participate in qualitative semi-structured interviews at 3 and 6 months post-PICU-discharge exploring parental/caregiver experiences of feeding their child after PICU. Statistical analysis of the survey data will consist of descriptive

and inferential statistics, plus qualitative analysis of any free text comments using thematic analysis.

Ethics and dissemination

This study will provide an insight and increase our understanding of the prevalence of feeding difficulties in previously healthy children admitted to PICU and parental/caregiver experiences. Multiple methods will be used to ensure that the findings are effectively disseminated to service users, clinicians, policy and academic audiences. The study has full ethical approval from the National Health Service Research Ethics Committee (Ref: 20/YH/0160) and full governance clearance.

Article summary

Strengths and limitations of this study

- A mixed methods design will provide new insights and a greater understanding into the prevalence and impact of feeding issues in previously healthy young children who survive PICU.
- Qualitative data collection methods will generate rich data progressing our understanding of this phenomenon.
- The longitudinal study design will allow us to explore the feeding survivorship journey experienced by families of children who have survived critical illness.
- The longitudinal study design may also however, have the potential for high attrition which may affect data at six months.

Introduction

Paediatric Intensive Care units (PICU) are busier, with admissions increasing by 15% over the last decade,(1, 2). Approximately 70% of the children are admitted due to emergency unplanned admissions,(2) causing a period of distress and crisis for families,(3). In developed countries, advances in medical care and technology mean that over 96% of PICU patients are discharged alive,(4). In recognition of this, the focus of critical care is changing to improving survivorship with a view to optimise physical, social, emotional, cognitive and functional outcomes for children and their families,(5).

However, up until now, there has been little focus on the impact an admission to intensive care (ICU) may have, on feeding and ability to self-feed following discharge. As is evident from adult ICU survivors, the pain and trauma of multiple oral procedures have been linked to dysphagia and other sensory feeding difficulties ,(6-10) along with difficulties in self-feeding, reduced appetite, altered taste and food preferences lasting up to three months post ICU discharge,(10, 11). Despite most PICUs in the United Kingdom (UK) incorporating early nutrition support via a nasogastric tube (NGT) within 12 – 24 hours of admission and continued for the duration of the admission,(12) the majority of children are unable to eat or drink orally throughout their PICU stay,(13). During their admission, children are exposed to multiple physical and environmental stressors, often involving up to 89 painful oral experiences, including the use of endotracheal tubes (ETT), nasogastric tube (NGT) insertion and frequent oral suctioning,(14).

Feeding is a complex process involving not only the physical aspect of oral feeding ability, but also the social aspect encompassing parental - child interactions,(15). Feeding difficulties are common among young children born prematurely or those with complex medical needs e.g. congenital heart disease (CHD). Associated risk factors include duration of intubation

with a ETT and mechanical ventilation, multiple oral interventions affecting oral motor skills, type of cardiac surgery with added risks associated with use of cardiopulmonary bypass and post-op chest open, prolonging mechanical ventilation,(16-20). The use of NGT's in young children with complex medical needs have been reported to negatively impact developmental milestone achievement with regards to establishing oral intake,(21-25). They may, as a result, cause altered oral sensory issues, difficulties in swallowing food, failure in feeding skill progression with regards to tastes and textures, and present as food refusal in some,(16, 22, 25, 26) causing parental distress around feeding and mealtimes,(27-29).

Despite a plethora of literature and research, there is no universally accepted definition of a paediatric feeding difficulty, (30) . Historically, feeding disorders have been defined in the *Diagnostic and Statistical Manual of Mental Disorders, 5th Edition*, (30)and in the *International Statistical Classification of Diseases and Related Health Problems, 10th Revision*, (30). Although these definitions incorporate nutritional complications found in some medical conditions and recognise oral feeding abilities, they fail to identify the multiple physical, non-organic and psycho-social factors,(31). Feeding difficulties as described by Kerzner and Levine, (28, 29, 32) go beyond diagnostic classifications and include food refusals; disruptive, stressful and prolonged mealtimes; lack of inappropriate self-feeding; failure to advance textures; vomiting and diarrhoea; gagging (and anticipatory gagging); and inappropriate nocturnal feeding, (29, 32). Furthermore, they recognise the importance of the impact that parental-child relationships and interactions with peers has on childhood feeding behaviours. Parental behaviours and feeding styles can directly influence perceived and actual feeding difficulties of young children,(25, 27). Parents play a pivotal role in shaping children's early feeding experiences, providing the physical foods, as well as the social interactions and model eating behaviours,(15).

The consequence an admission to PICU may impact the acquisition of normal feeding and eating skills of young children and normal parent-child relationships around mealtimes. The implications of this post-PICU-discharge for young children and their families is not known.

Methods and analysis

Study aims

The PIES study (Feeding and survivorship outcomes in previously healthy young Paediatric IntensivE Care Survivors) has six specific objectives:

1. To characterise and measure the prevalence of feeding difficulties in previously healthy children (≤ 4 years) who survive critical illness during the first 6 months after PICU discharge;
2. To identify clinical predictors for the development of feeding difficulties in previously healthy young children (≤ 4 years) who survive critical illness;
3. To identify parental/caregiver feeding styles for previously healthy young children (≤ 4 years) who survive critical illness;
4. To measure parental stress in parents/caregivers of previously healthy young children (≤ 4 years) who survive critical illness;
5. To identify behaviours of previously healthy young children (≤ 4 years) who survive critical illness;
6. To develop an in-depth understanding of how parents/caregivers of previously healthy young children (≤ 4 years old) who survive critical illness construct, experience and make sense of their survivorship journey from PICU admission, specifically looking at feeding experiences and parental-child relationships.

Study design

This multicenter longitudinal mixed method study has concurrent quantitative and qualitative components. Parents/caregivers of children will be asked to complete questionnaires considering aspects relating to; feeding difficulties, parental/caregiver stress, child and parental/caregivers feeding behaviours at the point of PICU-discharge and at 1, 3 and 6 months post-discharge. Parents/caregivers will also be invited to participate in qualitative semi-structured interviews at 3 and 6 months post-PICU-discharge which will explore parental/caregiver experiences of feeding their child post-PICU. See figure 1 for schematic overview of the study design.

Quantitative study

Data about the PICU admission of each child participant will be recorded onto an ALEA electronic Case Report Form (eCRF; https://www.aleaclinical.eu/), a secure password protected, web-based eCRF system. Data will include: length of PICU stay; length of intubation; length of mechanical invasive ventilation; number of (re) intubations; type of ETT (oral or nasal); length of non-invasive ventilation; inotrope requirement; mode of feeding during PICU admission; time from extubation to commence oral feeding; mode of feeding at PICU discharge; and evidence of gastric intolerance. Data will also be collected from each child's parent/caregiver prospectively over the first 6- months post-PICU, in a follow-up survey.

Study Measures

The outcome measures for the longitudinal follow-up survey have been selected based on their validity, reliability, use in previous paediatric populations and ease of use. Pre-existing validated questionnaires will be used to measure feeding difficulty assessment, parental stress, parental feeding styles and child behaviour. To obtain longitudinal outcome data and potentially identify acute and/or chronic feeding difficulties, data from the questionnaires will be collected

at four-time points: at PICU discharge (retrospective data), 1, 3 and 6 months after PICU discharge. The outcomes measures and time points are outlined in Table 1. The questionnaires have also been selected according to age of the child participant, in addition to tested psychometric properties.

Feeding difficulty assessment measures:

- Infant feeding questionnaire,(33) (7 items; up to 9 month old babies)
- Behavioral Pediatric Feeding Assessment Scale,(34) (35 items; 9 months old to 7 years).

Parental stress measure:

- Parental Stress Scale,(35) (18 items).

Parental feeding style measures:

- Infant feeding questionnaire,(36) (25 items; up to 2 years)
- Child feeding questionnaire,(37) (28 items; from 2 years onwards).

Child behaviour measures:

- Infant behaviour questionnaire – very short version,(38) (36 items; up to 12 months)
- Child behaviour questionnaire – very short version, (39) (35 items; from 1 year).

Table 1: Data collection measures and time points

Timepoint	Baseline (retrospective data)	1 month (after PICU discharge)	3 months (after PICU discharge)	6 months (after PICU discharge)
Enrolment:				
Eligibility screening	**X**			

(daily)				
Recruitment	**X**			
Assessments:				
Demographic information	**X**			
Routinely collected clinical PICU data	**X**			
Parental/caregivers reports of feeding history (prior to PICU admission)	**X**			
Feeding difficulty assessment measures				
Infant Feeding Questionnaire *or* Behavioral Pediatric Feeding Assessment Scale	**X**	**X**	**X**	**X**
Parental stress measure				
Parental Stress Scale	**X**	**X**	**X**	**X**
Parental feeding style measures				
Infant Feeding Questionnaire *or* Child Feeding Questionnaire	**X**	**X**	**X**	**X**
Child behaviour measures				
Infant Behavior Questionnaire (very-short version)	**X**	**X**	**X**	**X**

or Early Childhood Behavior Questionnaire				
Qualitative interviews:				
Invitation	**X**			
Interviews			**X**	**X**

Qualitative study

The main aim of the semi-structured qualitative interviews are to develop an in-depth understanding of how parents/caregivers of previously healthy young children (≤ 4 years old) who survive critical illness construct, experience and make sense of their survivorship journey from PICU admission, specifically looking at feeding experiences and parental-child behaviours. Parents will be interviewed at approximately 3 and 6 months post-PICU discharge so that they can describe how and/or if their experiences are changing (or have changed) along the PICU survivorship journey.

Sample and recruitment

Setting

Participants will be recruited from at least eight PICUs across the United Kingdom chosen to include variation in unit size, case mix, geographical location and patient demographic.

Eligibility criteria

The chosen inclusion criteria will allow recruitment of previously healthy young children (≤ 4 years) who are admitted to PICU both electively and in emergency situations. Participants will be eligible if they are parents/caregivers (aged ≥ 18 years of age) of a previously healthy

child aged ≤ 4years who has received invasive ventilation for 48 hours or more (including at referring hospital if applicable) and who are ready to be discharged from PICU. See Table 2 for full eligibility criteria.

Table 2: Eligibility criteria

Inclusion criteria	Rationale
Parents/caregivers (aged ≥ 18 years of age) of **previously healthy children** aged ≤ 4years who are ready to be discharged from PICU	Age limit required to comply with the Research Governance Framework for Health and Social Care (40)
Parents/caregivers who have sufficient language skills to read the Participant Information Sheet and to complete the questionnaires in English	Unable to translate study materials into different languages due to limited study resources
Children are included if they: • Are ≤ 4 years; • Have received invasive ventilation for 48 hours or more (including at referring hospital if applicable)	To cover children up to school age. Used as an indicator of critical illness and seen in adult ICU survivors to affect swallowing and feeding problems(8).
Exclusion criteria	**Rationale**
Aged >5 years or older	Age beyond preschool years
Children not invasively ventilated (so no ETT)	Unable to fulfil inclusion criteria
Children with previous feeding difficulties (children who were **not** fully orally fed prior to PICU admission or have document oral feeding	Unable to fulfil inclusion criteria and unable to consume sufficient nutrients orally

difficulties)	

Sample size

Quantitative study: The sample size is based on estimating prevalence to a certain level of precision as defined by a 95% confidence interval. Assuming a potentially low prevalence of just 20% (which is less than the NICU and CHD population owing to their underlying baseline disease,(16-20), a sample size of 204 child participants would be sufficient to estimate prevalence to within +/- 5.5%. Anticipating a 40% drop-out as often seen with online surveys,(41, 42), this requires an initial recruitment of 340 participants. We anticipate enrolling these 340 participants from at least eight PICUS in equal proportions (42 participants per site) over a 12-month recruitment phase. It is expected that recruitment will be higher during the winter months to account for seasonal admissions involving healthy children being admitted for bronchiolitis and other respiratory and/or septic illnesses. Recruitment centres will be encouraged to over recruit where possible.

Qualitative study: A realistic and pragmatic sample size of 15 to 20 parents/caregivers will be interviewed at 3 and 6 months after PICU discharge with the aim of increasing research knowledge in this field**.** It is not anticipated that data saturation will be achieved, as there are many different influences and variables surrounding the child's PICU admission and parent/caregivers feeding experiences and survivorship journeys.

Sampling strategy

Quantitative study: Initially, convenience sampling will be used to identify and recruit previously healthy children aged ≥ 37 weeks gestational age and ≤ 4 years who have survived an admission to PICU and their parents/caregivers. During the recruitment period, monthly progress will be monitored by the lead researcher (KM) and a proportional quota sampling

strategy will be used to recruit a sample representative to the UK PICU population in terms of age. Recruitment strategies will be employed against the population strata taken from annual UK PICU admission data,(4) (see Table 3). Both fathers and mothers will be asked to complete the parental questionnaires where possible, to increase our understanding of the experiences that fathers have after their child has survived intensive care.

Table 3: Proportional quota sampling strategy

Strata (age)	UK PICU population	Pro-rata	Quota sample
Less than 1 year	45%	153	217
1 year old	11%	37	53
2 years old	6%	20	28
3 and 4 years old	9%	30	42
Total	**70%**	**240 (70%)**	**340 (100%)**

Qualitative study: A purposeful sampling strategy will be used to interview a range of parents/caregivers based on reason for admission, age of child admitted to PICU and gender of parent (Table 4). This will ensure that not just mothers, parents/caregivers of planned surgery or parents/caregivers of babies are only interviewed for example.

Table 4: Sampling framework for interviews

Inclusion criteria	Rationale
Parents/caregivers of children enrolled into The PIES Study	To be able to compare experiences with quantitative data from the survey
Mothers and fathers	To obtain experiences of both mothers and fathers

Emergency and planned admission	To obtain experiences of parents/caregivers dealing with both planned and emergency admission as there is often psychological sequalae associated with emergency verses planned admissions to PICU (43)
Age of child: • ≤ 6 months (or pre-weaned babies) • > 6 months to 1 year • > 1 year to 2 years • > 2 years to 4 years	To obtain differing experiences of feeding during significant developmental feeding milestones for example weaning verses autonomous child self-feeding during pre-school years (44)

Study procedures

Quantitative study: Over a 12-month period, each site will screen daily the children admitted to PICU and invite all eligible children and their parents/caregivers to participate in the study. Site investigators (or their designated nominee) who are part of the PICU clinical care team will determine eligibility. Parents/caregivers could be approached to take part in the study when the child is still in PICU, near to or at discharge, on the High Dependency Unit or hospital ward soon after being discharged from PICU. Once informed consent has been obtained, parents/caregivers will be asked to complete baseline questionnaires (paper or online options available). Parent/caregiver contact details will be obtained and securely recorded on a password protected database to enable follow-up survey distribution at 1, 3 and 6 months. Follow-up survey data will be collected using either online or paper questionnaires as agreed by the parents/caregivers at recruitment. Online questionnaires will be managed through the iSurvey software (https://www.isurvey.soton.ac.uk/, University of Southampton. Two fortnightly

reminders will be sent for the follow-up surveys as reminder letters, telephone calls, messages or email by the lead researcher (KM) as agreed with the participant at recruitment. As there is such a small-time frame between 1 and 3 month assessments, if no response is received following the 1-month survey, participants will still be approached at 3 months. If there is no response at this point, they will not be approached again at 6 months.

Qualitative study: During recruitment into the multicentred survey, parents/caregivers will be invited to take part in the qualitative interviews. Those who consent to an interview will be approached by the lead researcher (KM) at the time in which reminders of the follow-up survey are sent (at 1, 3 and 6 months) either by reminder letters, telephone call, messages or email as agreed at survey enrolment. Semi-structured open-ended questions will be used as the primary method of data collection to allow the parent/caregiver to describe their story, communicate their experiences, feelings and PICU survivorship journey. In response to PPI feedback highlighting the lack of spare time that parents/caregivers of young children often face, telephone and internet (i.e. Microsoft teams: Microsoft 365, UK) interviews will be conducted at a time convenient for the parent/caregiver which could include evenings and weekends.

Data analysis

All data obtained will be analysed. In circumstances where participants are deemed lost to follow-up, any data supplied will be analysed and used where appropriate, even if it can only be used to describe the cohort at baseline. A pragmatic approach to missing data will be used, whereby data will be analysed as much as possible. Data from non-responders will be used within the analysis to observe for nonresponse bias.

Quantitative study data analysis

Descriptive statistics will be used to present the demographic data and information collected from the medical PICU admissions data. All child and parent/caregiver measures will be calculated, including means, SD, medians and IQRs for continuous variables and frequency counts and percentages for categorical data. Data will be examined for normality, outliers and for missing data. Statistical analysis will be completed using the IBM Statistical Package for Social Science (SPSS) and statistical significance will be set at $p < 0.05$.

Analyses related to the study specific objectives include the following:

Objective 1: To characterise and measure the prevalence of feeding difficulties in previously healthy children (≤ 4 years) who survive critical illness during the first 6 months after PICU discharge. From the feeding difficulty assessment measures, descriptive statistics (frequency counts and percentages) will be used to identify the numbers and types of feeding difficulties at each time point collected and for different age groups.

Objective 2: To identify clinical predictors for the development of feeding difficulties in previously healthy young children (≤ 4 years) who survive critical illness. The information from the routinely collected clinical PICU data will be used to identify any clinical predictors for the development of feeding difficulties, such as length of intubation and time to commence oral feeding. Statistical analysis will involve multiple +/- linear regressions to see if we can predict feeding difficulty questionnaire scores from the clinical variables.

Objective 3: To identify parental/caregiver feeding styles for previously healthy young children (≤ 4 years) who survive critical illness. Descriptive statistics will be initially performed to identify the frequency of participants in each parental feeding style, to identify the majority. This will then be repeated at each time point collected, to identify a change (or not) in parental feeding style across the 6 months from PICU discharge. If have enough data, differences between mother feeding styles and father feeding styles will be calculated using Mann-Whitney U (non-

parametric) or t-Test (parametric) tests as appropriate. The relationship between parental feeding style and feeding difficulty score will also be tested using the same statistical tests.

Objective 4: To measure parental stress in parents/caregivers of previously healthy young children (≤ 4 years) who survive critical illness. Using the scores from the parental stress scale, average parental stress scores for all participants will be calculated at all time points. Average parental stress score at each time point, for those parents of children with and without feeding difficulties, will also be presented to identify the trajectories of parental stress over time and between the two groups. Correlations between increasing feeding difficulty score and increasing parental stress score will be assessed using scatterplot graphs, and differences will be tested for statistical significance using Pearsons (parametric) or Spearmans (non-parametric) tests where appropriate.

Objective 5: To identify behaviours of previously healthy young children (≤ 4 years) who survive critical illness. Frequency of children in each temperament category from the Infant and Early Child Behavior questionnaires will be calculated and presented at each data collection time point, so observe for changes over time. The relationship between infant/child temperament and feeding difficulty score; and parental feeding style and parental stress score will be assessed using Mann-Whitney U (non- parametric) or t-Test (parametric) and regression models where appropriate.

Qualitative study data analysis

All interviews will be audio-recorded and transcribed verbatim. All data will be imported into a qualitative data analysis package (NVivo), which will assist in managing, sorting and coding the vast data set. Data analysis will be largely conducted by KM, with the other researchers (ASD, LVM) verifying the findings for consistencies and discrepancies to maximise credibility and reliability,(45). Data analysis will involve three stages:1) narrative analysis, 2) thematic analysis

and 3) integration and will look to answer study *objective 6: To develop an in-depth understanding of how parents/caregivers of previously healthy young children (≤ 4 years old) who survive critical illness construct, experience and make sense of their survivorship journey from PICU admission, specifically looking at feeding experiences and parental-child relationships.*

Stage 1: Narrative analysis: The first stage of analysis will involve analysing the content of the data from each participant's interview using the Clandinin and Connelly's (46) method of narrative inquiry. This framework uses three domains to structure the analysis: temporality, sociality and place,(47). The analysis focuses on the actual storylines that are told and emotions that are used to tell the story, the societal and cultural impact on the story and the influence of the place in which the experience occurs,(46). An additional consideration of the actual words and language, both verbal and nonverbal, used throughout the narrative will also be used during the analysis,(46).

Stage 2: Thematic analysis: The second stage of analysis will involve a thematic analysis approach, whereby repeated patterns across the stage 1 analysis will be identified, leading to the detection of codes and themes across the entire data set,(48). This will enable meaning and patterns to emerge from the data.

Stage 3: Data integration: The final step of the qualitative data analysis will involve integrating the narrative and thematic analysis. The individual stories will be re-told in a coherent manner and then the key themes across the entire data set will be presented. This will provide a detailed description and understanding of the survivorship journey of parents/caregivers of previously health children who survive critical illness.

Data integration strategy of quantitative and qualitative data

As a concurrent mixed methods design, the quantitative data from the survey and the qualitative data from the interviews will be analysed concurrently as they are collected and then

integrated to answer the overarching research questions and aims. The qualitative data will strengthen the survey findings by adding the human perspective, exploring behaviour, feelings and experiences of the parents/caregivers told by them,(49). The information gained from the interviews will assist interpretation and analysis of the survey results, drawing conclusions to the clinical significance of the results with implications for clinical practice,(50).

Public and patient involvement

Guided by the NIHR INVOLVE recommendations,(51), involvement of families of children recently discharged from PICU was sought during the study design process. Six parents volunteered to provide guidance and advice during an organised coffee morning. Collectively, the importance of the study was recognised, and recommendations made to the recruitment process and data collection methods. Feedback included using an online questionnaire for ease of use and to increase follow-up completion. The survey questions were also piloted by parents, assessing the clarity of the questionnaires and their instructions and to consider the burden of completing all four questionnaires. Offering home, telephone and internet interviews was also suggested for the interviews.

Ethics and Dissemination

Informed consent

Parents/caregivers will be approached to take part in The PIES study once the child meets the inclusion/exclusion criteria. After being given an ethically approved Participant Information Sheet (PIS), parents/caregivers will be given at least 48 hours to consider participation, unless they are happy to give informed consent before this time. It is anticipated that the children eligible for the study will be too young and/or too ill to participate directly in the consent process. Each parent/caregiver will complete a contact form that will record the

information needed for the follow-up survey distribution (e.g. mail addresses, telephone numbers) and informed consent will be obtained to allow the sharing of this personal data.

Researching sensitive and emotive topics

It is recognised that parents/caregivers of previously healthy young children who have survived critical illness may have psychological sequalae (i.e. post-traumatic stress disorder) following their child's admission to PICU,(43). Although not specifically asking about their PICU experience, completing the survey and taking part in the interviews may raise potentially distressing issues around difficult feeding and/or mealtime behaviours following the PICU admission. If any participant becomes distressed by recalling their experience during the interviews, the interview will be immediately stopped. The researcher (KM) will aim to debrief the situation at the time and will refer onto the relevant agencies such as Patient Advice and Liaison Services (PALS), clinical psychology team and their own or child's health team. The survey will encourage participants to inform the researcher of any problems or distress experienced during they survey completion. The researcher will be able to pinpoint sources of help through their local health care services where possible.

Burden

The survey is compiled of four separate pre-existing validated questionnaires, asked at four separate timepoints during the enrolment and follow-up (at recruitment, at 1, 3 and 6 months after PICU discharge). The questionnaires include Likert scales, yes/no answers and drop-down options. The survey questions and instructions have been piloted by parents of young children, assessing the clarity of the questionnaires, the instructions and consideration of the time and mental burden in completing all four questionnaires. Average time for survey completion was 15 minutes, with follow-up surveys thought to be quicker. We endeavour to reduce this burden by having the option of an online electronic survey available to parents and

by adding the feature where you can 'save and go back to later' option within the survey. The PIS will clearly state that there will be no financial gain from taking part in the study. Conversely, some participants might find taking part in the study beneficial because they will have the time and space to think about issues which are important to them.

Ethical review

The Yorkshire and The Humber – South Yorkshire Research Ethics Committee has reviewed the study protocol and provided favourable opinion (Ref: 20/YH/0160). The Health Research Authority has also approved the protocol (IRAS: 279171). This study has been extensively peer reviewed through the University of Southampton and forms the PhD study of the first author.

Methods of dissemination

This paper is part of the dissemination plan of the PIES study, by presenting the project background, providing a detailed description of methods and procedures used to collect and analyse the data. Other dissemination plans involve local, national and international audiences including academics, health care professionals, healthcare commissioners, charities and the public. Dissemination will include written and oral feedback to the PPI group, local PICU charity and each recruitment centre. Presentations to local and national research and clinical teams will take place, including research meetings and conferences. The findings from this study will contribute to addressing the significant gaps in the literature by investigating the prevalence of and predictors for feeding difficulties experienced by previously healthy young children who survive critical illness and explore the effect on parental feeding experiences, behaviours and stress. It is anticipated that the expected outputs of this proposed project will be in terms of high quality, peer-reviewed scientific publications and conference presentations. During the

informed consent process, parents/caregivers will be asked if they would like a lay summary of any study findings sent to them at the end of the study.

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Conflict of interest

None declared

Statement of authorship

Authors made the following contribution to the manuscript:

(1) KM formulated the original research idea, conducted the literature searching and is the chief investigator for the study,

(2) KM drafted the manuscript from the ethically approved protocol (which was originally supported by LVM and ASD)

(3) LVM, ASD and KM reviewed and revised the manuscript for important intellectual content, and (4) all authors provided final approval of the version to be submitted.

Data Statement

Technical appendix, statistical code, and dataset for The PIES study will be available from the University of Southampton Institutional Research Repository, ePrints Soton (https://eprints.soton.ac.uk/)

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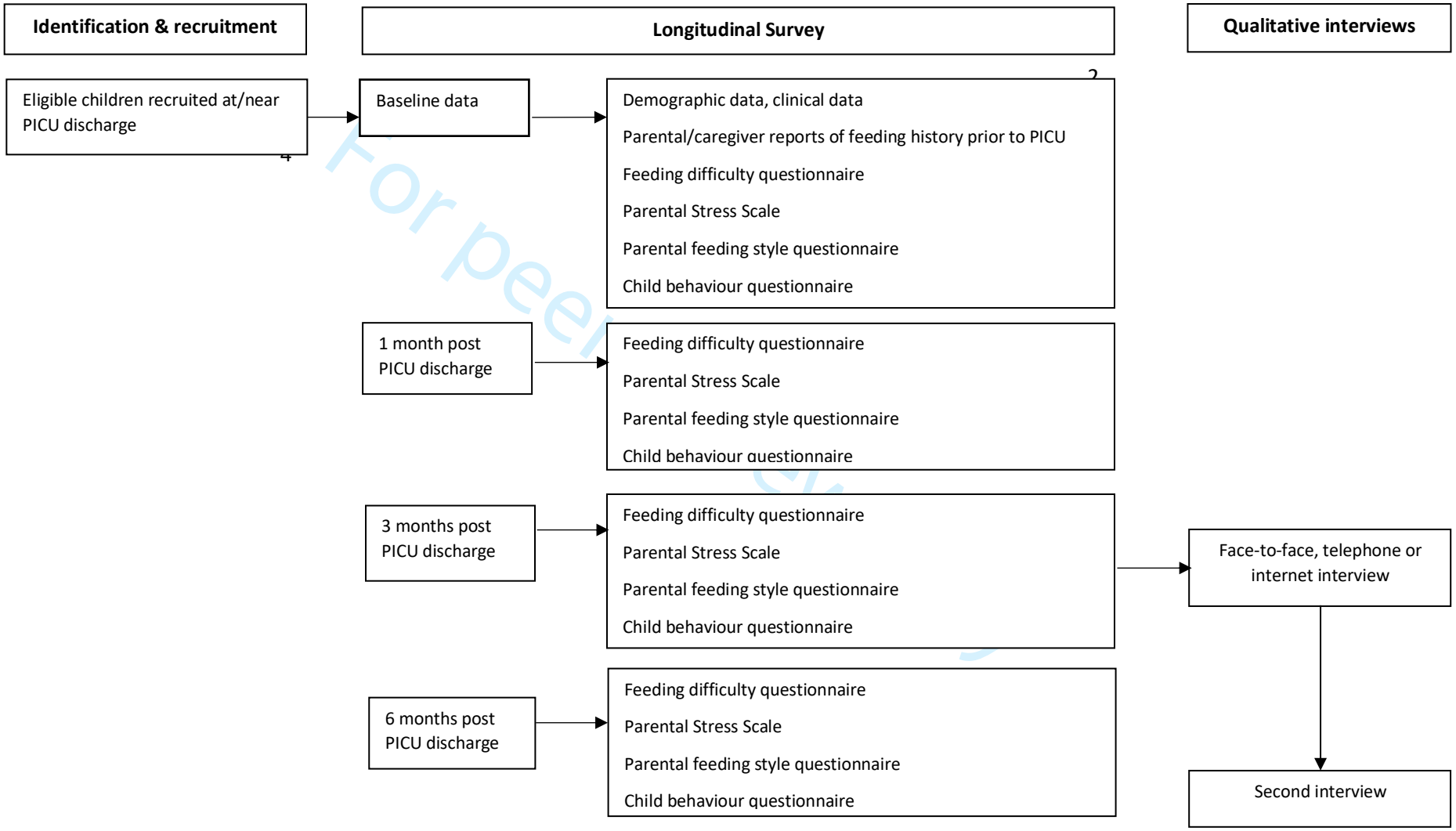
Figure 1: Overview of The PIES study design



Reporting checklist for protocol of a clinical trial.

Based on the SPIRIT guidelines.

Instructions to authors

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

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

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		Reporting Item	Page Number
Administrative information			
Title	#1	Descriptive title identifying the study design, population, interventions, and, if applicable, trial acronym	1

Trial registration	#2a	Trial identifier and registry name. If not yet registered, name of intended registry	N/A
Trial registration: data set	#2b	All items from the World Health Organization Trial Registration Data Set	NA
Protocol version	#3	Date and version identifier	3
Funding	#4	Sources and types of financial, material, and other support	27
Roles and responsibilities: contributorship	#5a	Names, affiliations, and roles of protocol contributors	1 and 25
Roles and responsibilities: sponsor contact information	#5b	Name and contact information for the trial sponsor	27
Roles and responsibilities: sponsor and funder	#5c	Role of study sponsor and funders, if any, in study design; collection, management, analysis, and interpretation of data; writing of the report; and the decision to submit the report for publication, including whether they will have ultimate authority over any of these activities	N/A
Roles and responsibilities: committees	#5d	Composition, roles, and responsibilities of the coordinating centre, steering committee, endpoint adjudication committee, data management team, and	N/A

		other individuals or groups overseeing the trial, if applicable (see Item 21a for data monitoring committee)	
Introduction			
Background and rationale	#6a	Description of research question and justification for undertaking the trial, including summary of relevant studies (published and unpublished) examining benefits and harms for each intervention	From page 4
Background and rationale: choice of comparators	#6b	Explanation for choice of comparators	N/A
Objectives	#7	Specific objectives or hypotheses	6
Trial design	#8	Description of trial design including type of trial (eg, parallel group, crossover, factorial, single group), allocation ratio, and framework (eg, superiority, equivalence, non-inferiority, exploratory)	7
Methods: Participants, interventions, and outcomes			
Study setting	#9	Description of study settings (eg, community clinic, academic hospital) and list of countries where data will be collected. Reference to where list of study sites can be obtained	7 and 10

Eligibility criteria	#10	Inclusion and exclusion criteria for participants. If applicable, eligibility criteria for study centres and individuals who will perform the interventions (eg, surgeons, psychotherapists)	11
Interventions: description	#11a	Interventions for each group with sufficient detail to allow replication, including how and when they will be administered	N/A
Interventions: modifications	#11b	Criteria for discontinuing or modifying allocated interventions for a given trial participant (eg, drug dose change in response to harms, participant request, or improving / worsening disease)	N/A
Interventions: adherance	#11c	Strategies to improve adherence to intervention protocols, and any procedures for monitoring adherence (eg, drug tablet return; laboratory tests)	N/A
Interventions: concomitant care	#11d	Relevant concomitant care and interventions that are permitted or prohibited during the trial	N/A
Outcomes	#12	Primary, secondary, and other outcomes, including the specific measurement variable (eg, systolic blood pressure), analysis metric (eg, change from baseline, final value, time to event), method of aggregation (eg, median, proportion), and time point for each outcome. Explanation of the clinical relevance of chosen efficacy and harm outcomes is strongly recommended	7

Participant timeline	#13	Time schedule of enrolment, interventions (including any run-ins and washouts), assessments, and visits for participants. A schematic diagram is highly recommended (see Figure)	8
Sample size	#14	Estimated number of participants needed to achieve study objectives and how it was determined, including clinical and statistical assumptions supporting any sample size calculations	12
Recruitment	#15	Strategies for achieving adequate participant enrolment to reach target sample size	14
Methods: Assignment of interventions (for controlled trials)			
Allocation: sequence generation	#16a	Method of generating the allocation sequence (eg, computer-generated random numbers), and list of any factors for stratification. To reduce predictability of a random sequence, details of any planned restriction (eg, blocking) should be provided in a separate document that is unavailable to those who enrol participants or assign interventions	N/A
Allocation concealment mechanism	#16b	Mechanism of implementing the allocation sequence (eg, central telephone; sequentially numbered, opaque,	N/A

		sealed envelopes), describing any steps to conceal the sequence until interventions are assigned	
Allocation: implementation	#16c	Who will generate the allocation sequence, who will enrol participants, and who will assign participants to interventions	N/A
Blinding (masking)	#17a	Who will be blinded after assignment to interventions (eg, trial participants, care providers, outcome assessors, data analysts), and how	N/A
Blinding (masking): emergency unblinding	#17b	If blinded, circumstances under which unblinding is permissible, and procedure for revealing a participant's allocated intervention during the trial	N/A
Methods: Data collection, management, and analysis			
Data collection plan	#18a	Plans for assessment and collection of outcome, baseline, and other trial data, including any related processes to promote data quality (eg, duplicate measurements, training of assessors) and a description of study instruments (eg, questionnaires, laboratory tests) along with their reliability and validity, if known. Reference to where data collection forms can be found, if not in the protocol	15

Data collection plan: retention	#18b	Plans to promote participant retention and complete follow-up, including list of any outcome data to be collected for participants who discontinue or deviate from intervention protocols	15
Data management	#19	Plans for data entry, coding, security, and storage, including any related processes to promote data quality (eg, double data entry; range checks for data values). Reference to where details of data management procedures can be found, if not in the protocol	N/A
Statistics: outcomes	#20a	Statistical methods for analysing primary and secondary outcomes. Reference to where other details of the statistical analysis plan can be found, if not in the protocol	15 onwards
Statistics: additional analyses	#20b	Methods for any additional analyses (eg, subgroup and adjusted analyses)	15 onwards
Statistics: analysis population and missing data	#20c	Definition of analysis population relating to protocol non-adherence (eg, as randomised analysis), and any statistical methods to handle missing data (eg, multiple imputation)	15
Methods: Monitoring			
Data monitoring: formal committee	#21a	Composition of data monitoring committee (DMC); summary of its role and reporting structure; statement of whether it is independent from the sponsor and	N/A

		competing interests; and reference to where further details about its charter can be found, if not in the protocol. Alternatively, an explanation of why a DMC is not needed	
Data monitoring: interim analysis	#21b	Description of any interim analyses and stopping guidelines, including who will have access to these interim results and make the final decision to terminate the trial	N/A
Harms	#22	Plans for collecting, assessing, reporting, and managing solicited and spontaneously reported adverse events and other unintended effects of trial interventions or trial conduct	No
Auditing	#23	Frequency and procedures for auditing trial conduct, if any, and whether the process will be independent from investigators and the sponsor	No
Ethics and dissemination			
Research ethics approval	#24	Plans for seeking research ethics committee / institutional review board (REC / IRB) approval	21
Protocol amendments	#25	Plans for communicating important protocol modifications (eg, changes to eligibility criteria, outcomes, analyses) to relevant parties (eg, investigators, REC / IRBs, trial participants, trial registries, journals, regulators)	21

Consent or assent	#26a	Who will obtain informed consent or assent from potential trial participants or authorised surrogates, and how (see Item 32)	14 and 19
Consent or assent: ancillary studies	#26b	Additional consent provisions for collection and use of participant data and biological specimens in ancillary studies, if applicable	N/A
Confidentiality	#27	How personal information about potential and enrolled participants will be collected, shared, and maintained in order to protect confidentiality before, during, and after the trial	14/15
Declaration of interests	#28	Financial and other competing interests for principal investigators for the overall trial and each study site	N/A
Data access	#29	Statement of who will have access to the final trial dataset, and disclosure of contractual agreements that limit such access for investigators	26
Ancillary and post trial care	#30	Provisions, if any, for ancillary and post-trial care, and for compensation to those who suffer harm from trial participation	N/A
Dissemination policy: trial results	#31a	Plans for investigators and sponsor to communicate trial results to participants, healthcare professionals, the public, and other relevant groups (eg, via publication, reporting in results databases, or other data sharing arrangements), including any publication restrictions	21

Dissemination policy: authorship	#31b	Authorship eligibility guidelines and any intended use of professional writers	N/A
Dissemination policy: reproducible research	#31c	Plans, if any, for granting public access to the full protocol, participant-level dataset, and statistical code	N/A
Appendices			
Informed consent materials	#32	Model consent form and other related documentation given to participants and authorised surrogates	No
Biological specimens	#33	Plans for collection, laboratory evaluation, and storage of biological specimens for genetic or molecular analysis in the current trial and for future use in ancillary studies, if applicable	N/A

BMJ Open

Protocol for a multicentre longitudinal mixed methods study: Feeding and survivorship outcomes in previously healthy young Paediatric IntensivE Care Survivors – The PIES study

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Title: Protocol for a multicentre longitudinal mixed methods study: Feeding and survivorship outcomes in previously healthy young Paediatric IntensivE Care Survivors – The PIES study

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Keywords: feeding difficulties, children, critical illness, survivors

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Abstract

Introduction

An admission to Paediatric Intensive Care (PICU) is associated with multiple physical and environmental stressors, often involving many negative and painful oral experiences. Evidence from children with complex medical conditions suggest that feeding difficulties post-PICU stay are common, causing significant parental anxiety. Adult intensive care (ICU) survivor studies suggest feeding issues lasting up to 3 months post discharge from ICU. There is, however, a paucity of evidence regarding feeding outcomes for previously healthy children following a PICU admission and whether painful oral experiences during an admission contribute to feeding difficulties post-discharge, negatively impacting on parental/caregiver anxiety.

Methods and analysis

This longitudinal mixed method study will explore the impact of feeding difficulties, identifying any clinical risk factors during the first 6 months of PICU-discharge in previously healthy young children (≤ 4 years). Parents/caregivers of children will be asked to complete questionnaires relating to; feeding difficulties, parental/caregiver stress, child and parental/caregivers feeding behaviours, at the point of PICU-discharge, 1, 3 and 6 months post-discharge. Parents/caregivers will be invited to participate in qualitative semi-structured interviews at 3 and 6 months post-PICU-discharge exploring parental/caregiver experiences of feeding their child after PICU. Statistical analysis of the survey data will consist of descriptive and inferential statistics, plus qualitative analysis of any free text comments using thematic analysis.

Ethics and dissemination

This study will provide an insight and increase our understanding of the prevalence of feeding difficulties in previously healthy children admitted to PICU and parental/caregiver

experiences. Multiple methods will be used to ensure that the findings are effectively disseminated to service users, clinicians, policy and academic audiences. The study has full ethical approval from the National Health Service Research Ethics Committee (Ref: 20/YH/0160) and full governance clearance.

Article summary

Strengths:

- A strength of this study is that it is the first multicentre, longitudinal study to investigate feeding and survivorship outcomes in young paediatric intensive care (PICU) survivors, in the first 6-months post-discharge.
- By using a mixed methods design, this study will provide a greater breadth of understanding into the prevalence and impact of feeding issues in previously healthy young children who survive PICU.
- A strength of this study's qualitative data collection method (interviews with parents/caregivers) lies in its ability to generate a rich narrative data set exploring the survivorship journey of families post-PICU.
- The longitudinal study design will allow us to explore any feeding difficulties over a 6-month period post-PICU, potentially identifying transient and persistent problems.

Limitations:

- A limitation to the study's longitudinal design lies in its potential for high attrition which may affect data at six months, challenging the internal validity of the reported results.

Introduction

Paediatric intensive care unit (PICU) admissions have increased by 15% over the last decade,(1, 2). Approximately 70% are admitted due to emergency unplanned admissions,(2) causing a period of distress and crisis for families,(3). In developed countries, advances in medical care and technology mean that over 96% of PICU patients are discharged alive,(4) although morbidity amongst childhood survivors is high ,(5). As a result, the focus of critical care has moved to improving survivorship, aiming to optimise physical, social, emotional, cognitive and functional outcomes for children and their families,(6).

Until now, there has been little focus on the impact an admission to PICU may have on oral feeding ability in survivors of critical illness. During an admission to PICU, children are exposed to multiple physical and environmental stressors, involving up to 89 painful oral experiences, including the use of endotracheal tubes (ETT), extubations and re-intubations, nasogastric tube (NGT) insertion and frequent oral suctioning,(7). These traumatic and often painful oral experiences have been linked to swallowing and eating difficulties in adult survivors of intensive care ,(8-12) with difficulties in self-feeding, reduced appetite, altered taste and food preferences lasting up to three months post ICU discharge,(12, 13).

Despite most PICUs in the United Kingdom (UK) incorporating early nutritional support within 24 hours of admission (14, 15), it is usual for children not to eat or drink orally during their intensive care admission,(16). Nasogastric tube feeding is routinely used during critical illness as a primary method of delivering nutrition support (16), resulting in young children missing out on normal oral feeding experiences,(17, 18). The impact of prolonged NGT feeding is well described, with evidence indicating that children under 1-year-of age can take up to 2 years to establish oral feeding if they are NGT fed for significant periods of time,(19, 20).

Feeding is a complex learned behaviour, occurring during infancy involving developmental maturation to coordinate the process of sucking, swallowing and breathing. This then advances into chewing and texture control, (21).There is also a social aspect of feeding, involving parental - child interactions,(22) with parental behaviours and feeding styles directly influencing feeding behaviours of young children,(20, 23). Parental feeding styles have been shown to influence food enjoyment, fussiness, food responsiveness, food neophobia, and self-regulation in children,(22). Parental feeding interactions and practices during childhood cancer treatment, for example, include pressurising children to eat, using food as rewards and bribes and being overindulgent, with the stress of eating having a negative effect on the parental-child relationship (3, 24). There is, however, no evidence looking at feeding difficulties and parental-child feeding interactions associated with feeding in the previously healthy PICU population (25). Although there is some information describing feeding outcomes in children born prematurely and young children with CHD, there remains a lack of high-quality evidence. The consequence of an admission to PICU on the ability of young children to eat and drink initially after PICU discharge and then once home, and the implications this has for young children and their families, is not known.

Methods and analysis

Study aims

The PIES study (Feeding and survivorship outcomes in previously healthy young Paediatric IntensivE Care Survivors) has six specific objectives:

1. To characterise and measure the prevalence of feeding difficulties in previously healthy children (≤ 4 years) who survive critical illness during the first 6 months after PICU discharge;

2. To identify clinical predictors for the development of feeding difficulties in previously healthy young children (≤ 4 years) who survive critical illness;
3. To identify parental/caregiver feeding styles for previously healthy young children (≤ 4 years) who survive critical illness;
4. To measure parental stress in parents/caregivers of previously healthy young children (≤ 4 years) who survive critical illness;
5. To identify behaviours of previously healthy young children (≤ 4 years) who survive critical illness;
6. To develop an in-depth understanding of how parents/caregivers of previously healthy young children (≤ 4 years old) who survive critical illness construct, experience and make sense of their survivorship journey from PICU admission, specifically looking at feeding experiences and parental-child relationships.

Study design

Based on the research question and objectives, a prospective, longitudinal mixed methods design will be used. Quantitative and qualitative data will be collected simultaneously over several times points, analysed separately and then integrated giving equal emphasis to each strand,(26). Parents/caregivers of children will be asked to take part in a longitudinal survey, completing questionnaires considering aspects relating to; feeding difficulties, parental/caregiver stress, child and parental/caregivers feeding behaviours at the point of PICU-discharge and at 1, 3 and 6 months post-discharge. Parents/caregivers will also be invited to participate in qualitative semi-structured interviews at 3 and 6 months post-PICU-discharge, which will explore parental/caregiver experiences of feeding their child post-PICU. Routinely collected clinical data about the PICU admission will additionally be collected. See figure 1 for schematic overview of the study design.

Setting

Participants will be recruited from up to ten PICUs across the United Kingdom chosen to include variation in unit size, case mix, geographical location and patient demographic.

Sample and recruitment

Eligibility criteria

The chosen inclusion criteria will allow recruitment of previously healthy young children (≤ 4 years) who are admitted to PICU both electively and in emergency situations. Participants will be eligible if they are parents/caregivers (aged ≥ 18 years of age) of a previously healthy child aged ≤ 4years who has received invasive ventilation for 48 hours or more (including at referring hospital if applicable) (Table 1).

Table 1: Eligibility criteria

Inclusion criteria	Rationale
Parents/caregivers (aged ≥ 18 years of age) of **previously healthy children** aged ≤ 4years who are ready to be discharged from PICU	Age limit required to comply with the Research Governance Framework for Health and Social Care (27)
Parents/caregivers who have sufficient language skills to read the Participant Information Sheet and to complete the questionnaires in English	Unable to translate study materials into different languages due to limited study resources
Children are included if they: • Are ≤ 4 years;	To cover children up to school age. Used as an indicator of critical illness and seen in adult ICU survivors to affect swallowing and feeding problems(10).

• Have received invasive ventilation for 48 hours or more (including at referring hospital if applicable)	
Exclusion criteria	**Rationale**
Aged >5 years or older	Age beyond preschool years
Children not invasively ventilated (so no ETT)	Unable to fulfil inclusion criteria
Children with previous feeding difficulties (children who were **not** fully orally fed prior to PICU admission or have document oral feeding difficulties)	Unable to fulfil inclusion criteria and unable to consume sufficient nutrients orally

A limit of ≤ 4 year of age has been set because the majority of children admitted to PICU are under school age, with children under 5 years of age spending the most number of days in PICU,(4). Furthermore, the skills and behaviours learnt in the first few years of life are seen as imperative for future eating skills, attitudes and behaviours needed for future adult health,(28). Additionally, by studying this age range, any feeding difficulties that may occur during critical time-sensitive developmental feeding milestone windows, may also be identified,(29). These include:

- The initial feeding skill that is required to successfully breast or bottle feed at birth;
- To identify feeding difficulties that might occur during the weaning to complementary food stage (4 to 6 months of age), for example involving problems with textures, tastes, and chewing;

- To identify feeding difficulties that might occur during the transition to autonomous child self-feeding during pre-school years;
- To identify extreme cases of behaviour often associated with picky or fussy behaviour in preschool aged children.
- Once children start school (> 4 years of age), parents often have less control over lunchtime behaviours and food intake, (30).

The exclusion of non-English speaking families is a limitation of the study design in terms of selection bias and may affect the generalisability of the results. This will be investigated in the interpretations of the study results and implications for clinical practice.

Sample size

Quantitative study: The sample size is based on estimating prevalence to a certain level of precision as defined by a 95% confidence interval. Assuming a potentially low prevalence of just 20% (which is less than the NICU and CHD population owing to their underlying baseline disease,(31-35)), a sample size of 204 child participants would be sufficient to estimate feeding difficulty prevalence. Anticipating a 40% drop-out, as often seen with online surveys,(36, 37), an initial recruitment of 340 participants is required. We anticipate enrolling those participants from 10 PICUs over a 12-month period. It is expected that recruitment numbers will vary across the sites and across the recruitment period, accounting for seasonal admissions involving healthy children being admitted for bronchiolitis and other respiratory and/or septic illness in the winter months. Recruitment targets will be discussed at each site set up, with the allowance of over-recruiting in larger sites where possible.

Qualitative study: A realistic and pragmatic sample size of 15 to 20 parents/caregivers will be interviewed at 3 and 6 months after PICU discharge, with the aim of increasing research knowledge in this unknown field. We recognise that we may not achieve data saturation with

this sample size, as there are many different influences and variables surrounding the child's PICU admission, parent/caregivers feeding experiences and survivorship journeys. However, this limitation will be acknowledged, investigated and discussed in the data analysis and future reporting of any study results, including the impact this may have on the study's credibility and generalisability.

Sampling strategy

Quantitative study: Initially, convenience sampling will be used to identify and recruit previously healthy children aged ≥ 37 weeks gestational age and ≤ 4 years who have survived an admission to PICU and their parents/caregivers. During the recruitment period, monthly progress will be monitored by the lead researcher (KM) and a proportional quota sampling strategy will be used to recruit a sample representative to the UK PICU population in terms of age. Recruitment strategies will be employed against the population strata taken from annual UK PICU admission data,(4) (Table 2). To increase our understanding of the experiences that both fathers and mothers have after their child has survived intensive care, we are encouraging both fathers and mothers to complete the parental questionnaires where possible.

Table 2: Proportional quota sampling strategy

Strata (age)	UK PICU population	Pro-rata	Quota sample
Less than 1 year	45%	153	217
1 year old	11%	37	53
2 years old	6%	20	28
3 and 4 years old	9%	30	42
Total	**70%**	**240 (70%)**	**340 (100%)**

Qualitative study: A purposeful sampling strategy will be used to interview a range of parents/caregivers based on reason for admission, age of child admitted to PICU and gender of parent (Table 3). This will ensure that not just mothers, or parents/caregivers of planned surgery or parents/caregivers of babies are only interviewed, for example.

Table 3: Sampling framework for interviews

Inclusion criteria	Rationale
Parents/caregivers of children enrolled into The PIES Study	To be able to compare experiences with quantitative data from the survey
Mothers and fathers	To obtain experiences of both mothers and fathers
Emergency and planned admission	To obtain experiences of parents/caregivers dealing with both planned and emergency admission as there is often psychological sequalae associated with emergency verses planned admissions to PICU (38)
Age of child: • ≤ 6 months (or pre-weaned babies) • > 6 months to 1 year • > 1 year to 2 years • > 2 years to 4 years	To obtain differing experiences of feeding during significant developmental feeding milestones for example weaning verses autonomous child self-feeding during pre-school years (39)

Study Measures

Longitudinal follow-up survey

The outcome measures for the longitudinal follow-up survey have been selected based on their validity, reliability, use in previous paediatric populations and ease of use for participants. Pre-existing validated questionnaires will be used to measure feeding difficulty assessment, parental stress, parental feeding styles and child behaviour. To obtain longitudinal outcome data and potentially identify acute and/or chronic feeding difficulties, data from the questionnaires will be collected at four-time points: at PICU discharge (retrospective data), 1, 3 and 6 months after PICU discharge. The outcomes measures and time points are outlined in Table 4. The questionnaires have also been selected according to age of the child participant, in addition to tested psychometric properties.

Feeding difficulty assessment measures:

- Infant feeding questionnaire,(40) (7 items; up to 9 month old babies)
- Behavioral Pediatric Feeding Assessment Scale,(41) (35 items; 9 months old to 7 years).

Parental stress measure:

- Parental Stress Scale,(42) (18 items).

Parental feeding style measures:

- Infant feeding questionnaire,(43) (25 items; up to 2 years)
- Child feeding questionnaire,(44) (28 items; from 2 years onwards).

Child behaviour measures

- Infant behaviour questionnaire – very short version,(45) (36 items; up to 12 months)
- Child behaviour questionnaire – very short version, (46) (35 items; from 1 year)

Demographic Information:

At each survey, parental factors, family variables and socio-economic data will be collected to identify any relationship between family background and the development of feeding difficulties for young survivors of critical illness. This includes parental/caregiver:

- Ethnic origin
- Age
- Gender
- Highest level of education
- Living situation
- Employment status
- Siblings in household.

Routinely collected clinical PICU data:

For all recruited patients, data already recorded during the child's PICU admission will be captured on a paper or electronic Case Report Form completed by the RC research nurse, a clinical team member delegated by the local PI or by the Chief Investigator at a later date. The variables of interest have been identified as:

- Length of PICU stay (in hours)
- Length of intubation (in hours)
- Length of mechanical invasive ventilation (in hours)
- Number of (re) intubations
- Type of ETT (oral or nasal)

- Length of non-invasive ventilation (in hours and mode)
- Inotrope requirement (yes/no)
- Mode of feeding during PICU admission (enteral, bolus or continuous, parental nutrition, oral diet, location of feeding tube)
- Time from extubation to commence oral feeding (in hours)
- Mode of feeding at PICU discharge
- Documented evidence of gastric intolerance (vomiting, diarrhea, abdominal distention).

Table 4: Data collection measures and time points

Timepoint	Baseline (retrospective data)	1 month (after PICU discharge)	3 months (after PICU discharge)	6 months (after PICU discharge)
Enrolment:				
Eligibility screening (daily)	**X**			
Recruitment	**X**			
Assessments:				
Demographic information	**X**			
Routinely collected clinical PICU data	**X**			
Parental/caregivers reports of feeding history (prior to PICU admission)	**X**			

Feeding difficulty assessment measures				
Infant Feeding Questionnaire *or* Behavioral Pediatric Feeding Assessment Scale	**X**	**X**	**X**	**X**
Parental stress measure				
Parental Stress Scale	**X**	**X**	**X**	**X**
Parental feeding style measures				
Infant Feeding Questionnaire *or* Child Feeding Questionnaire	**X**	**X**	**X**	**X**
Child behaviour measures				
Infant Behavior Questionnaire (very-short version) *or* Early Childhood Behavior Questionnaire	**X**	**X**	**X**	**X**
Qualitative interviews:				
Invitation	**X**			
Interviews			**X**	**X**

Qualitative study

The main aim of the semi-structured qualitative interviews are to develop an in-depth understanding of how parents/caregivers of previously healthy young children (≤ 4 years old) who survive critical illness construct, experience and make sense of their survivorship journey from PICU admission, specifically looking at feeding experiences and parental-child behaviours. Parents will be interviewed at approximately 3 and 6 months post-PICU discharge so that they can describe how and/or if their experiences are changing (or have changed) along the PICU survivorship journey.

Study procedures

Quantitative study: Over a 12-month period, each site will screen all children admitted to PICU and invite all eligible children and their parents/caregivers to participate in the study. Site investigators (or their designated nominee) who are part of the PICU clinical care team will determine eligibility. Parents/caregivers could be approached to take part in the study when the child is still in PICU, near to or at discharge, on the High Dependency Unit or hospital ward soon after being discharged from PICU. Once informed consent has been obtained, parents/caregivers will be asked to complete baseline questionnaires (paper or online options available). Parent/caregiver contact details will be obtained and securely recorded on a password protected database to enable follow-up survey distribution at 1, 3 and 6 months. Follow-up survey data will be collected using either online or paper questionnaires as agreed by the parents/caregivers at recruitment. Two fortnightly reminders will be sent for the follow-up surveys as reminder letters, telephone calls, messages or email by the lead researcher (KM) as agreed with the participant at recruitment. As there is such a small-time frame between 1 and 3 month assessments, if no response is received following the 1-month survey, participants will

still be approached at 3 months. If there is no response at this point however, they will not be approached again at 6 months.

Qualitative study: During recruitment into the multicentred survey, parents/caregivers will be invited to take part in the qualitative interviews. Those who consent to an interview will be approached by the lead researcher (KM) at the time in which reminders of the follow-up survey are sent (at 1, 3 and 6 months) either by reminder letters, telephone call, messages or email as agreed at recruitment. Semi-structured open-ended questions will be used as the primary method of data collection to allow the parent/caregiver to describe their story, communicate their experiences, feelings and PICU survivorship journey. In response to PPI feedback highlighting the lack of spare time that parents/caregivers of young children often face, telephone and internet (i.e. Microsoft teams: Microsoft 365, UK) interviews will be conducted at a time convenient for the parent/caregiver which could include evenings and weekends.

Data analysis

All data obtained will be analysed. In circumstances where participants are deemed lost to follow-up, any data supplied will be analysed and used where appropriate, even if it can only be used to describe the cohort at baseline. A pragmatic approach to missing data will be used, whereby data will be analysed as much as possible. Data from non-responders will be used within the analysis to observe for nonresponse bias.

Quantitative study data analysis

Descriptive statistics will be used to present the demographic data information taken from the routinely collected clinical PICU data. All child and parent/caregiver outcome measures will be calculated, including means, SD, medians and IQRs for continuous variables and

frequency counts and percentages for categorical data. Data will be examined for normality, outliers and for missing data. Statistical analysis will be completed using the IBM Statistical Package for Social Science (SPSS) and statistical significance will be set at $p < 0.05$.

Analyses related to the study specific objectives include the following:

Objective 1: To characterise and measure the prevalence of feeding difficulties in previously healthy children (≤ 4 years) who survive critical illness during the first 6 months after PICU discharge. From the feeding difficulty assessment measures, descriptive statistics (frequency counts and percentages) will be used to identify the numbers and types of feeding difficulties at each time point collected and for different age groups.

Objective 2: To identify clinical predictors for the development of feeding difficulties in previously healthy young children (≤ 4 years) who survive critical illness. The information from the routinely collected clinical PICU data will be used to identify any clinical predictors for the development of feeding difficulties, such as length of intubation and time to commence oral feeding. Statistical analysis will involve multiple +/- linear regressions to see if we can predict feeding difficulty questionnaire scores from the clinical variables.

Objective 3: To identify parental/caregiver feeding styles for previously healthy young children (≤ 4 years) who survive critical illness. Descriptive statistics will be initially performed to identify the frequency of participants in each parental feeding style, to identify the majority. This will then be repeated at each time point collected, to identify a change (or not) in parental feeding style across the 6 months from PICU discharge. If have enough data, differences between mother feeding styles and father feeding styles will be calculated using Mann-Whitney U (non- parametric) or t-Test (parametric) tests as appropriate. The relationship between parental feeding style and feeding difficulty score will also be tested using the same statistical tests.

Objective 4: To measure parental stress in parents/caregivers of previously healthy young children (≤ 4 years) who survive critical illness. Using the scores from the parental stress scale, average parental stress scores for all participants will be calculated at all time points. Average parental stress score at each time point, for those parents of children with and without feeding difficulties, will also be presented to identify the trajectories of parental stress over time and between the two groups. Correlation and regression analysis will be used to investigate relationships between increasing feeding difficulty score and increasing parental stress score

Objective 5: To identify behaviours of previously healthy young children (≤ 4 years) who survive critical illness. Frequency of children in each temperament category from the Infant and Early Child Behavior questionnaires will be calculated and presented at each data collection time point, so observe for changes over time. The relationship between infant/child temperament and feeding difficulty score; and parental feeding style and parental stress score will be assessed using Mann-Whitney U (non- parametric) or t-Test (parametric) and regression models where appropriate.

Qualitative study data analysis

All interviews will be audio-recorded and transcribed verbatim. All data will be imported into a qualitative data analysis package (NVivo), which will assist in managing, sorting and coding the vast data set. Data analysis will be largely conducted by KM, with the other researchers (ASD, LVM) verifying the findings for consistencies and discrepancies to maximise credibility and reliability,(47). Data analysis will involve three stages:1) narrative analysis, 2) thematic analysis and 3) integration and will look to answer study *objective 6: To develop an in-depth understanding of how parents/caregivers of previously healthy young children (≤ 4 years old) who survive critical illness construct, experience and make sense of their survivorship journey from PICU admission, specifically looking at feeding experiences and parental-child relationships.*

Stage 1: Narrative analysis: The first stage of analysis will involve analysing the content of the data from each participant's interview using the Clandinin and Connelly's (48) method of narrative inquiry. This framework uses three domains to structure the analysis: temporality, sociality and place,(49). The analysis focuses on the actual storylines that are told and emotions that are used to tell the story, the societal and cultural impact on the story and the influence of the place in which the experience occurs,(48). An additional consideration of the actual words and language, both verbal and nonverbal, used throughout the narrative will also be used during the analysis,(48).

Stage 2: Thematic analysis: The second stage of analysis will involve a thematic analysis approach, whereby repeated patterns across the stage 1 analysis will be identified, leading to the detection of codes and themes across the entire data set,(50). This will enable meaning and patterns to emerge from the data.

Stage 3: Data integration: The final step of the qualitative data analysis will involve integrating the narrative and thematic analysis. The individual stories will be re-told in a coherent manner and then the key themes across the entire data set will be presented. This will provide a detailed description and understanding of the survivorship journey of parents/caregivers of previously health children who survive critical illness.

Data integration strategy of quantitative and qualitative data

The quantitative data from the survey and the qualitative data from the interviews will be analysed concurrently as they are collected and then integrated to answer the overarching research questions and aims. The qualitative data will strengthen the survey findings by adding the human perspective, exploring behaviour, feelings and experiences of the parents/caregivers

told by them,(51). The information gained from the interviews will assist interpretation and analysis of the survey results, drawing conclusions to the clinical significance of the results with implications for clinical practice,(52).

Public and patient involvement

Guided by the NIHR INVOLVE recommendations,(53), involvement of families of children recently discharged from PICU was sought during the study design process. Six parents volunteered to provide guidance and advice during an organised coffee morning. Collectively, the importance of the study was recognised, and recommendations made to the recruitment process and data collection methods. Feedback included using an online questionnaire for ease of use and to increase follow-up completion. The survey questions were also piloted by parents, assessing the clarity of the questionnaires and their instructions and to consider the burden of completing all four questionnaires. Offering home, telephone and internet interviews was also suggested for the interviews.

Ethics and Dissemination

Informed consent

Parents/caregivers will be approached to take part in The PIES study once the child meets the inclusion/exclusion criteria. After being given an ethically approved Participant Information Sheet (PIS), parents/caregivers will be given at least 48 hours to consider participation, unless they are happy to give informed consent before this time. It is anticipated that the children eligible for the study will be too young and/or too ill to participate directly in the consent process. Each parent/caregiver will complete a contact form that will record the

information needed for the follow-up survey distribution (e.g. mail addresses, telephone numbers) and informed consent will be obtained to allow the sharing of this personal data.

Researching sensitive and emotive topics

It is recognised that parents/caregivers of previously healthy young children who have survived critical illness may have psychological sequalae (i.e. post-traumatic stress disorder) following their child's admission to PICU,(38). Although not specifically asking about their PICU experience, completing the survey and taking part in the interviews may raise potentially distressing issues around difficult feeding and/or mealtime behaviours following the PICU admission. Initial instances of distress will be dealt by the researcher and supported by the PICU psychology team at the researchers host institution. The researcher will also signpost the participants to the Patient Advice and Liaison Services (PALS), clinical psychology team based at Southampton Children's Hospital and other local healthcare teams.

Burden

The survey is compiled of four separate pre-existing validated questionnaires, asked at four separate timepoints during the enrolment and follow-up (at recruitment, at 1, 3 and 6 months after PICU discharge). The questionnaires include Likert scales, yes/no answers and drop-down options. The survey questions and instructions have been piloted by parents of young children, assessing the clarity of the questionnaires, the instructions and consideration of the time and mental burden in completing all four questionnaires. Average time for survey completion was 15 minutes, with follow-up surveys thought to be quicker. We endeavour to reduce this burden by having the option of an online electronic survey available to parents and by adding the feature where you can 'save and go back to later' option within the survey. The PIS will clearly state that there will be no financial gain from taking part in the study. Conversely,

some participants might find taking part in the study beneficial because they will have the time and space to think about issues which are important to them.

Ethical review

The Yorkshire and The Humber – South Yorkshire Research Ethics Committee has reviewed the study protocol and provided favourable opinion (Ref: 20/YH/0160). The Health Research Authority has also approved the protocol (IRAS: 279171). This study has been extensively peer reviewed through the University of Southampton and forms the PhD study of the first author.

Methods of dissemination

This paper is part of the dissemination plan of the PIES study, by presenting the project background, providing a detailed description of methods and procedures used to collect and analyse the data. Other dissemination plans involve local, national and international audiences including academics, health care professionals, healthcare commissioners, charities and the public. Dissemination will include written and oral feedback to the PPI group, local PICU charity and each recruitment centre. Presentations to local and national research and clinical teams will take place, including research meetings and conferences. The findings from this study will contribute to addressing the significant gaps in the literature by investigating the prevalence of and predictors for feeding difficulties experienced by previously healthy young children who survive critical illness and explore the effect on parental feeding experiences, behaviours and stress. It is anticipated that the expected outputs of this proposed project will be in terms of high quality, peer-reviewed scientific publications and conference presentations. During the informed consent process, parents/caregivers will be asked if they would like a lay summary of any study findings sent to them at the end of the study.

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Conflict of interest

None declared

Statement of authorship

Authors made the following contribution to the manuscript:

(1) KM formulated the original research idea, conducted the literature searching and is the chief investigator for the study,

(2) KM drafted the manuscript from the ethically approved protocol (which was originally supported by LVM and ASD)

(3) LVM, ASD and KM reviewed and revised the manuscript for important intellectual content, and (4) all authors provided final approval of the version to be submitted.

Data Statement

Technical appendix, statistical code, and dataset for The PIES study will be available from the University of Southampton Institutional Research Repository, ePrints Soton (https://eprints.soton.ac.uk/)

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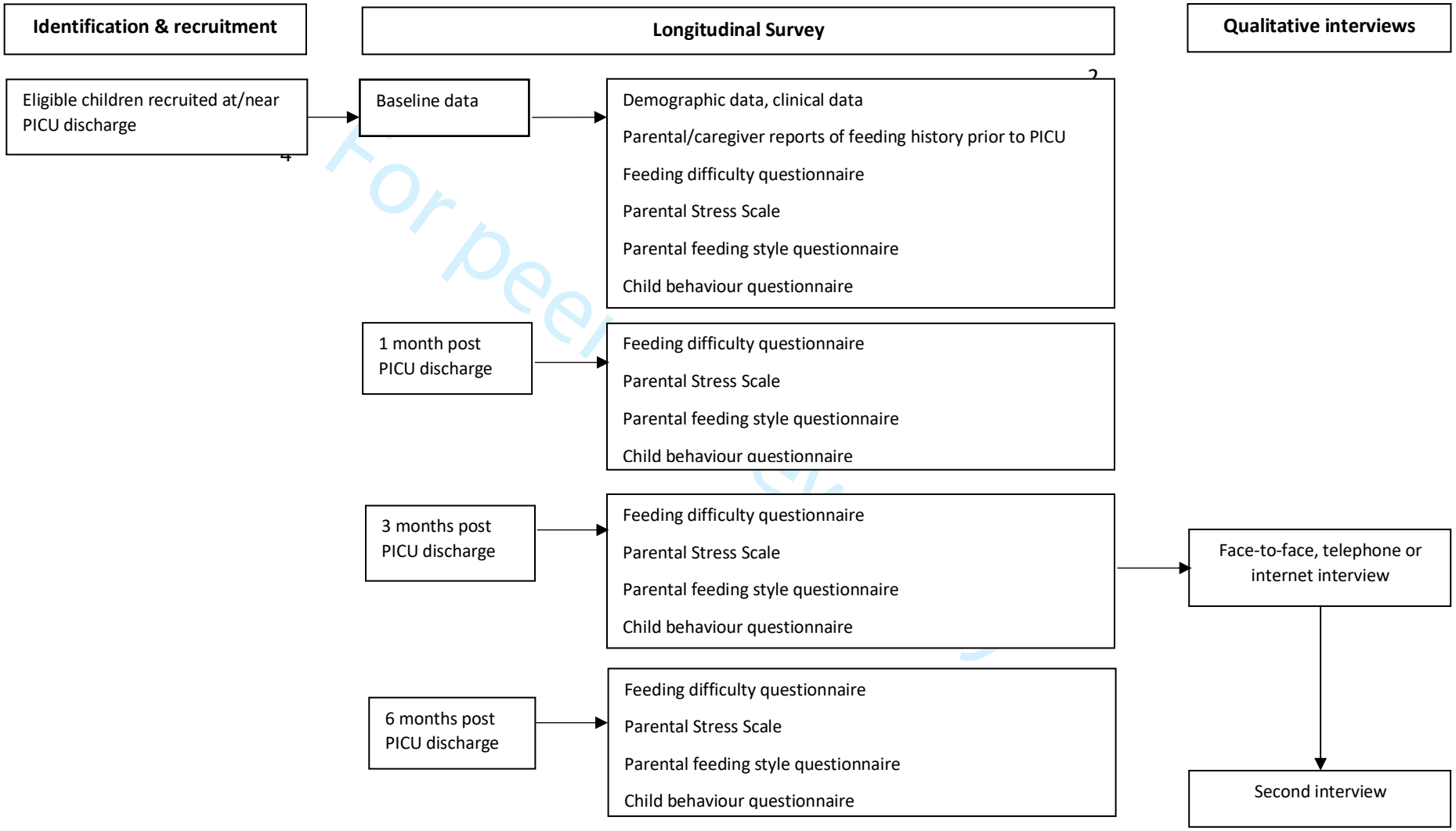
Figure 1 for schematic overview of the study design

638

Figure 1: Overview of The PIES study design



Reporting checklist for protocol of a clinical trial.

Based on the SPIRIT guidelines.

Instructions to authors

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

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

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		Reporting Item	Page Number
Administrative information			
Title	#1	Descriptive title identifying the study design, population, interventions, and, if applicable, trial acronym	1

Trial registration	#2a	Trial identifier and registry name. If not yet registered, name of intended registry	N/A
Trial registration: data set	#2b	All items from the World Health Organization Trial Registration Data Set	NA
Protocol version	#3	Date and version identifier	3
Funding	#4	Sources and types of financial, material, and other support	27
Roles and responsibilities: contributorship	#5a	Names, affiliations, and roles of protocol contributors	1 and 25
Roles and responsibilities: sponsor contact information	#5b	Name and contact information for the trial sponsor	27
Roles and responsibilities: sponsor and funder	#5c	Role of study sponsor and funders, if any, in study design; collection, management, analysis, and interpretation of data; writing of the report; and the decision to submit the report for publication, including whether they will have ultimate authority over any of these activities	N/A
Roles and responsibilities: committees	#5d	Composition, roles, and responsibilities of the coordinating centre, steering committee, endpoint adjudication committee, data management team, and	N/A

		other individuals or groups overseeing the trial, if applicable (see Item 21a for data monitoring committee)	
Introduction			
Background and rationale	#6a	Description of research question and justification for undertaking the trial, including summary of relevant studies (published and unpublished) examining benefits and harms for each intervention	From page 4
Background and rationale: choice of comparators	#6b	Explanation for choice of comparators	N/A
Objectives	#7	Specific objectives or hypotheses	6
Trial design	#8	Description of trial design including type of trial (eg, parallel group, crossover, factorial, single group), allocation ratio, and framework (eg, superiority, equivalence, non-inferiority, exploratory)	7
Methods: Participants, interventions, and outcomes			
Study setting	#9	Description of study settings (eg, community clinic, academic hospital) and list of countries where data will be collected. Reference to where list of study sites can be obtained	7 and 10

Eligibility criteria	#10	Inclusion and exclusion criteria for participants. If applicable, eligibility criteria for study centres and individuals who will perform the interventions (eg, surgeons, psychotherapists)	11
Interventions: description	#11a	Interventions for each group with sufficient detail to allow replication, including how and when they will be administered	N/A
Interventions: modifications	#11b	Criteria for discontinuing or modifying allocated interventions for a given trial participant (eg, drug dose change in response to harms, participant request, or improving / worsening disease)	N/A
Interventions: adherance	#11c	Strategies to improve adherence to intervention protocols, and any procedures for monitoring adherence (eg, drug tablet return; laboratory tests)	N/A
Interventions: concomitant care	#11d	Relevant concomitant care and interventions that are permitted or prohibited during the trial	N/A
Outcomes	#12	Primary, secondary, and other outcomes, including the specific measurement variable (eg, systolic blood pressure), analysis metric (eg, change from baseline, final value, time to event), method of aggregation (eg, median, proportion), and time point for each outcome. Explanation of the clinical relevance of chosen efficacy and harm outcomes is strongly recommended	7

Participant timeline	#13	Time schedule of enrolment, interventions (including any run-ins and washouts), assessments, and visits for participants. A schematic diagram is highly recommended (see Figure)	8
Sample size	#14	Estimated number of participants needed to achieve study objectives and how it was determined, including clinical and statistical assumptions supporting any sample size calculations	12
Recruitment	#15	Strategies for achieving adequate participant enrolment to reach target sample size	14
Methods: Assignment of interventions (for controlled trials)			
Allocation: sequence generation	#16a	Method of generating the allocation sequence (eg, computer-generated random numbers), and list of any factors for stratification. To reduce predictability of a random sequence, details of any planned restriction (eg, blocking) should be provided in a separate document that is unavailable to those who enrol participants or assign interventions	N/A
Allocation concealment mechanism	#16b	Mechanism of implementing the allocation sequence (eg, central telephone; sequentially numbered, opaque,	N/A

		sealed envelopes), describing any steps to conceal the sequence until interventions are assigned	
Allocation: implementation	#16c	Who will generate the allocation sequence, who will enrol participants, and who will assign participants to interventions	N/A
Blinding (masking)	#17a	Who will be blinded after assignment to interventions (eg, trial participants, care providers, outcome assessors, data analysts), and how	N/A
Blinding (masking): emergency unblinding	#17b	If blinded, circumstances under which unblinding is permissible, and procedure for revealing a participant's allocated intervention during the trial	N/A
Methods: Data collection, management, and analysis			
Data collection plan	#18a	Plans for assessment and collection of outcome, baseline, and other trial data, including any related processes to promote data quality (eg, duplicate measurements, training of assessors) and a description of study instruments (eg, questionnaires, laboratory tests) along with their reliability and validity, if known. Reference to where data collection forms can be found, if not in the protocol	15

Data collection plan: retention	#18b	Plans to promote participant retention and complete follow-up, including list of any outcome data to be collected for participants who discontinue or deviate from intervention protocols	15
Data management	#19	Plans for data entry, coding, security, and storage, including any related processes to promote data quality (eg, double data entry; range checks for data values). Reference to where details of data management procedures can be found, if not in the protocol	N/A
Statistics: outcomes	#20a	Statistical methods for analysing primary and secondary outcomes. Reference to where other details of the statistical analysis plan can be found, if not in the protocol	15 onwards
Statistics: additional analyses	#20b	Methods for any additional analyses (eg, subgroup and adjusted analyses)	15 onwards
Statistics: analysis population and missing data	#20c	Definition of analysis population relating to protocol non-adherence (eg, as randomised analysis), and any statistical methods to handle missing data (eg, multiple imputation)	15
Methods: Monitoring			
Data monitoring: formal committee	#21a	Composition of data monitoring committee (DMC); summary of its role and reporting structure; statement of whether it is independent from the sponsor and	N/A

		competing interests; and reference to where further details about its charter can be found, if not in the protocol. Alternatively, an explanation of why a DMC is not needed	
Data monitoring: interim analysis	#21b	Description of any interim analyses and stopping guidelines, including who will have access to these interim results and make the final decision to terminate the trial	N/A
Harms	#22	Plans for collecting, assessing, reporting, and managing solicited and spontaneously reported adverse events and other unintended effects of trial interventions or trial conduct	No
Auditing	#23	Frequency and procedures for auditing trial conduct, if any, and whether the process will be independent from investigators and the sponsor	No
Ethics and dissemination			
Research ethics approval	#24	Plans for seeking research ethics committee / institutional review board (REC / IRB) approval	21
Protocol amendments	#25	Plans for communicating important protocol modifications (eg, changes to eligibility criteria, outcomes, analyses) to relevant parties (eg, investigators, REC / IRBs, trial participants, trial registries, journals, regulators)	21

Consent or assent	#26a	Who will obtain informed consent or assent from potential trial participants or authorised surrogates, and how (see Item 32)	14 and 19
Consent or assent: ancillary studies	#26b	Additional consent provisions for collection and use of participant data and biological specimens in ancillary studies, if applicable	N/A
Confidentiality	#27	How personal information about potential and enrolled participants will be collected, shared, and maintained in order to protect confidentiality before, during, and after the trial	14/15
Declaration of interests	#28	Financial and other competing interests for principal investigators for the overall trial and each study site	N/A
Data access	#29	Statement of who will have access to the final trial dataset, and disclosure of contractual agreements that limit such access for investigators	26
Ancillary and post trial care	#30	Provisions, if any, for ancillary and post-trial care, and for compensation to those who suffer harm from trial participation	N/A
Dissemination policy: trial results	#31a	Plans for investigators and sponsor to communicate trial results to participants, healthcare professionals, the public, and other relevant groups (eg, via publication, reporting in results databases, or other data sharing arrangements), including any publication restrictions	21

Dissemination policy: authorship	#31b	Authorship eligibility guidelines and any intended use of professional writers	N/A
Dissemination policy: reproducible research	#31c	Plans, if any, for granting public access to the full protocol, participant-level dataset, and statistical code	N/A
Appendices			
Informed consent materials	#32	Model consent form and other related documentation given to participants and authorised surrogates	No
Biological specimens	#33	Plans for collection, laboratory evaluation, and storage of biological specimens for genetic or molecular analysis in the current trial and for future use in ancillary studies, if applicable	N/A