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

Journal:	<i>BMJ Open</i>
Manuscript ID	bmjopen-2020-041234
Article Type:	Protocol
Date Submitted by the Author:	03-Jun-2020
Complete List of Authors:	Morton, Kathryn; University Hospital Southampton NHS Foundation Trust, PICU; University of Southampton, School of Health Sciences Darlington, Anne-Sophie; University of Southampton, School of Health Sciences Marino, LV; University Hospital Southampton NHS Foundation Trust, Department of Dietetics/SLT,
Keywords:	NUTRITION & DIETETICS, Paediatric intensive & critical care < ANAESTHETICS, PAEDIATRICS

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1 **Title:** Protocol for a multicentre longitudinal mixed methods study: Feeding and survivorship
2 outcomes in previously healthy young Paediatric Intensive Care Survivors – The PIES study
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49 **Keywords:** feeding difficulties, children, critical illness, survivors
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10 27
11
12 28 **Abstract**

13
14 29 **Introduction**

15
16 30 An admission to Paediatric Intensive Care (PICU) is associated with multiple physical and
17
18 31 environmental stressors, often involving many negative and painful oral experiences. Evidence
19
20 32 from children with complex medical conditions suggest that feeding difficulties post-PICU stay
21
22 33 are common, causing significant parental anxiety. Adult intensive care (ICU) survivor studies
23
24 34 suggest feeding issues lasting up to 3 months post discharge from ICU. There is, however, a
25
26 35 paucity of evidence regarding feeding outcomes for previously healthy children following a PICU
27
28 36 admission and whether painful oral experiences during an admission contribute to feeding
29
30 37 difficulties post-discharge, negatively impacting on parental/caregiver anxiety.
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33

34 38 **Methods and analysis**

35
36 39 This longitudinal concurrent mixed method study will explore the impact of feeding
37
38 40 difficulties, identifying any clinical risk factors during the first 6 months of PICU-discharge in
39
40 41 previously healthy young children (≤ 4 years). Parents/caregivers of children will be asked to
41
42 42 complete questionnaires relating to; feeding difficulties, parental/caregiver stress, child and
43
44 43 parental/caregivers feeding behaviours, at the point of PICU-discharge, 1, 3 and 6 months post-
45
46 44 discharge. Parents/caregivers will be invited to participate in qualitative semi-structured
47
48 45 interviews at 3 and 6 months post-PICU-discharge exploring parental/caregiver experiences of
49
50 46 feeding their child after PICU. Statistical analysis of the survey data will consist of descriptive
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3 47 and inferential statistics, plus qualitative analysis of any free text comments using thematic
4
5 48 analysis.
6

7 49 **Ethics and dissemination**

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9
10 50 This study will provide an insight and increase our understanding of the prevalence of
11
12 51 feeding difficulties in previously healthy children admitted to PICU and parental/caregiver
13
14 52 experiences. Multiple methods will be used to ensure that the findings are effectively
15
16 53 disseminated to service users, clinicians, policy and academic audiences. The study has full
17
18 54 ethical approval from the National Health Service Research Ethics Committee (Ref: 20/YH/0160)
19
20
21 55 and full governance clearance.
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24 56

25 57 **Article summary**

26 58 27 59 **Strengths and limitations of this study**

- 28
29
30 60 • A mixed methods design will provide new insights and a greater understanding into the
31
32 61 prevalence and impact of feeding issues in previously healthy young children who
33
34 62 survive PICU.
35
36
37 63 • Qualitative data collection methods will generate rich data progressing our
38
39 64 understanding of this phenomenon.
40
41 65 • The longitudinal study design will allow us to explore the feeding survivorship journey
42
43 66 experienced by families of children who have survived critical illness.
44
45
46 67 • The longitudinal study design may also however, have the potential for high attrition
47
48 68 which may affect data at six months.
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72 Introduction

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

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

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

1
2
3 96 with a ETT and mechanical ventilation, multiple oral interventions affecting oral motor skills,
4
5 97 type of cardiac surgery with added risks associated with use of cardiopulmonary bypass and
6
7 98 post-op chest open, prolonging mechanical ventilation,(16-20). The use of NGT's in young
8
9 99 children with complex medical needs have been reported to negatively impact developmental
10
11 100 milestone achievement with regards to establishing oral intake,(21-25). They may, as a result,
12
13 101 cause altered oral sensory issues, difficulties in swallowing food, failure in feeding skill
14
15 102 progression with regards to tastes and textures, and present as food refusal in some,(16, 22, 25,
16
17 103 26) causing parental distress around feeding and mealtimes,(27-29).

20
21 104 Despite a plethora of literature and research, there is no universally accepted definition
22
23 105 of a paediatric feeding difficulty, (30) . Historically, feeding disorders have been defined in the
24
25 106 *Diagnostic and Statistical Manual of Mental Disorders, 5th Edition*, (30)and in the *International*
26
27 107 *Statistical Classification of Diseases and Related Health Problems, 10th Revision*, (30). Although
28
29 108 these definitions incorporate nutritional complications found in some medical conditions and
30
31 109 recognise oral feeding abilities, they fail to identify the multiple physical, non-organic and
32
33 110 psycho-social factors,(31). Feeding difficulties as described by Kerzner and Levine, (28, 29, 32) go
34
35 111 beyond diagnostic classifications and include food refusals; disruptive, stressful and prolonged
36
37 112 mealtimes; lack of inappropriate self-feeding; failure to advance textures; vomiting and
38
39 113 diarrhoea; gagging (and anticipatory gagging); and inappropriate nocturnal feeding, (29, 32).
40
41 114 Furthermore, they recognise the importance of the impact that parental-child relationships and
42
43 115 interactions with peers has on childhood feeding behaviours. Parental behaviours and feeding
44
45 116 styles can directly influence perceived and actual feeding difficulties of young children,(25, 27).
46
47 117 Parents play a pivotal role in shaping children's early feeding experiences, providing the physical
48
49 118 foods, as well as the social interactions and model eating behaviours,(15).

1
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3 119 The consequence an admission to PICU may impact the acquisition of normal feeding
4
5 120 and eating skills of young children and normal parent-child relationships around mealtimes. The
6
7 121 implications of this post-PICU-discharge for young children and their families is not known.
8
9

10 122 **Methods and analysis**

11 12 123 **Study aims**

13
14 124 The PIES study (Feeding and survivorship outcomes in previously healthy young
15
16 125 Paediatric Intensive Care Survivors) has six specific objectives:

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18
19 126 1. To characterise and measure the prevalence of feeding difficulties in previously healthy
20
21 127 children (≤ 4 years) who survive critical illness during the first 6 months after PICU
22
23 128 discharge;
- 24
25 129 2. To identify clinical predictors for the development of feeding difficulties in previously
26
27 130 healthy young children (≤ 4 years) who survive critical illness;
- 28
29 131 3. To identify parental/caregiver feeding styles for previously healthy young children (≤ 4
30
31 132 years) who survive critical illness;
- 32
33 133 4. To measure parental stress in parents/caregivers of previously healthy young children (≤ 4
34
35 134 years) who survive critical illness;
- 36
37 135 5. To identify behaviours of previously healthy young children (≤ 4 years) who survive
38
39 136 critical illness;
- 40
41 137 6. To develop an in-depth understanding of how parents/caregivers of previously healthy
42
43 138 young children (≤ 4 years old) who survive critical illness construct, experience and make
44
45 139 sense of their survivorship journey from PICU admission, specifically looking at feeding
46
47 140 experiences and parental-child relationships.

48 49 50 51 52 141 **Study design**

1
2
3 142 This multicenter longitudinal mixed method study has concurrent quantitative and
4
5 143 qualitative components. Parents/caregivers of children will be asked to complete questionnaires
6
7 144 considering aspects relating to; feeding difficulties, parental/caregiver stress, child and
8
9 145 parental/caregivers feeding behaviours at the point of PICU-discharge and at 1, 3 and 6 months
10
11 146 post-discharge. Parents/caregivers will also be invited to participate in qualitative semi-
12
13 147 structured interviews at 3 and 6 months post-PICU-discharge which will explore
14
15 148 parental/caregiver experiences of feeding their child post-PICU. See figure 1 for schematic
16
17 149 overview of the study design.

21 150 **Quantitative study**

22
23 151 Data about the PICU admission of each child participant will be recorded onto an ALEA
24
25 152 electronic Case Report Form (eCRF; <https://www.aleaclinical.eu/>), a secure password
26
27 153 protected, web-based eCRF system. Data will include: length of PICU stay; length of intubation;
28
29 154 length of mechanical invasive ventilation; number of (re) intubations; type of ETT (oral or nasal);
30
31 155 length of non-invasive ventilation; inotrope requirement; mode of feeding during PICU
32
33 156 admission; time from extubation to commence oral feeding; mode of feeding at PICU discharge;
34
35 157 and evidence of gastric intolerance. Data will also be collected from each child's
36
37 158 parent/caregiver prospectively over the first 6- months post-PICU, in a follow-up survey.

42 159 **Study Measures**

43
44
45 160 The outcome measures for the longitudinal follow-up survey have been selected based
46
47 161 on their validity, reliability, use in previous paediatric populations and ease of use. Pre-existing
48
49 162 validated questionnaires will be used to measure feeding difficulty assessment, parental stress,
50
51 163 parental feeding styles and child behaviour. To obtain longitudinal outcome data and potentially
52
53 164 identify acute and/or chronic feeding difficulties, data from the questionnaires will be collected
54
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3 165 at four-time points: at PICU discharge (retrospective data), 1, 3 and 6 months after PICU
4
5 166 discharge. The outcomes measures and time points are outlined in Table 1. The questionnaires
6
7 167 have also been selected according to age of the child participant, in addition to tested
8
9
10 168 psychometric properties.

11
12
13 169 Feeding difficulty assessment measures:

- 14
15
16 170 • Infant feeding questionnaire,(33) (7 items; up to 9 month old babies)
17
18 171 • Behavioral Pediatric Feeding Assessment Scale,(34) (35 items; 9 months old to 7 years).

19
20
21 172 Parental stress measure:

- 22
23
24 173 • Parental Stress Scale,(35) (18 items).

25
26
27 174 Parental feeding style measures:

- 28
29
30 175 • Infant feeding questionnaire,(36) (25 items; up to 2 years)
31
32 176 • Child feeding questionnaire,(37) (28 items; from 2 years onwards).

33
34
35 177 Child behaviour measures:

- 36
37
38 178 • Infant behaviour questionnaire – very short version,(38) (36 items; up to 12 months)
39
40 179 • Child behaviour questionnaire – very short version, (39) (35 items; from 1 year).

41
42
43 180 **Table 1: Data collection measures and time points**

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

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(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 <i>or</i> 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 <i>or</i> Child Feeding Questionnaire	X	X	X	X
Child behaviour measures				
Infant Behavior Questionnaire (very-short version)	X	X	X	X

<i>or</i>				
Early Childhood Behavior Questionnaire				
Qualitative interviews:				
Invitation	X			
Interviews			X	X

181

182 **Qualitative study**

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

190 **Sample and recruitment**

191 **Setting**

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

195 **Eligibility criteria**

196 The chosen inclusion criteria will allow recruitment of previously healthy young children
 197 (≤ 4 years) who are admitted to PICU both electively and in emergency situations. Participants
 198 will be eligible if they are parents/caregivers (aged ≥ 18 years of age) of a previously healthy

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

202 **Table 2: Eligibility criteria**

Inclusion criteria	Rationale
Parents/caregivers (aged ≥ 18 years of age) of previously healthy children aged ≤ 4 years 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: <ul style="list-style-type: none"> • 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)	
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203

204 Sample size

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

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

221 Sampling strategy

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

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

231 **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%)

232
 233 *Qualitative study:* A purposeful sampling strategy will be used to interview a range of
 234 parents/caregivers based on reason for admission, age of child admitted to PICU and gender of
 235 parent (Table 4). This will ensure that not just mothers, parents/caregivers of planned surgery or
 236 parents/caregivers of babies are only interviewed for example.

237 **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 sequelae associated with emergency verses planned admissions to PICU (43)
Age of child: <ul style="list-style-type: none"> • ≤ 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)

238

239 **Study procedures**

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

1
2
3 252 reminders will be sent for the follow-up surveys as reminder letters, telephone calls, messages
4
5 253 or email by the lead researcher (KM) as agreed with the participant at recruitment. As there is
6
7 254 such a small-time frame between 1 and 3 month assessments, if no response is received
8
9 255 following the 1-month survey, participants will still be approached at 3 months. If there is no
10
11 256 response at this point, they will not be approached again at 6 months.
12
13

14 257 *Qualitative study:* During recruitment into the multicentred survey, parents/caregivers
15
16 258 will be invited to take part in the qualitative interviews. Those who consent to an interview will
17
18 259 be approached by the lead researcher (KM) at the time in which reminders of the follow-up
19
20 260 survey are sent (at 1, 3 and 6 months) either by reminder letters, telephone call, messages or
21
22 261 email as agreed at survey enrolment. Semi-structured open-ended questions will be used as the
23
24 262 primary method of data collection to allow the parent/caregiver to describe their story,
25
26 263 communicate their experiences, feelings and PICU survivorship journey. In response to PPI
27
28 264 feedback highlighting the lack of spare time that parents/caregivers of young children often
29
30 265 face, telephone and internet (i.e. Microsoft teams: Microsoft 365, UK) interviews will be
31
32 266 conducted at a time convenient for the parent/caregiver which could include evenings and
33
34 267 weekends.
35
36
37
38

39 268 **Data analysis**

40
41 269 All data obtained will be analysed. In circumstances where participants are deemed lost
42
43 270 to follow-up, any data supplied will be analysed and used where appropriate, even if it can only
44
45 271 be used to describe the cohort at baseline. A pragmatic approach to missing data will be used,
46
47 272 whereby data will be analysed as much as possible. Data from non-responders will be used
48
49 273 within the analysis to observe for nonresponse bias.
50
51

52 274 **Quantitative study data analysis**

1
2
3 275 Descriptive statistics will be used to present the demographic data and information
4
5 276 collected from the medical PICU admissions data. All child and parent/caregiver measures will
6
7 277 be calculated, including means, SD, medians and IQRs for continuous variables and frequency
8
9 278 counts and percentages for categorical data. Data will be examined for normality, outliers and
10
11 279 for missing data. Statistical analysis will be completed using the IBM Statistical Package for Social
12
13
14 280 Science (SPSS) and statistical significance will be set at $p < 0.05$.

15
16
17 281 Analyses related to the study specific objectives include the following:

18
19 282 *Objective 1: To characterise and measure the prevalence of feeding difficulties in previously*
20
21 283 *healthy children (≤ 4 years) who survive critical illness during the first 6 months after PICU*
22
23 284 *discharge. From the feeding difficulty assessment measures, descriptive statistics (frequency*
24
25 285 *counts and percentages) will be used to identify the numbers and types of feeding difficulties at*
26
27
28 286 *each time point collected and for different age groups.*

29
30 287 *Objective 2: To identify clinical predictors for the development of feeding difficulties in previously*
31
32 288 *healthy young children (≤ 4 years) who survive critical illness. The information from the routinely*
33
34 289 *collected clinical PICU data will be used to identify any clinical predictors for the development of*
35
36 290 *feeding difficulties, such as length of intubation and time to commence oral feeding. Statistical*
37
38 291 *analysis will involve multiple +/- linear regressions to see if we can predict feeding difficulty*
39
40 292 *questionnaire scores from the clinical variables.*

41
42
43 293 *Objective 3: To identify parental/caregiver feeding styles for previously healthy young children (\leq*
44
45 294 *4 years) who survive critical illness. Descriptive statistics will be initially performed to identify*
46
47 295 *the frequency of participants in each parental feeding style, to identify the majority. This will*
48
49 296 *then be repeated at each time point collected, to identify a change (or not) in parental feeding*
50
51 297 *style across the 6 months from PICU discharge. If have enough data, differences between*
52
53 298 *mother feeding styles and father feeding styles will be calculated using Mann-Whitney U (non-*
54
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2
3 299 parametric) or t-Test (parametric) tests as appropriate. The relationship between parental
4
5 300 feeding style and feeding difficulty score will also be tested using the same statistical tests.
6
7 301 *Objective 4: To measure parental stress in parents/caregivers of previously healthy young*
8
9 302 *children (≤ 4 years) who survive critical illness.* Using the scores from the parental stress scale,
10
11 303 average parental stress scores for all participants will be calculated at all time points. Average
12
13 304 parental stress score at each time point, for those parents of children with and without feeding
14
15 305 difficulties, will also be presented to identify the trajectories of parental stress over time and
16
17 306 between the two groups. Correlations between increasing feeding difficulty score and increasing
18
19 307 parental stress score will be assessed using scatterplot graphs, and differences will be tested for
20
21 308 statistical significance using Pearsons (parametric) or Spearmans (non-parametric) tests where
22
23 309 appropriate.

24
25 310 *Objective 5: To identify behaviours of previously healthy young children (≤ 4 years) who survive*
26
27 311 *critical illness.* Frequency of children in each temperament category from the Infant and Early
28
29 312 Child Behavior questionnaires will be calculated and presented at each data collection time
30
31 313 point, so observe for changes over time. The relationship between infant/child temperament
32
33 314 and feeding difficulty score; and parental feeding style and parental stress score will be assessed
34
35 315 using Mann-Whitney U (non- parametric) or t-Test (parametric) and regression models where
36
37 316 appropriate.

317 **Qualitative study data analysis**

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

1
2
3 323 and 3) integration and will look to answer study *objective 6: To develop an in-depth*
4
5 324 *understanding of how parents/caregivers of previously healthy young children (≤ 4 years old)*
6
7 325 *who survive critical illness construct, experience and make sense of their survivorship journey*
8
9
10 326 *from PICU admission, specifically looking at feeding experiences and parental-child relationships.*

11
12 327 Stage 1: Narrative analysis: The first stage of analysis will involve analysing the content of the
13
14 328 data from each participant's interview using the Clandinin and Connelly's (46) method of
15
16 329 narrative inquiry. This framework uses three domains to structure the analysis: temporality,
17
18 330 sociality and place,(47). The analysis focuses on the actual storylines that are told and emotions
19
20 331 that are used to tell the story, the societal and cultural impact on the story and the influence of
21
22 332 the place in which the experience occurs,(46). An additional consideration of the actual words
23
24 333 and language, both verbal and nonverbal, used throughout the narrative will also be used during
25
26 334 the analysis,(46).

27
28
29
30 335 Stage 2: Thematic analysis: The second stage of analysis will involve a thematic analysis
31
32 336 approach, whereby repeated patterns across the stage 1 analysis will be identified, leading to
33
34 337 the detection of codes and themes across the entire data set,(48). This will enable meaning and
35
36 338 patterns to emerge from the data.

37
38
39 339 Stage 3: Data integration: The final step of the qualitative data analysis will involve integrating
40
41 340 the narrative and thematic analysis. The individual stories will be re-told in a coherent manner
42
43 341 and then the key themes across the entire data set will be presented. This will provide a detailed
44
45 342 description and understanding of the survivorship journey of parents/caregivers of previously
46
47 343 health children who survive critical illness.

344 **Data integration strategy of quantitative and qualitative data**

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

1
2
3 347 integrated to answer the overarching research questions and aims. The qualitative data will
4
5 348 strengthen the survey findings by adding the human perspective, exploring behaviour, feelings
6
7 349 and experiences of the parents/caregivers told by them,(49). The information gained from the
8
9
10 350 interviews will assist interpretation and analysis of the survey results, drawing conclusions to
11
12 351 the clinical significance of the results with implications for clinical practice,(50).

14 352 **Public and patient involvement**

16 353 Guided by the NIHR INVOLVE recommendations,(51), involvement of families of children
17
18 354 recently discharged from PICU was sought during the study design process. Six parents
19
20
21 355 volunteered to provide guidance and advice during an organised coffee morning. Collectively,
22
23 356 the importance of the study was recognised, and recommendations made to the recruitment
24
25 357 process and data collection methods. Feedback included using an online questionnaire for ease
26
27
28 358 of use and to increase follow-up completion. The survey questions were also piloted by parents,
29
30 359 assessing the clarity of the questionnaires and their instructions and to consider the burden of
31
32 360 completing all four questionnaires. Offering home, telephone and internet interviews was also
33
34
35 361 suggested for the interviews.

36 362 **Ethics and Dissemination**

39 363 **Informed consent**

41 364 Parents/caregivers will be approached to take part in The PIES study once the child
42
43 365 meets the inclusion/exclusion criteria. After being given an ethically approved Participant
44
45 366 Information Sheet (PIS), parents/caregivers will be given at least 48 hours to consider
46
47
48 367 participation, unless they are happy to give informed consent before this time. It is anticipated
49
50 368 that the children eligible for the study will be too young and/or too ill to participate directly in
51
52 369 the consent process. Each parent/caregiver will complete a contact form that will record the
53
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2
3 370 information needed for the follow-up survey distribution (e.g. mail addresses, telephone
4
5 371 numbers) and informed consent will be obtained to allow the sharing of this personal data.
6

7
8 372 **Researching sensitive and emotive topics**
9

10 373 It is recognised that parents/caregivers of previously healthy young children who have
11
12 374 survived critical illness may have psychological sequelae (i.e. post-traumatic stress disorder)
13
14 375 following their child's admission to PICU,(43). Although not specifically asking about their PICU
15
16 376 experience, completing the survey and taking part in the interviews may raise potentially
17
18 377 distressing issues around difficult feeding and/or mealtime behaviours following the PICU
19
20 378 admission. If any participant becomes distressed by recalling their experience during the
21
22 379 interviews, the interview will be immediately stopped. The researcher (KM) will aim to debrief
23
24 380 the situation at the time and will refer onto the relevant agencies such as Patient Advice and
25
26 381 Liaison Services (PALS), clinical psychology team and their own or child's health team. The
27
28 382 survey will encourage participants to inform the researcher of any problems or distress
29
30 383 experienced during they survey completion. The researcher will be able to pinpoint sources of
31
32 384 help through their local health care services where possible.
33
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35

36
37 385 **Burden**
38

39 386 The survey is compiled of four separate pre-existing validated questionnaires, asked at
40
41 387 four separate timepoints during the enrolment and follow-up (at recruitment, at 1, 3 and 6
42
43 388 months after PICU discharge). The questionnaires include Likert scales, yes/no answers and
44
45 389 drop-down options. The survey questions and instructions have been piloted by parents of
46
47 390 young children, assessing the clarity of the questionnaires, the instructions and consideration of
48
49 391 the time and mental burden in completing all four questionnaires. Average time for survey
50
51 392 completion was 15 minutes, with follow-up surveys thought to be quicker. We endeavour to
52
53 393 reduce this burden by having the option of an online electronic survey available to parents and
54
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1
2
3 394 by adding the feature where you can 'save and go back to later' option within the survey. The
4
5 395 PIS will clearly state that there will be no financial gain from taking part in the study. Conversely,
6
7 396 some participants might find taking part in the study beneficial because they will have the time
8
9 397 and space to think about issues which are important to them.

11 398 **Ethical review**

12
13
14 399 The Yorkshire and The Humber – South Yorkshire Research Ethics Committee has
15
16 400 reviewed the study protocol and provided favourable opinion (Ref: 20/YH/0160). The Health
17
18 401 Research Authority has also approved the protocol (IRAS: 279171). This study has been
19
20
21 402 extensively peer reviewed through the University of Southampton and forms the PhD study of
22
23 403 the first author.

24 404 **Methods of dissemination**

25
26
27
28 405 This paper is part of the dissemination plan of the PIES study, by presenting the project
29
30 406 background, providing a detailed description of methods and procedures used to collect and
31
32 407 analyse the data. Other dissemination plans involve local, national and international audiences
33
34 408 including academics, health care professionals, healthcare commissioners, charities and the
35
36 409 public. Dissemination will include written and oral feedback to the PPI group, local PICU charity
37
38 410 and each recruitment centre. Presentations to local and national research and clinical teams will
39
40 411 take place, including research meetings and conferences. The findings from this study will
41
42 412 contribute to addressing the significant gaps in the literature by investigating the prevalence of
43
44 413 and predictors for feeding difficulties experienced by previously healthy young children who
45
46 414 survive critical illness and explore the effect on parental feeding experiences, behaviours and
47
48 415 stress. It is anticipated that the expected outputs of this proposed project will be in terms of
49
50 416 high quality, peer-reviewed scientific publications and conference presentations. During the
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417 informed consent process, parents/caregivers will be asked if they would like a lay summary of
418 any study findings sent to them at the end of the study.

For peer review only

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7 560

8
9
10 561 **Acknowledgements**

11
12 562 The PIES study protocol was developed by KM, LVM and ASD. The corresponding author would
13
14 563 like to acknowledge LVM and ASD in their supervisory support during KM's PhD in which The
15
16 564 PIES Study has been developed. KM would like to acknowledge the University of Southampton
17
18 565 and University Hospital Southampton NHS Foundation Trust in supporting and funding her PhD
19
20 566 through the Wessex Clinical Doctoral Research Fellowship scheme, and the clinical team at
21
22 567 Southampton Children's Hospital PICU in allowing KM the clinical backfill time to undertake her
23
24 568 PhD. Furthermore, KM would like to acknowledge Kevin Wheeler (Clinical Informatics Research
25
26 569 Unit, Southampton) for his support and patience in developing the PIES study data capture and
27
28 570 management though the ALEA database/eCRF.
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33
34 572 **Conflict of interest**

35
36 573 None declared
37
38 574

39
40 575 **Statement of authorship**

41
42 576 Authors made the following contribution to the manuscript:

43
44 577 (1) KM formulated the original research idea, conducted the literature searching and is the
45
46 578 chief investigator for the study,

47
48 579 (2) KM drafted the manuscript from the ethically approved protocol (which was originally
49
50 580 supported by LVM and ASD)
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3 581 (3) LVM, ASD and KM reviewed and revised the manuscript for important intellectual
4
5 582 content, and (4) all authors provided final approval of the version to be submitted.
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9
10 584 **Data Statement**

11
12 585 Technical appendix, statistical code, and dataset for The PIES study will be available from the
13
14 586 University of Southampton Institutional Research Repository, ePrints Soton
15
16 587 (<https://eprints.soton.ac.uk/>)
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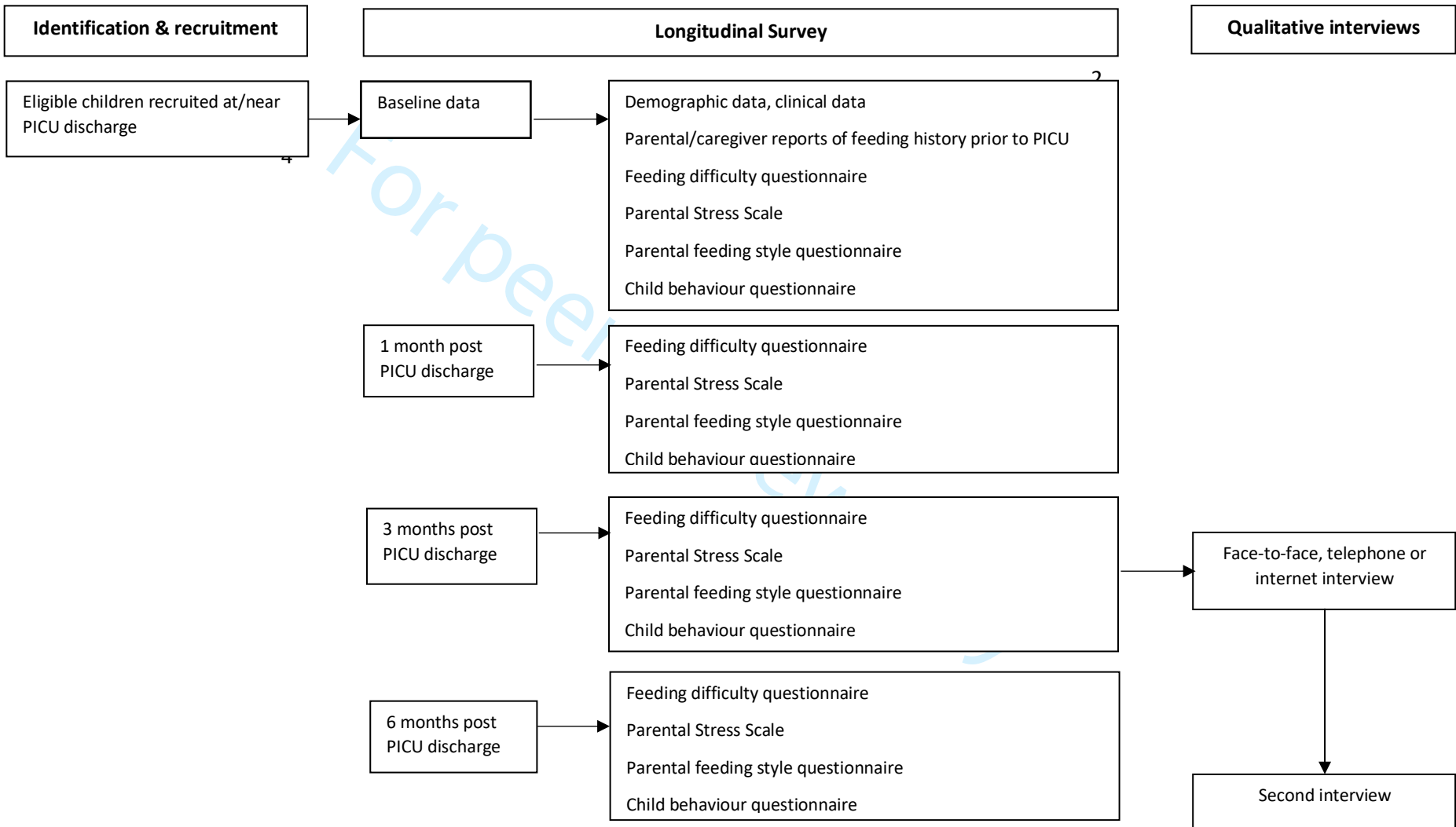
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21 589 **Funding**

22
23 590 This report describes independent research arising from a personal Clinical Doctoral Research
24
25 591 Fellowship for Kathryn Morton, supported jointly by the University of Southampton and
26
27 592 University Hospital Southampton NHS Foundation Trust, England.
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1 **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.

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

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

Chan A-W, Tetzlaff JM, Altman DG, Laupacis A, Gøtzsche PC, Krleža-Jerić K, Hróbjartsson A, Mann H, Dickersin K, Berlin J, Doré C, Parulekar W, Summerskill W, Groves T, Schulz K, Sox H, Rockhold FW, Rennie D, Moher D. SPIRIT 2013 Statement: Defining standard protocol items for clinical trials. *Ann Intern Med.* 2013;158(3):200-207

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

1	Trial registration	#2a	Trial identifier and registry name. If not yet registered,	N/A
2			name of intended registry	
3				
4				
5				
6	Trial registration:	#2b	All items from the World Health Organization Trial	NA
7	data set		Registration Data Set	
8				
9				
10				
11	Protocol version	#3	Date and version identifier	3
12				
13				
14				
15	Funding	#4	Sources and types of financial, material, and other	27
16			support	
17				
18				
19				
20	Roles and	#5a	Names, affiliations, and roles of protocol contributors	1 and 25
21	responsibilities:			
22				
23	contributorship			
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28	Roles and	#5b	Name and contact information for the trial sponsor	27
29	responsibilities:			
30				
31	sponsor contact			
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33	information			
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38	Roles and	#5c	Role of study sponsor and funders, if any, in study	N/A
39	responsibilities:		design; collection, management, analysis, and	
40			interpretation of data; writing of the report; and the	
41	sponsor and funder		decision to submit the report for publication, including	
42			whether they will have ultimate authority over any of	
43			these activities	
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52	Roles and	#5d	Composition, roles, and responsibilities of the	N/A
53	responsibilities:		coordinating centre, steering committee, endpoint	
54			adjudication committee, data management team, and	
55	committees			
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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

1	Eligibility criteria	#10	Inclusion and exclusion criteria for participants. If	11
2			applicable, eligibility criteria for study centres and	
3			individuals who will perform the interventions (eg,	
4			surgeons, psychotherapists)	
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11	Interventions:	#11a	Interventions for each group with sufficient detail to allow	N/A
12			replication, including how and when they will be	
13	description		administered	
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19	Interventions:	#11b	Criteria for discontinuing or modifying allocated	N/A
20			interventions for a given trial participant (eg, drug dose	
21	modifications		change in response to harms, participant request, or	
22			improving / worsening disease)	
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29	Interventions:	#11c	Strategies to improve adherence to intervention	N/A
30			protocols, and any procedures for monitoring adherence	
31	adherence		(eg, drug tablet return; laboratory tests)	
32				
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36	Interventions:	#11d	Relevant concomitant care and interventions that are	N/A
37			permitted or prohibited during the trial	
38	concomitant care			
39				
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41				
42	Outcomes	#12	Primary, secondary, and other outcomes, including the	7
43			specific measurement variable (eg, systolic blood	
44			pressure), analysis metric (eg, change from baseline,	
45			final value, time to event), method of aggregation (eg,	
46			median, proportion), and time point for each outcome.	
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53			Explanation of the clinical relevance of chosen efficacy	
54			and harm outcomes is strongly recommended	
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1	Participant timeline	#13	Time schedule of enrolment, interventions (including any	8
2			run-ins and washouts), assessments, and visits for	
3			participants. A schematic diagram is highly	
4			recommended (see Figure)	
5				
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11	Sample size	#14	Estimated number of participants needed to achieve	12
12			study objectives and how it was determined, including	
13			clinical and statistical assumptions supporting any	
14			sample size calculations	
15				
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21	Recruitment	#15	Strategies for achieving adequate participant enrolment	14
22			to reach target sample size	
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26	Methods:			
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28	Assignment of			
29	interventions (for			
30	controlled trials)			
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36	Allocation: sequence	#16a	Method of generating the allocation sequence (eg,	N/A
37	generation		computer-generated random numbers), and list of any	
38			factors for stratification. To reduce predictability of a	
39			random sequence, details of any planned restriction (eg,	
40			blocking) should be provided in a separate document that	
41			is unavailable to those who enrol participants or assign	
42			interventions	
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53	Allocation	#16b	Mechanism of implementing the allocation sequence (eg,	N/A
54	concealment		central telephone; sequentially numbered, opaque,	
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58	mechanism			
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sealed envelopes), describing any steps to conceal the sequence until interventions are assigned

Allocation: [#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): [#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

1	Data collection plan:	#18b	Plans to promote participant retention and complete	15
2				
3	retention		follow-up, including list of any outcome data to be	
4			collected for participants who discontinue or deviate from	
5			intervention protocols	
6				
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11	Data management	#19	Plans for data entry, coding, security, and storage,	N/A
12			including any related processes to promote data quality	
13			(eg, double data entry; range checks for data values).	
14			Reference to where details of data management	
15			procedures can be found, if not in the protocol	
16				
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23	Statistics: outcomes	#20a	Statistical methods for analysing primary and secondary	15
24			outcomes. Reference to where other details of the	onwards
25			statistical analysis plan can be found, if not in the	
26			protocol	
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33	Statistics: additional	#20b	Methods for any additional analyses (eg, subgroup and	15
34	analyses		adjusted analyses)	onwards
35				
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38				
39	Statistics: analysis	#20c	Definition of analysis population relating to protocol non-	15
40	population and		adherence (eg, as randomised analysis), and any	
41	missing data		statistical methods to handle missing data (eg, multiple	
42			imputation)	
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48	Methods: Monitoring			
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50				
51	Data monitoring:	#21a	Composition of data monitoring committee (DMC);	N/A
52	formal committee		summary of its role and reporting structure; statement of	
53			whether it is independent from the sponsor and	
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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

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10	Data monitoring:	#21b	Description of any interim analyses and stopping
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12	interim analysis		guidelines, including who will have access to these
13			interim results and make the final decision to terminate
14			the trial
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20	Harms	#22	Plans for collecting, assessing, reporting, and managing
21			solicited and spontaneously reported adverse events and
22			other unintended effects of trial interventions or trial
23			conduct
24			
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30	Auditing	#23	Frequency and procedures for auditing trial conduct, if
31			any, and whether the process will be independent from
32			investigators and the sponsor
33			
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38	Ethics and		
39			
40	dissemination		
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42			
43	Research ethics	#24	Plans for seeking research ethics committee / institutional
44			review board (REC / IRB) approval
45	approval		
46			
47			
48	Protocol	#25	Plans for communicating important protocol modifications
49			(eg, changes to eligibility criteria, outcomes, analyses) to
50	amendments		relevant parties (eg, investigators, REC / IRBs, trial
51			participants, trial registries, journals, regulators)
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1	Consent or assent	#26a	Who will obtain informed consent or assent from potential	14 and
2			trial participants or authorised surrogates, and how (see	19
3			Item 32)	
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8	Consent or assent:	#26b	Additional consent provisions for collection and use of	N/A
9	ancillary studies		participant data and biological specimens in ancillary	
10			studies, if applicable	
11				
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16	Confidentiality	#27	How personal information about potential and enrolled	14/15
17			participants will be collected, shared, and maintained in	
18			order to protect confidentiality before, during, and after	
19			the trial	
20				
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26	Declaration of	#28	Financial and other competing interests for principal	N/A
27	interests		investigators for the overall trial and each study site	
28				
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31	Data access	#29	Statement of who will have access to the final trial	26
32			dataset, and disclosure of contractual agreements that	
33			limit such access for investigators	
34				
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39	Ancillary and post	#30	Provisions, if any, for ancillary and post-trial care, and for	N/A
40	trial care		compensation to those who suffer harm from trial	
41			participation	
42				
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46				
47	Dissemination policy:	#31a	Plans for investigators and sponsor to communicate trial	21
48	trial results		results to participants, healthcare professionals, the	
49			public, and other relevant groups (eg, via publication,	
50			reporting in results databases, or other data sharing	
51			arrangements), including any publication restrictions	
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1 Dissemination policy: [#31b](#) Authorship eligibility guidelines and any intended use of N/A
 2
 3 authorship professional writers
 4
 5

6 Dissemination policy: [#31c](#) Plans, if any, for granting public access to the full N/A
 7
 8 reproducible protocol, participant-level dataset, and statistical code
 9
 10 research
 11
 12

13 Appendices

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 16
 17 Informed consent [#32](#) Model consent form and other related documentation No
 18
 19 materials given to participants and authorised surrogates
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 21

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 23 Biological specimens [#33](#) Plans for collection, laboratory evaluation, and storage of N/A
 24
 25 biological specimens for genetic or molecular analysis in
 26
 27 the current trial and for future use in ancillary studies, if
 28
 29 applicable
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 33 None The SPIRIT checklist is distributed under the terms of the Creative Commons Attribution
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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

Journal:	<i>BMJ Open</i>
Manuscript ID	bmjopen-2020-041234.R1
Article Type:	Protocol
Date Submitted by the Author:	22-Oct-2020
Complete List of Authors:	Morton, Kathryn; University Hospital Southampton NHS Foundation Trust, PICU; University of Southampton, School of Health Sciences Darlington, Anne-Sophie; University of Southampton, School of Health Sciences Marino, LV; University Hospital Southampton NHS Foundation Trust, Department of Dietetics/SLT,
Primary Subject Heading:	Intensive care
Secondary Subject Heading:	Paediatrics, Nutrition and metabolism
Keywords:	NUTRITION & DIETETICS, Paediatric intensive & critical care < ANAESTHETICS, PAEDIATRICS, Paediatric intensive & critical care < INTENSIVE & CRITICAL CARE, Paediatric intensive & critical care < PAEDIATRICS

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

3
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21
22 **Keywords:** feeding difficulties, children, critical illness, survivors

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For peer review only

29 **Abstract**

30 **Introduction**

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

39 **Methods and analysis**

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

50 **Ethics and dissemination**

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

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

For peer review only

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2
3 59 **Article summary**

4 60

5 61 **Strengths:**

- 6
7
8 62 • A strength of this study is that it is the first multicentre, longitudinal study to investigate
9
10 63 feeding and survivorship outcomes in young paediatric intensive care (PICU) survivors, in the
11
12 64 first 6-months post-discharge.
13
14 65 • By using a mixed methods design, this study will provide a greater breadth of understanding
15
16 66 into the prevalence and impact of feeding issues in previously healthy young children who
17
18 67 survive PICU.
19
20
21 68 • A strength of this study's qualitative data collection method (interviews with
22
23 69 parents/caregivers) lies in its ability to generate a rich narrative data set exploring the
24
25 70 survivorship journey of families post-PICU.
26
27
28 71 • The longitudinal study design will allow us to explore any feeding difficulties over a 6-month
29
30 72 period post-PICU, potentially identifying transient and persistent problems.
31
32

33 73 **Limitations:**

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36
37 74 • A limitation to the study's longitudinal design lies in its potential for high attrition which
38
39 75 may affect data at six months, challenging the internal validity of the reported results.
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42 76

77 Introduction

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

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

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

1
2
3 100 Feeding is a complex learned behaviour, occurring during infancy involving
4
5 101 developmental maturation to coordinate the process of sucking, swallowing and breathing. This
6
7 102 then advances into chewing and texture control, (21). There is also a social aspect of feeding,
8
9 103 involving parental - child interactions,(22) with parental behaviours and feeding styles directly
10
11 104 influencing feeding behaviours of young children,(20, 23). Parental feeding styles have been
12
13 105 shown to influence food enjoyment, fussiness, food responsiveness, food neophobia, and self-
14
15 106 regulation in children,(22). Parental feeding interactions and practices during childhood cancer
16
17 107 treatment, for example, include pressurising children to eat, using food as rewards and bribes
18
19 108 and being overindulgent, with the stress of eating having a negative effect on the parental-child
20
21 109 relationship (3, 24). There is, however, no evidence looking at feeding difficulties and parental-
22
23 110 child feeding interactions associated with feeding in the previously healthy PICU population (25).
24
25
26
27 111 Although there is some information describing feeding outcomes in children born prematurely
28
29 112 and young children with CHD, there remains a lack of high-quality evidence. The consequence of
30
31 113 an admission to PICU on the ability of young children to eat and drink initially after PICU
32
33 114 discharge and then once home, and the implications this has for young children and their
34
35 115 families, is not known.
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41 117 **Methods and analysis**

42 118 **Study aims**

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45 119 The PIES study (Feeding and survivorship outcomes in previously healthy young
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47 120 Paediatric Intensive Care Survivors) has six specific objectives:
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49
50 121 1. To characterise and measure the prevalence of feeding difficulties in previously healthy
51
52 122 children (≤ 4 years) who survive critical illness during the first 6 months after PICU
53
54 123 discharge;
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3 124 2. To identify clinical predictors for the development of feeding difficulties in previously
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5 125 healthy young children (≤ 4 years) who survive critical illness;
6
7 126 3. To identify parental/caregiver feeding styles for previously healthy young children (≤ 4
8
9 127 years) who survive critical illness;
10
11 128 4. To measure parental stress in parents/caregivers of previously healthy young children (\leq
12
13 129 4 years) who survive critical illness;
14
15 130 5. To identify behaviours of previously healthy young children (≤ 4 years) who survive
16
17 131 critical illness;
18
19 132 6. To develop an in-depth understanding of how parents/caregivers of previously healthy
20
21 133 young children (≤ 4 years old) who survive critical illness construct, experience and make
22
23 134 sense of their survivorship journey from PICU admission, specifically looking at feeding
24
25 135 experiences and parental-child relationships.
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30 **Study design**

31
32 137 Based on the research question and objectives, a prospective, longitudinal mixed
33
34 138 methods design will be used. Quantitative and qualitative data will be collected simultaneously
35
36 139 over several times points, analysed separately and then integrated giving equal emphasis to
37
38 140 each strand,(26). Parents/caregivers of children will be asked to take part in a longitudinal
39
40 141 survey, completing questionnaires considering aspects relating to; feeding difficulties,
41
42 142 parental/caregiver stress, child and parental/caregivers feeding behaviours at the point of PICU-
43
44 143 discharge and at 1, 3 and 6 months post-discharge. Parents/caregivers will also be invited to
45
46 144 participate in qualitative semi-structured interviews at 3 and 6 months post-PICU-discharge,
47
48 145 which will explore parental/caregiver experiences of feeding their child post-PICU. Routinely
49
50 146 collected clinical data about the PICU admission will additionally be collected. See figure 1 for
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52 147 schematic overview of the study design.
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148 **Setting**

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

151 **Sample and recruitment**152 **Eligibility criteria**

153 The chosen inclusion criteria will allow recruitment of previously healthy young children
 154 (≤ 4 years) who are admitted to PICU both electively and in emergency situations. Participants
 155 will be eligible if they are parents/caregivers (aged ≥ 18 years of age) of a previously healthy
 156 child aged ≤ 4 years who has received invasive ventilation for 48 hours or more (including at
 157 referring hospital if applicable) (Table 1).

158 **Table 1: Eligibility criteria**

Inclusion criteria	Rationale
Parents/caregivers (aged ≥ 18 years of age) of previously healthy children aged ≤ 4 years 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: <ul style="list-style-type: none"> • 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).

<ul style="list-style-type: none"> • 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

159

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

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

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3 172 • To identify feeding difficulties that might occur during the transition to
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5 173 autonomous child self-feeding during pre-school years;
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7 174 • To identify extreme cases of behaviour often associated with picky or fussy
8
9 175 behaviour in preschool aged children.
10
11 176 • Once children start school (> 4 years of age), parents often have less control
12
13 177 over lunchtime behaviours and food intake, (30).
14
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16 178 The exclusion of non-English speaking families is a limitation of the study design in terms of
17
18 179 selection bias and may affect the generalisability of the results. This will be investigated in the
19
20 180 interpretations of the study results and implications for clinical practice.
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22

23 181 **Sample size**

24
25 182 Quantitative study: The sample size is based on estimating prevalence to a certain level
26
27 183 of precision as defined by a 95% confidence interval. Assuming a potentially low prevalence of
28
29 184 just 20% (which is less than the NICU and CHD population owing to their underlying baseline
30
31 185 disease,(31-35)), a sample size of 204 child participants would be sufficient to estimate feeding
32
33 186 difficulty prevalence. Anticipating a 40% drop-out, as often seen with online surveys,(36, 37), an
34
35 187 initial recruitment of 340 participants is required. We anticipate enrolling those participants
36
37 188 from 10 PICUs over a 12-month period. It is expected that recruitment numbers will vary across
38
39 189 the sites and across the recruitment period, accounting for seasonal admissions involving
40
41 190 healthy children being admitted for bronchiolitis and other respiratory and/or septic illness in
42
43 191 the winter months. Recruitment targets will be discussed at each site set up, with the allowance
44
45 192 of over-recruiting in larger sites where possible.
46
47

48
49 193 Qualitative study: A realistic and pragmatic sample size of 15 to 20 parents/caregivers
50
51 194 will be interviewed at 3 and 6 months after PICU discharge, with the aim of increasing research
52
53 195 knowledge in this unknown field. We recognise that we may not achieve data saturation with
54
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196 this sample size, as there are many different influences and variables surrounding the child's
 197 PICU admission, parent/caregivers feeding experiences and survivorship journeys. However, this
 198 limitation will be acknowledged, investigated and discussed in the data analysis and future
 199 reporting of any study results, including the impact this may have on the study's credibility and
 200 generalisability.

201 **Sampling strategy**

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

212 **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%)

213

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

218 **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 sequelae associated with emergency verses planned admissions to PICU (38)
Age of child: <ul style="list-style-type: none"> • ≤ 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)

219

220 Study Measures

221 Longitudinal follow-up survey

1
2
3 222 The outcome measures for the longitudinal follow-up survey have been selected based
4
5 223 on their validity, reliability, use in previous paediatric populations and ease of use for
6
7 224 participants. Pre-existing validated questionnaires will be used to measure feeding difficulty
8
9 225 assessment, parental stress, parental feeding styles and child behaviour. To obtain longitudinal
10
11 226 outcome data and potentially identify acute and/or chronic feeding difficulties, data from the
12
13 227 questionnaires will be collected at four-time points: at PICU discharge (retrospective data), 1, 3
14
15 228 and 6 months after PICU discharge. The outcomes measures and time points are outlined in
16
17 229 Table 4. The questionnaires have also been selected according to age of the child participant, in
18
19 230 addition to tested psychometric properties.
20
21
22
23

24 231 Feeding difficulty assessment measures:

- 25
26
27 232 • Infant feeding questionnaire,(40) (7 items; up to 9 month old babies)
28
29 233 • Behavioral Pediatric Feeding Assessment Scale,(41) (35 items; 9 months old to 7 years).
30
31

32 234 Parental stress measure:

- 33
34
35 235 • Parental Stress Scale,(42) (18 items).
36
37

38 236 Parental feeding style measures:

- 39
40
41 237 • Infant feeding questionnaire,(43) (25 items; up to 2 years)
42
43 238 • Child feeding questionnaire,(44) (28 items; from 2 years onwards).
44
45

46 239 Child behaviour measures

- 47
48
49 240 • Infant behaviour questionnaire – very short version,(45) (36 items; up to 12 months)
50
51 241 • Child behaviour questionnaire – very short version, (46) (35 items; from 1 year)
52
53

54 242 **Demographic Information:**
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1
2
3 243 At each survey, parental factors, family variables and socio-economic data will be
4
5 244 collected to identify any relationship between family background and the development of
6
7 245 feeding difficulties for young survivors of critical illness. This includes parental/caregiver:

- 10 246
- Ethnic origin
- 13 247
- Age
- 16 248
- Gender
- 19 249
- Highest level of education
- 22 250
- Living situation
- 25 251
- Employment status
- 28 252
- Siblings in household.

31 253 **Routinely collected clinical PICU data:**

34 254 For all recruited patients, data already recorded during the child's PICU admission will
35
36 255 be captured on a paper or electronic Case Report Form completed by the RC research nurse,
37
38 256 a clinical team member delegated by the local PI or by the Chief Investigator at a later date.

40
41 257 The variables of interest have been identified as:

- 43 258
- Length of PICU stay (in hours)
- 46 259
- Length of intubation (in hours)
- 49 260
- Length of mechanical invasive ventilation (in hours)
- 52 261
- Number of (re) intubations
- 55 262
- Type of ETT (oral or nasal)

- 1
2
3 263 • Length of non-invasive ventilation (in hours and mode)
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5
6 264 • Inotrope requirement (yes/no)
7
8
9 265 • Mode of feeding during PICU admission (enteral, bolus or continuous, parental
10
11 266 nutrition, oral diet, location of feeding tube)
12
13
14 267 • Time from extubation to commence oral feeding (in hours)
15
16
17 268 • Mode of feeding at PICU discharge
18
19
20 269 • Documented evidence of gastric intolerance (vomiting, diarrhea, abdominal
21
22 270 distention).
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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 <i>or</i> 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 <i>or</i> Child Feeding Questionnaire	X	X	X	X
Child behaviour measures				
Infant Behavior Questionnaire (very-short version) <i>or</i> Early Childhood Behavior Questionnaire	X	X	X	X
Qualitative interviews:				
Invitation	X			
Interviews			X	X

273

274 **Qualitative study**

1
2
3 275 The main aim of the semi-structured qualitative interviews are to develop an in-depth
4
5 276 understanding of how parents/caregivers of previously healthy young children (≤ 4 years old)
6
7 277 who survive critical illness construct, experience and make sense of their survivorship journey
8
9
10 278 from PICU admission, specifically looking at feeding experiences and parental-child behaviours.
11
12 279 Parents will be interviewed at approximately 3 and 6 months post-PICU discharge so that they
13
14 280 can describe how and/or if their experiences are changing (or have changed) along the PICU
15
16 281 survivorship journey.
17
18
19 282

21 283 **Study procedures**

22
23 284 Quantitative study: Over a 12-month period, each site will screen all children admitted
24
25 285 to PICU and invite all eligible children and their parents/caregivers to participate in the study.
26
27 286 Site investigators (or their designated nominee) who are part of the PICU clinical care team will
28
29 287 determine eligibility. Parents/caregivers could be approached to take part in the study when the
30
31 288 child is still in PICU, near to or at discharge, on the High Dependency Unit or hospital ward soon
32
33 289 after being discharged from PICU. Once informed consent has been obtained,
34
35 290 parents/caregivers will be asked to complete baseline questionnaires (paper or online options
36
37 291 available). Parent/caregiver contact details will be obtained and securely recorded on a
38
39 292 password protected database to enable follow-up survey distribution at 1, 3 and 6 months.
40
41 293 Follow-up survey data will be collected using either online or paper questionnaires as agreed by
42
43 294 the parents/caregivers at recruitment. Two fortnightly reminders will be sent for the follow-up
44
45 295 surveys as reminder letters, telephone calls, messages or email by the lead researcher (KM) as
46
47 296 agreed with the participant at recruitment. As there is such a small-time frame between 1 and 3
48
49 297 month assessments, if no response is received following the 1-month survey, participants will
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1
2
3 298 still be approached at 3 months. If there is no response at this point however, they will not be
4
5 299 approached again at 6 months.

6
7 300 *Qualitative study:* During recruitment into the multicentred survey, parents/caregivers
8
9 301 will be invited to take part in the qualitative interviews. Those who consent to an interview will
10
11 302 be approached by the lead researcher (KM) at the time in which reminders of the follow-up
12
13 303 survey are sent (at 1, 3 and 6 months) either by reminder letters, telephone call, messages or
14
15 304 email as agreed at recruitment. Semi-structured open-ended questions will be used as the
16
17 305 primary method of data collection to allow the parent/caregiver to describe their story,
18
19 306 communicate their experiences, feelings and PICU survivorship journey. In response to PPI
20
21 307 feedback highlighting the lack of spare time that parents/caregivers of young children often
22
23 308 face, telephone and internet (i.e. Microsoft teams: Microsoft 365, UK) interviews will be
24
25 309 conducted at a time convenient for the parent/caregiver which could include evenings and
26
27 310 weekends.

311 312 **Data analysis**

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

318 **Quantitative study data analysis**

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

1
2
3 322 frequency counts and percentages for categorical data. Data will be examined for normality,
4
5 323 outliers and for missing data. Statistical analysis will be completed using the IBM Statistical
6
7 324 Package for Social Science (SPSS) and statistical significance will be set at $p < 0.05$.

8
9
10 325 Analyses related to the study specific objectives include the following:

11
12 326 *Objective 1: To characterise and measure the prevalence of feeding difficulties in*
13
14 327 *previously healthy children (≤ 4 years) who survive critical illness during the first 6 months after*
15
16 328 *PICU discharge. From the feeding difficulty assessment measures, descriptive statistics*
17
18 329 *(frequency counts and percentages) will be used to identify the numbers and types of feeding*
19
20 330 *difficulties at each time point collected and for different age groups.*

21
22
23 331 *Objective 2: To identify clinical predictors for the development of feeding difficulties in*
24
25 332 *previously healthy young children (≤ 4 years) who survive critical illness. The information from*
26
27 333 *the routinely collected clinical PICU data will be used to identify any clinical predictors for the*
28
29 334 *development of feeding difficulties, such as length of intubation and time to commence oral*
30
31 335 *feeding. Statistical analysis will involve multiple +/- linear regressions to see if we can predict*
32
33 336 *feeding difficulty questionnaire scores from the clinical variables.*

34
35
36
37 337 *Objective 3: To identify parental/caregiver feeding styles for previously healthy young*
38
39 338 *children (≤ 4 years) who survive critical illness. Descriptive statistics will be initially performed to*
40
41 339 *identify the frequency of participants in each parental feeding style, to identify the majority.*
42
43 340 *This will then be repeated at each time point collected, to identify a change (or not) in parental*
44
45 341 *feeding style across the 6 months from PICU discharge. If have enough data, differences*
46
47 342 *between mother feeding styles and father feeding styles will be calculated using Mann-Whitney*
48
49 343 *U (non- parametric) or t-Test (parametric) tests as appropriate. The relationship between*
50
51 344 *parental feeding style and feeding difficulty score will also be tested using the same statistical*
52
53 345 *tests.*

1
2
3 346 *Objective 4: To measure parental stress in parents/caregivers of previously healthy*
4
5 347 *young children (≤ 4 years) who survive critical illness. Using the scores from the parental stress*
6
7 348 *scale, average parental stress scores for all participants will be calculated at all time points.*
8
9 349 *Average parental stress score at each time point, for those parents of children with and without*
10
11 350 *feeding difficulties, will also be presented to identify the trajectories of parental stress over time*
12
13 351 *and between the two groups. Correlation and regression analysis will be used to investigate*
14
15 352 *relationships between increasing feeding difficulty score and increasing parental stress score*

16
17 353 *Objective 5: To identify behaviours of previously healthy young children (≤ 4 years) who*
18
19 354 *survive critical illness. Frequency of children in each temperament category from the Infant and*
20
21 355 *Early Child Behavior questionnaires will be calculated and presented at each data collection time*
22
23 356 *point, so observe for changes over time. The relationship between infant/child temperament*
24
25 357 *and feeding difficulty score; and parental feeding style and parental stress score will be assessed*
26
27 358 *using Mann-Whitney U (non- parametric) or t-Test (parametric) and regression models where*
28
29 359 *appropriate.*

30 360 **Qualitative study data analysis**

31
32 361 *All interviews will be audio-recorded and transcribed verbatim. All data will be imported*
33
34 362 *into a qualitative data analysis package (NVivo), which will assist in managing, sorting and coding*
35
36 363 *the vast data set. Data analysis will be largely conducted by KM, with the other researchers*
37
38 364 *(ASD, LVM) verifying the findings for consistencies and discrepancies to maximise credibility and*
39
40 365 *reliability,(47). Data analysis will involve three stages:1) narrative analysis, 2) thematic analysis*
41
42 366 *and 3) integration and will look to answer study objective 6: To develop an in-depth*
43
44 367 *understanding of how parents/caregivers of previously healthy young children (≤ 4 years old)*
45
46 368 *who survive critical illness construct, experience and make sense of their survivorship journey*
47
48 369 *from PICU admission, specifically looking at feeding experiences and parental-child relationships.*

370

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

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

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

388

389 **Data integration strategy of quantitative and qualitative data**

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

1
2
3 394 told by them,(51). The information gained from the interviews will assist interpretation and
4
5 395 analysis of the survey results, drawing conclusions to the clinical significance of the results with
6
7 396 implications for clinical practice,(52).
8
9

10 397

11 398 **Public and patient involvement**

12
13
14 399 Guided by the NIHR INVOLVE recommendations,(53), involvement of families of children
15
16 400 recently discharged from PICU was sought during the study design process. Six parents
17
18 401 volunteered to provide guidance and advice during an organised coffee morning. Collectively,
19
20 402 the importance of the study was recognised, and recommendations made to the recruitment
21
22 403 process and data collection methods. Feedback included using an online questionnaire for ease
23
24 404 of use and to increase follow-up completion. The survey questions were also piloted by parents,
25
26 405 assessing the clarity of the questionnaires and their instructions and to consider the burden of
27
28 406 completing all four questionnaires. Offering home, telephone and internet interviews was also
29
30 407 suggested for the interviews.
31
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33

34 408

35 409 **Ethics and Dissemination**

36 410 **Informed consent**

37
38
39 411 Parents/caregivers will be approached to take part in The PIES study once the child
40
41 412 meets the inclusion/exclusion criteria. After being given an ethically approved Participant
42
43 413 Information Sheet (PIS), parents/caregivers will be given at least 48 hours to consider
44
45 414 participation, unless they are happy to give informed consent before this time. It is anticipated
46
47 415 that the children eligible for the study will be too young and/or too ill to participate directly in
48
49 416 the consent process. Each parent/caregiver will complete a contact form that will record the
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2
3 417 information needed for the follow-up survey distribution (e.g. mail addresses, telephone
4
5 418 numbers) and informed consent will be obtained to allow the sharing of this personal data.
6

7
8 419 **Researching sensitive and emotive topics**
9

10
11 420 It is recognised that parents/caregivers of previously healthy young children who have
12
13 421 survived critical illness may have psychological sequelae (i.e. post-traumatic stress disorder)
14
15 422 following their child's admission to PICU,(38). Although not specifically asking about their PICU
16
17 423 experience, completing the survey and taking part in the interviews may raise potentially
18
19 424 distressing issues around difficult feeding and/or mealtime behaviours following the PICU
20
21 425 admission. Initial instances of distress will be dealt by the researcher and supported by the PICU
22
23 426 psychology team at the researchers host institution. The researcher will also signpost the
24
25 427 participants to the Patient Advice and Liaison Services (PALS), clinical psychology team based at
26
27 428 Southampton Children's Hospital and other local healthcare teams.
28
29
30

31
32 429 **Burden**
33

34
35 430 The survey is compiled of four separate pre-existing validated questionnaires, asked at
36
37 431 four separate timepoints during the enrolment and follow-up (at recruitment, at 1, 3 and 6
38
39 432 months after PICU discharge). The questionnaires include Likert scales, yes/no answers and
40
41 433 drop-down options. The survey questions and instructions have been piloted by parents of
42
43 434 young children, assessing the clarity of the questionnaires, the instructions and consideration of
44
45 435 the time and mental burden in completing all four questionnaires. Average time for survey
46
47 436 completion was 15 minutes, with follow-up surveys thought to be quicker. We endeavour to
48
49 437 reduce this burden by having the option of an online electronic survey available to parents and
50
51 438 by adding the feature where you can 'save and go back to later' option within the survey. The
52
53 439 PIS will clearly state that there will be no financial gain from taking part in the study. Conversely,
54
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1
2
3 440 some participants might find taking part in the study beneficial because they will have the time
4
5 441 and space to think about issues which are important to them.
6

7 442 **Ethical review**

8
9
10 443 The Yorkshire and The Humber – South Yorkshire Research Ethics Committee has
11
12 444 reviewed the study protocol and provided favourable opinion (Ref: 20/YH/0160). The Health
13
14 445 Research Authority has also approved the protocol (IRAS: 279171). This study has been
15
16 446 extensively peer reviewed through the University of Southampton and forms the PhD study of
17
18 447 the first author.
19
20

21 448

22 23 449 **Methods of dissemination**

24
25 450 This paper is part of the dissemination plan of the PIES study, by presenting the project
26
27 451 background, providing a detailed description of methods and procedures used to collect and
28
29 452 analyse the data. Other dissemination plans involve local, national and international audiences
30
31 453 including academics, health care professionals, healthcare commissioners, charities and the
32
33 454 public. Dissemination will include written and oral feedback to the PPI group, local PICU charity
34
35 455 and each recruitment centre. Presentations to local and national research and clinical teams will
36
37 456 take place, including research meetings and conferences. The findings from this study will
38
39 457 contribute to addressing the significant gaps in the literature by investigating the prevalence of
40
41 458 and predictors for feeding difficulties experienced by previously healthy young children who
42
43 459 survive critical illness and explore the effect on parental feeding experiences, behaviours and
44
45 460 stress. It is anticipated that the expected outputs of this proposed project will be in terms of
46
47 461 high quality, peer-reviewed scientific publications and conference presentations. During the
48
49 462 informed consent process, parents/caregivers will be asked if they would like a lay summary of
50
51 463 any study findings sent to them at the end of the study.
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8 604 **Acknowledgements**

9
10 605 The PIES study protocol was developed by KM, LVM and ASD. The corresponding author would
11
12 606 like to acknowledge LVM and ASD in their supervisory support during KM's PhD in which The
13
14 607 PIES Study has been developed. KM would like to acknowledge the University of Southampton
15
16 608 and University Hospital Southampton NHS Foundation Trust in supporting and funding her PhD
17
18 609 through the Wessex Clinical Doctoral Research Fellowship scheme, and the clinical team at
19
20 610 Southampton Children's Hospital PICU in allowing KM the clinical backfill time to undertake her
21
22 611 PhD. Furthermore, KM would like to acknowledge Kevin Wheeler (Clinical Informatics Research
23
24 612 Unit, Southampton) for his support and patience in developing the PIES study data capture and
25
26 613 management through the ALEA database/eCRF.
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32 615 **Conflict of interest**

33
34 616 None declared
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39 618 **Statement of authorship**

40
41 619 Authors made the following contribution to the manuscript:

- 42
43 620 (1) KM formulated the original research idea, conducted the literature searching and is the
44
45 621 chief investigator for the study,
46
47 622 (2) KM drafted the manuscript from the ethically approved protocol (which was originally
48
49 623 supported by LVM and ASD)
50
51 624 (3) LVM, ASD and KM reviewed and revised the manuscript for important intellectual
52
53 625 content, and (4) all authors provided final approval of the version to be submitted.
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5 627 **Data Statement**
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7 628 Technical appendix, statistical code, and dataset for The PIES study will be available from the
8

9
10 629 University of Southampton Institutional Research Repository, ePrints Soton
11

12 630 (<https://eprints.soton.ac.uk/>)
13

14 631
15

16
17 632 **Funding**
18

19 633 This report describes independent research arising from a personal Clinical Doctoral Research
20

21 634 Fellowship for Kathryn Morton, supported jointly by the University of Southampton and
22

23 635 University Hospital Southampton NHS Foundation Trust, England.
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28 637 **Figure 1 for schematic overview of the study design**
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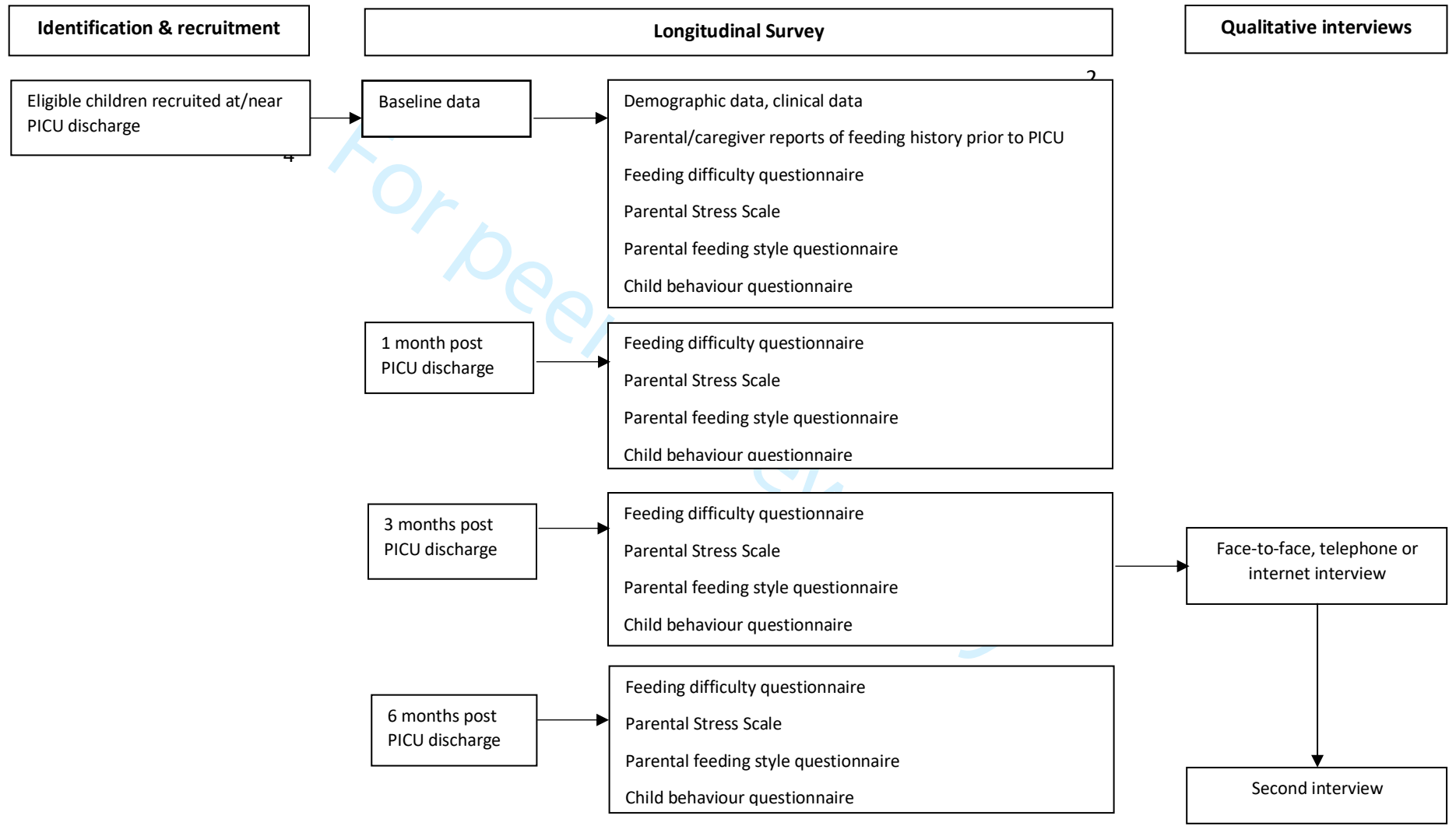
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For peer review only

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1 **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.

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

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

Chan A-W, Tetzlaff JM, Altman DG, Laupacis A, Gøtzsche PC, Krleža-Jerić K, Hróbjartsson A, Mann H, Dickersin K, Berlin J, Doré C, Parulekar W, Summerskill W, Groves T, Schulz K, Sox H, Rockhold FW, Rennie D, Moher D. SPIRIT 2013 Statement: Defining standard protocol items for clinical trials. *Ann Intern Med.* 2013;158(3):200-207

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

1	Trial registration	#2a	Trial identifier and registry name. If not yet registered,	N/A
2			name of intended registry	
3				
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6	Trial registration:	#2b	All items from the World Health Organization Trial	NA
7	data set		Registration Data Set	
8				
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11	Protocol version	#3	Date and version identifier	3
12				
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15	Funding	#4	Sources and types of financial, material, and other	27
16			support	
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20	Roles and	#5a	Names, affiliations, and roles of protocol contributors	1 and 25
21	responsibilities:			
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23	contributorship			
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28	Roles and	#5b	Name and contact information for the trial sponsor	27
29	responsibilities:			
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31	sponsor contact			
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33	information			
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38	Roles and	#5c	Role of study sponsor and funders, if any, in study	N/A
39	responsibilities:		design; collection, management, analysis, and	
40			interpretation of data; writing of the report; and the	
41	sponsor and funder		decision to submit the report for publication, including	
42			whether they will have ultimate authority over any of	
43			these activities	
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52	Roles and	#5d	Composition, roles, and responsibilities of the	N/A
53	responsibilities:		coordinating centre, steering committee, endpoint	
54			adjudication committee, data management team, and	
55	committees			
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1 other individuals or groups overseeing the trial, if
 2
 3 applicable (see Item 21a for data monitoring committee)
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 5

6 Introduction

9 Background and [#6a](#) Description of research question and justification for
 10
 11 rationale undertaking the trial, including summary of relevant
 12
 13 studies (published and unpublished) examining benefits
 14
 15 and harms for each intervention
 16
 17 From
 18 page 4

19 Background and [#6b](#) Explanation for choice of comparators
 20
 21 rationale: choice of
 22
 23 comparators
 24
 25 N/A

26 Objectives [#7](#) Specific objectives or hypotheses
 27
 28 6

29 Trial design [#8](#) Description of trial design including type of trial (eg,
 30
 31 parallel group, crossover, factorial, single group),
 32
 33 allocation ratio, and framework (eg, superiority,
 34
 35 equivalence, non-inferiority, exploratory)
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39 Methods:

41 Participants,
 42
 43 interventions, and
 44
 45 outcomes
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 47
 48

49 Study setting [#9](#) Description of study settings (eg, community clinic,
 50
 51 academic hospital) and list of countries where data will
 52
 53 be collected. Reference to where list of study sites can
 54
 55 be obtained
 56
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 60 7 and 10

1	Eligibility criteria	#10	Inclusion and exclusion criteria for participants. If	11
2			applicable, eligibility criteria for study centres and	
3			individuals who will perform the interventions (eg,	
4			surgeons, psychotherapists)	
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11	Interventions:	#11a	Interventions for each group with sufficient detail to allow	N/A
12			replication, including how and when they will be	
13	description		administered	
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19	Interventions:	#11b	Criteria for discontinuing or modifying allocated	N/A
20			interventions for a given trial participant (eg, drug dose	
21	modifications		change in response to harms, participant request, or	
22			improving / worsening disease)	
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29	Interventions:	#11c	Strategies to improve adherence to intervention	N/A
30			protocols, and any procedures for monitoring adherence	
31	adherence		(eg, drug tablet return; laboratory tests)	
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36	Interventions:	#11d	Relevant concomitant care and interventions that are	N/A
37			permitted or prohibited during the trial	
38	concomitant care			
39				
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41				
42	Outcomes	#12	Primary, secondary, and other outcomes, including the	7
43			specific measurement variable (eg, systolic blood	
44			pressure), analysis metric (eg, change from baseline,	
45			final value, time to event), method of aggregation (eg,	
46			median, proportion), and time point for each outcome.	
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53			Explanation of the clinical relevance of chosen efficacy	
54			and harm outcomes is strongly recommended	
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1	Participant timeline	#13	Time schedule of enrolment, interventions (including any	8
2			run-ins and washouts), assessments, and visits for	
3			participants. A schematic diagram is highly	
4			recommended (see Figure)	
5				
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11	Sample size	#14	Estimated number of participants needed to achieve	12
12			study objectives and how it was determined, including	
13			clinical and statistical assumptions supporting any	
14			sample size calculations	
15				
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21	Recruitment	#15	Strategies for achieving adequate participant enrolment	14
22			to reach target sample size	
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26	Methods:			
27				
28	Assignment of			
29	interventions (for			
30	controlled trials)			
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36	Allocation: sequence	#16a	Method of generating the allocation sequence (eg,	N/A
37	generation		computer-generated random numbers), and list of any	
38			factors for stratification. To reduce predictability of a	
39			random sequence, details of any planned restriction (eg,	
40			blocking) should be provided in a separate document that	
41			is unavailable to those who enrol participants or assign	
42			interventions	
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53	Allocation	#16b	Mechanism of implementing the allocation sequence (eg,	N/A
54	concealment		central telephone; sequentially numbered, opaque,	
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58	mechanism			
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sealed envelopes), describing any steps to conceal the sequence until interventions are assigned

Allocation: [#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): [#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

1	Data collection plan:	#18b	Plans to promote participant retention and complete	15
2				
3	retention		follow-up, including list of any outcome data to be	
4			collected for participants who discontinue or deviate from	
5			intervention protocols	
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11	Data management	#19	Plans for data entry, coding, security, and storage,	N/A
12			including any related processes to promote data quality	
13			(eg, double data entry; range checks for data values).	
14			Reference to where details of data management	
15			procedures can be found, if not in the protocol	
16				
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23	Statistics: outcomes	#20a	Statistical methods for analysing primary and secondary	15
24			outcomes. Reference to where other details of the	onwards
25			statistical analysis plan can be found, if not in the	
26			protocol	
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33	Statistics: additional	#20b	Methods for any additional analyses (eg, subgroup and	15
34	analyses		adjusted analyses)	onwards
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39	Statistics: analysis	#20c	Definition of analysis population relating to protocol non-	15
40	population and		adherence (eg, as randomised analysis), and any	
41	missing data		statistical methods to handle missing data (eg, multiple	
42			imputation)	
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48	Methods: Monitoring			
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51	Data monitoring:	#21a	Composition of data monitoring committee (DMC);	N/A
52	formal committee		summary of its role and reporting structure; statement of	
53			whether it is independent from the sponsor and	
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1 competing interests; and reference to where further
 2 details about its charter can be found, if not in the
 3 protocol. Alternatively, an explanation of why a DMC is
 4 not needed
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10	Data monitoring:	#21b	Description of any interim analyses and stopping	N/A
11	interim analysis		guidelines, including who will have access to these	
12			interim results and make the final decision to terminate	
13			the trial	
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20	Harms	#22	Plans for collecting, assessing, reporting, and managing	No
21			solicited and spontaneously reported adverse events and	
22			other unintended effects of trial interventions or trial	
23			conduct	
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30	Auditing	#23	Frequency and procedures for auditing trial conduct, if	No
31			any, and whether the process will be independent from	
32			investigators and the sponsor	
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38	Ethics and			
39	dissemination			
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43	Research ethics	#24	Plans for seeking research ethics committee / institutional	21
44	approval		review board (REC / IRB) approval	
45				
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48	Protocol	#25	Plans for communicating important protocol modifications	21
49	amendments		(eg, changes to eligibility criteria, outcomes, analyses) to	
50			relevant parties (eg, investigators, REC / IRBs, trial	
51			participants, trial registries, journals, regulators)	
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1	Consent or assent	#26a	Who will obtain informed consent or assent from potential	14 and
2			trial participants or authorised surrogates, and how (see	19
3			Item 32)	
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9	Consent or assent:	#26b	Additional consent provisions for collection and use of	N/A
10	ancillary studies		participant data and biological specimens in ancillary	
11			studies, if applicable	
12				
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16	Confidentiality	#27	How personal information about potential and enrolled	14/15
17			participants will be collected, shared, and maintained in	
18			order to protect confidentiality before, during, and after	
19			the trial	
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26	Declaration of	#28	Financial and other competing interests for principal	N/A
27	interests		investigators for the overall trial and each study site	
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31	Data access	#29	Statement of who will have access to the final trial	26
32			dataset, and disclosure of contractual agreements that	
33			limit such access for investigators	
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39	Ancillary and post	#30	Provisions, if any, for ancillary and post-trial care, and for	N/A
40	trial care		compensation to those who suffer harm from trial	
41			participation	
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47	Dissemination policy:	#31a	Plans for investigators and sponsor to communicate trial	21
48	trial results		results to participants, healthcare professionals, the	
49			public, and other relevant groups (eg, via publication,	
50			reporting in results databases, or other data sharing	
51			arrangements), including any publication restrictions	
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1 Dissemination policy: [#31b](#) Authorship eligibility guidelines and any intended use of N/A
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 3 authorship professional writers
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6 Dissemination policy: [#31c](#) Plans, if any, for granting public access to the full N/A
 7
 8 reproducible protocol, participant-level dataset, and statistical code
 9
 10 research
 11
 12

13 Appendices

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 16
 17 Informed consent [#32](#) Model consent form and other related documentation No
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 19 materials given to participants and authorised surrogates
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 23 Biological specimens [#33](#) Plans for collection, laboratory evaluation, and storage of N/A
 24
 25 biological specimens for genetic or molecular analysis in
 26
 27 the current trial and for future use in ancillary studies, if
 28
 29 applicable
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 33 None The SPIRIT checklist is distributed under the terms of the Creative Commons Attribution
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 36
 37 tool made by the [EQUATOR Network](#) in collaboration with [Penelope.ai](#)
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