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Research Priorities for Pediatric Intensive Care Nutrition Within the United Kingdom: A National Institute of Health Research James Lind Alliance Priority Setting Partnership

OBJECTIVES: To determine research priorities in PICU nutrition, which represent the shared priorities of patients, parents, carers, and PICU healthcare professionals within the United Kingdom.

DESIGN: A national multiphase priority setting methodology in partnership with the James Lind Alliance delivered over 16 months (June 2020–September 2021). Part 1: a national scoping survey asked respondents to submit their research uncertainties related to PICU nutrition. Part 2: summarizing and evidence-checking the submitted uncertainties. Part 3: interim prioritization survey. Part 4: consensus workshop.

SETTING: PICU.

PARTICIPANTS: Patients, parents, and carers of patients who had been admitted to PICU, and PICU healthcare professionals involved in the treatment of these patients within the United Kingdom.

INTERVENTIONS: None.

MEASUREMENTS AND MAIN RESULTS: A national scoping survey asked respondents to submit their research uncertainties related to PICU nutrition. In the first survey, 165 topic ideas were suggested (12% by parents/carers and 88% by PICU healthcare professionals). These were categorized into 57 summary questions. The existing evidence was searched to ensure that the proposed summary questions had not already been answered. Forty were judged to be true uncertainties following a systematic literature review. These 40 uncertainties were grouped into eight themes for the second interim survey, which asked respondents to prioritize their top research questions. One hundred and forty participants contributed to this second interim survey. A final shortlist of 25 questions was derived, with the top 18 questions taken to a multistakeholder workshop where a consensus was reached on the top 10 priorities.

CONCLUSIONS: This research identified important research gaps in the management of patients in PICU. Areas that need to be addressed as a priority include energy requirements in ventilated neonates, nutritional supplementation of probiotics to manage and prevent sepsis, the impact of postintensive care syndrome on nutrition and growth, and when to commence parenteral (IV) nutrition. The challenge now is to refine and deliver answers to these research priorities.

KEY WORDS: James Lind Alliance; National Institute of Health Research; nutrition support; paediatric intensive care; paediatric nutrition; research priorities

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The James Lind Alliance (JLA) is a nonprofit organization hosted by the National Institute of Health Research (NIHR) with the aim of raising awareness of research, which is directly relevant and of potential benefit to

patients and healthcare professionals. The guiding principle is to bring together patients, parents, carers, and healthcare professionals to identify and agree on which research uncertainties are most important. To date, there have been over 60 priority setting partnerships (PSPs) across a range of disciplines with over 100 research topics addressed as a direct result of the JLA PSPs (1).

Optimal nutrition is essential for critically ill children but remains an area that has not been well investigated and is a controversial topic within pediatric intensive care (2). There is a lack of methodologically robust trials to inform evidence-based guidelines leading to diverse practices in PICU worldwide (3). Consequently, nutritional practices on PICU continue to be driven largely by expert opinion or consensus, with very few practices supported by high-level evidence (4).

Preillness nutritional state affects both the ability to perform rehabilitation and subsequent clinical outcomes during and beyond the PICU stay (5). Critically ill infants and children have limited macronutrient stores and relatively higher energy requirements compared with adults (6). Undernutrition at PICU admission was predictive of 60-day mortality and longer time to discharge alive from the PICU (7). PICU-acquired faltering growth is a well-documented phenomenon, and the consequence of a profound metabolic shift in response to inflammatory stress and subsequent catabolism, coupled with severe fluid restriction, results in loss of body mass (8).

Other contributing issues to declining nutritional status on PICU include fasting for medical interventions and procedures, and trial extubation; and withholding feeds for perceived feed intolerance (9). The adverse clinical outcomes resulting from malnutrition are electrolyte and nutrient deficiencies, immunosuppression, muscle weakness, a longer duration of mechanical ventilation, and higher risk of hospital-acquired infection, all of which increase the risk of mortality (10). Furthermore, postadmission to PICU can also impact on a child's longer term feeding and swallowing function due to a decline in physical functioning. These difficulties can not only increase length of stay but have a wider psychosocial impact on the child and family (11).

The aim of this work is to establish the top 10 research priorities for PICU nutrition within the United Kingdom, which represent the shared interests and priorities of patients, parents, carers, and healthcare professionals. This PICU nutrition PSP was funded by the British Dietetic Association.

MATERIALS AND METHODS

The PICU nutrition PSP was delivered over 16 months (June 2020–September 2021). Using a multiphase methodology consisting of four components: part 1: a national scoping survey asked respondents to submit their research uncertainties related to PICU nutrition; part 2: summarizing and evidence-checking the submitted uncertainties; part 3: interim prioritization survey; and part 4: consensus workshop with representatives from parents, carers, and PICU healthcare professionals to discuss and agree the top 10 priorities. An overview of the methodology is shown in **Figure 1**. The design of PSP scoping reviews and consensus meetings do not come under the remit for Health Research Association ethical approval, within the U.K. Policy Framework for Health and Social Care Research (<https://www.jla.nihr.ac.uk/jla-guidebook/downloads/JLA-Guidebook-Version-10-March-2021.pdf>).

Steering Group and Partner Organizations

The research lead for dietetics (G.O.) initiated the PSP and guided the appointment of a steering group to oversee and contribute to the process. The steering group consisted of parents of patients who had experienced PICU and PICU healthcare professionals who had links to relevant partner organizations to enable wide dissemination of surveys including the Paediatric Critical Care Society, Royal College of Nursing, British Dietetic Association Paediatric Group, Royal College of Speech and Language Therapists, and Chartered Society of Physiotherapy. Healthcare professionals on the steering group were recruited from the Paediatric Critical Care Society, and parents were recruited directly from a pediatric ward, and the other had previously supported a PICU study that was led by Nottingham University hospital.

Steering group members attended monthly meetings on a voluntary basis and were expected to commit to the whole process where possible. A JLA adviser (S.K.) supported and guided the PSP to follow the JLA process and adhere to its principles. This meant ensuring that it was undertaken in a fair and transparent way, encouraging equal contributions from parents, carers, and healthcare professionals. This is an important aspect of the JLA process and ensures that all voices are heard and respected throughout the process. An information specialist (G.O.) managed the data

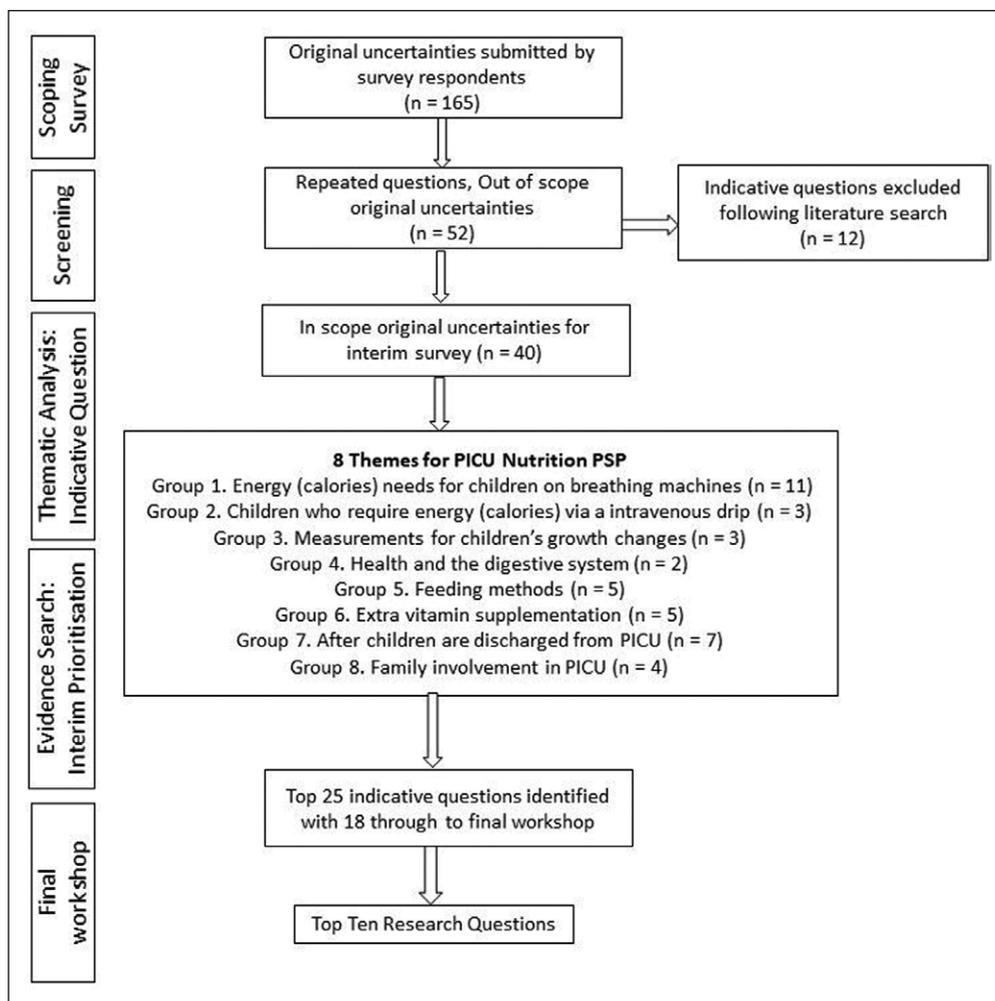


Figure 1. Flowchart to illustrate the James Lind Alliance Priority Setting Partnership (PSP) methodology.

and performed the analysis. This was overseen and advised by the steering group.

Scoping Survey and Identification of Themes

An initial scoping survey asked respondents to submit their research uncertainties:

- 1) What are your questions relating to experiences, knowledge, and support around feeding and drinking (including feeding tube and IV nutrition) during and after the child's time in hospital?
- 2) Any other comments relating to feeding during and after your/their time in PICU.

Additional optional questions were asked pertaining to basic demographic information including, ethnic group, gender, residence in the United Kingdom, and to identify themselves as either previous/current patient on PICU, family member of someone who is or was on PICU, or a PICU healthcare professional. The survey

was circulated via the steering group and associated governing organizations as an open invitation. The survey was available online via Survey Monkey but can still be viewed at <https://www.jla.nihr.ac.uk/priority-setting-partnerships/paediatric-intensive-care-nutrition>.

A pilot phase was undertaken consisting of both healthcare professionals and parents ($n = 10$) to ensure that the survey was clearly written, understandable to all groups, and easy to complete. All submissions were subjected to thematic analysis to define themes and subthemes. The process included initial data immersion (reading and re-reading the submissions), coding of common ideas/themes, identification and naming of themes and subthemes,

and a final review to refine the overarching themes.

The thematic analysis was undertaken by the information specialist (G.O.) and decisions verified by members of the steering group. To do this, the steering group were given the opportunity to review all the submissions under each theme/subtheme. These were then referred to during the verification process.

Indicative Questions and Evidence Search

The overarching themes from the thematic analysis were used to generate a smaller number of representative summary questions. These were derived from the original submissions and were designed to summarize the submissions within each subtheme. The information specialist undertook this process. The summary questions were then reviewed by the steering group along with a selection of the original uncertainties to ensure they were a true representation and to ensure

that the language used was understandable to all stakeholder groups. For each summary question, a review of the current research evidence was undertaken to ensure that the proposed summary questions were “true uncertainties” and had not already been answered by research. To fully incorporate the relevant literature, a thorough electronic screening was conducted by G.O., and scanning was focused on key elements of each summary question.

Eligibility Criteria

For the selection of the papers, the following inclusion criteria were defined: 1) all research uncertainties related to PICU nutrition in children from 0 to 17 years and 2) all stages of the patient’s pathway were eligible including the immediate PICU care and out-of-hospital care (postintensive care). We excluded from the review studies regarding preterm neonates and adult intensive care or nutrition-related questions not relevant to intensive care. The decisions about whether submissions were in or out-of-scope were made by the information specialist and subsequently verified by the steering group.

The following databases were used to scan the data: PubMed, Embase-biomedical literature database, MedRxiv, Scholar, Scopus, Web of Science, and the Cochrane Central Register of Controlled Trials (www.cochranelibrary.com/about/central-landing-page.html) databases were searched up to May 8, 2021. We followed the Preferred Reporting Items for Systematic Reviews and Meta-Analysis reporting guidelines (12). A worked example has been provided for the summary question relating to energy calculation for mechanically ventilated children (**Supplemental Fig. 1**, <http://links.lww.com/CCX/A937>).

The research strategy adopted included different combinations of the following terms: “intubated,” “mechanical ventilation,” “critically ill,” “indirect calorimetry,” “energy,” “calories,” “children,” “pediatric,” “infants,” and “newborn.” The complete search strategies adopted by the electronic database are reported in Supplemental Figure 1 (<http://links.lww.com/CCX/A937>).

Study Selection

All studies identified with the electronic searches were listed by citation, title, authors, and abstract. Duplicates were identified and then removed. Summary questions were excluded if the steering group agreed that

high-quality evidence was found (e.g., large clinical trials either published or in-progress, published meta-analyses, or published national evidence-based guidelines). Summary questions that did not meet the NIHR JLA classification as evidence went through to the interim prioritization.

Interim Prioritization Survey

The survey was available in an online format and went through a pilot phase with the steering group and lay people to ensure the questions were understandable ($n = 9$). The second survey first asked respondents to select as many of the 40 summary questions they felt were important. The 40 summary questions appeared randomly for each responder to reduce risk of fatigue selection toward the latter summary questions. In the second section of the interim prioritization, survey respondents were asked to select a maximum of 10 questions (1 most important to 10 lower importance). Each respondent’s results were then calculated using an average ranking for each answer choice, which was then combined with the average ranking score of other respondents to produce a ranked position—ranked from positions 1 (highest priority) to 40.

The top 25 were calculated using the combined average ranking for healthcare professionals patients, parents, and carers. The results were reviewed by the steering group who decided to take the top 18 to the consensus workshop. In face-to-face JLA final workshops, typically 25 questions are discussed. However, a limitation of online “zoom” workshops is the size of the screen; therefore, the JLA has recommended a maximum of 18 questions are reviewed and discussed.

Prior to the workshop, all participants were requested to rank the 18 question independently with particular focus on their top and bottom three research priorities.

Consensus Workshop

The consensus workshop was a 1-day multistakeholder event involving parents of children who were on or had been on PICU and PICU healthcare professionals. Due to COVID-19 restrictions, the workshop was delivered on a virtual platform (Zoom), which has the capacity for breakout groups; each group was led by JLA facilitator—three groups were formed, consisting of nine healthcare professionals and five parents. Each group discussed individual’s chosen top and bottom three

questions from the 18 questions. The combined results of the breakout group discussions were presented to the whole group. These were considered before a further round of small group discussions. Finally, the whole group came back together to establish a consensus on the top 10 research priorities for PICU nutrition. The role of the JLA facilitator at this stage was to ensure that parents were well supported with information and with practical support on the day. As places in the consensus workshop were limited, some of the steering group did not participate in the final workshop. This decision was based on overrepresentation from either an institution or profession.

Patient and Public Involvement

Patients, parents, and carer representatives were actively involved throughout the whole process: from the initial stages of planning and overseeing the study as part of the steering group to participation in the final workshop to ensure that the patient and parent “voice” was represented in the final prioritization. The steering group made efforts to approach a diverse range of patient, parent, and carer groups across several settings to encourage responses to the surveys. The dissemination strategy will include a plain English summary alongside the scientific publication, which will be circulated to the partner organizations and PPI groups. Our acknowledgement section specifically recognizes and praises the parents who were involved throughout the PSP process.

RESULTS

One hundred and sixty-five research uncertainties were submitted by 90 respondents to the first scoping survey. After removal of “out-of-scope” and repeated uncertainties, 52 uncertainties remained. Respondents were located throughout the United Kingdom. Forty-five percentage of respondents were based in London and South East of England: 11% West Midlands, 12% East Midlands, 12% South West, 10% Yorkshire and North West, 4% East of England, 2% Scotland, and 2% Republic of Ireland. Eighty-eight percent of respondents identified themselves as PICU healthcare professionals and 12% as parents/carers (**Table 1**). Eighty-two percent of respondents are identified as White/White other and 12% are identified as Asian/Asian other. A full breakdown of the ethnic diversity of respondents is outlined in **Table 2**.

TABLE 1.
Percentage of Respondents Who Were Parent or Carer, Patient, or Healthcare Professional for Scoping and Interim Survey

Respondent	Scoping Survey (%)	Interim Second Survey (%)
Parent/carers	12	14
Patient	0	4
Dietitian	35	11
Doctor	22	21
Nurse	19	32
Pharmacist	0	1
Physiotherapist	6	1
Speech language therapist	6	16
Total	100	100

Twelve indicative questions were excluded following a search of the research evidence, leaving 40 indicative questions for the interim prioritization survey. The 40 uncertainties relating to PICU Nutrition were grouped into eight themes:

- 1) Group 1: energy (calories) needs for children on breathing machines in PICU
- 2) Group 2: children who require energy (calories) via an IV drip (parenteral nutrition) in PICU
- 3) Group 3: measurements for children’s growth changes in PICU
- 4) Group 4: health and the digestive system in PICU
- 5) Group 5: feeding methods in PICU
- 6) Group 6: extra vitamin supplementation in PICU
- 7) Group 7: nutrition after children are discharged from PICU
- 8) Group 8: family involvement in PICU.

The second prioritization survey received 140 responses, of which 82% identified themselves as PICU healthcare professional, 14% parents/carers, and 4% patients (**Table 1**). Considering the underrepresentation of parents/carers in the interim survey, an independent average ranking calculation was performed on responses from only parents/carers and patients to elicit their top 10 questions. These questions were automatically prioritized for the final workshop. The remaining 15 questions required to generate the top 25 were calculated using average ranking for the combined score of parents/carers, patients, and healthcare professionals (**Table 3** for priorities 1–10, **Table 4** for priorities 11–18, and **Table 5** for priorities 19–25). The full list of the 40 original

TABLE 2.
Ethnic Diversity of Respondents for the Scoping and Interim Survey Divided Into Parents or Carers and Healthcare Professionals

Respondent	Scoping Survey (%)	Interim Second Survey (%)
Parents/carers		
Black, African, Caribbean, or Black British–African, Caribbean	8	25
Asian or Asian British–Indian, Pakistani, Bangladeshi	42	9
White–English, Welsh, Scottish, Northern Irish, British, or Irish	50	49
Mixed or multiple ethnic groups–White and Black Caribbean	0	17
Total	100	100
PICU healthcare profession		
Black, African, Caribbean, or Black British–African, Caribbean	3	0
Asian or Asian British–Indian, Pakistani, Bangladeshi	7	8
White–English, Welsh, Scottish, Northern Irish, British, or Irish	86	87
Mixed or Multiple ethnic groups–White and Black Caribbean	4	0
Chinese Asian/Asian other	0	3
Arab	0	2
Total	100	100
Combined parents/healthcare profession		
Black, African, Caribbean, or Black British–African, Caribbean	2	5
Asian or Asian British–Indian, Pakistani, Bangladeshi	12	8
White–English, Welsh, Scottish, Northern Irish, British, or Irish	82	83
Mixed or Multiple ethnic groups–White and Black Caribbean	4	
Chinese Asian/Asian other	0	2
Arab	0	2
Total	100	100

TABLE 3.
Top 10 Research Priority Questions for Paediatric Intensive Care Nutrition

1	Group 1. Can energy needs of babies on breathing machines be more accurately measured using indirect calorimetry?
2	Group 7. What are the long term feeding problems in relation to Post Intensive Care Syndrome once a child is discharged home from intensive care?
3	Group 7. Does a high protein feed formula combined with early mobilization reduce muscle wasting in children on breathing machines?
4	Group 8. Can parents' nutritional beliefs and preferences be better understood by healthcare professional and included into the care of their child on breathing machines?
5	Group 2. When should intravenous nutrition start in very underweight critically ill children who DO NOT have a working digestive system?
6	Group 5. What is the definition of feed intolerance in children on breathing machines?
7	Group 4. Does giving probiotics (healthy bacteria) reduce the risk of hospital acquired infections in children on breathing machines?
8	Group 7. Does a child's swallowing change as a result of having needed a breathing tube
9	Group 8. What strategies should be in place on PICU to help with parental bonding with their baby when breast feeding is not possible?
10	Group 1. Do the energy (calorie) needs change for children who have been on a breathing machine for more than 5 d with no change in activity level?

TABLE 4.
Shortlisted Top 11–18 Research Priorities Questions as Agreed at the Consensus Workshop

11	Group 5. Is feeding into the small bowel (postpyloric/jejunal) better tolerated than feeding into stomach in children who are receiving noninvasive ventilation (such as face mask–continuous positive airway pressure/BiPAP)?
12	Group 7. What is the impact of postintensive care syndrome on growth?
13	Group 5. Is bolus feeding better than slow continuous pump feeding in children on breathing machines?
14	Group 7. Can nonnutritive feeding (use of dummies/pacifier) reduce feeding aversion for infants on breathing machines?
15	Group 5. Can a low carbohydrate diet reduce illness related stress (sepsis) to infection (such as hyperlactatemia and hyperglycemia) in children on breathing machines?
16	Group 3. Can specific types of proteins (branch chain amino acids) reduce muscle loss in children who are on breathing machines for more than 7 d?
17	Group 4. Does giving probiotics in children on breathing machines reduce inflammation (cytokines)?
18	Group 4. Is there a safe dose of probiotics (healthy bacteria) for children with low immune function (immunosuppression or immunocompromised) on breathing machines?

uncertainties can be found at this website: <https://www.jla.nihr.ac.uk/priority-setting-partnerships/paediatric-intensive-care-nutrition/>.

DISCUSSION

We have reported the results of a U.K. PSP with the JLA and identified the research priorities around PICU nutrition. These research priorities represent the shared interests of the multiple stakeholders affected by PICU: patients, parents, carers, and healthcare professionals. The top 10 priorities emphasize the lack of evidence to guide postintensive care nutritional management and highlight several unanswered questions related to: the use of nutritional supplements containing probiotics in an acute setting and effective ways to measure energy expenditure in

infants. Furthermore, parents'/carers' nutritional beliefs need to be heard on intensive care, this was specifically raised within the workshop and related to cultural beliefs (halal/kosher), and nutritional preferences such as veganism or access to real food blended diets. Responses have been submitted from across the United Kingdom, and we feel the top 10 summary questions reflect many of the key areas where there is a gap in practice (research uncertainties) in relation to PICU nutrition.

This is the first study to report national research priorities around PICU nutrition in partnership with the JLA. Our nutrition-focused priorities echo research priorities highlighted by Tume et al (13)—although their study adopted a modified 3-round Delphi process and did not include patients or parents/ carers, they did identify a paucity in evidence in accuracy in assessment of

TABLE 5.
Priority Research Questions 19–25—Not Taken Through for Discussion to Consensus Workshop

19	Group 1. How useful is carbon dioxide production (respiratory quotient) in directing nutrition care in children on breathing machines?
20	Group 1. Is there a need for a nutritional screening tool to identify risk of malnutrition in children who are on a breathing machine?
21	Group 1. How should energy (calorie) needs be calculated in children with obesity who are on a breathing machine?
22	Group 2. Should nutrition be limited in the early phase of infection/trauma to promote the body's natural recovery?
23	Group 1. What is the energy (calorie) and protein need for children who are on a breathing machine and need continuous kidney dialysis?
24	Group 1. What is the energy (calorie) and protein needs for children who are on a specialized machine that adds oxygen to the blood (extracorporeal membrane oxygenation)?
25	Group 6. Should vitamin D be supplemented in all children on breathing machines to help with lung function?

energy requirements in all phases of critical illness and the need to better define enteral feeding intolerance and management. However, clarity and consistency are still required regarding the definition of fundamental nutrition outcomes on PICU including energy targets, nutrition parameters, and feeding tolerance (14).

Parents/carers of children who had been on PICU were actively involved at all stages of the process to ensure that the patient and parent voice were heard and remained at the center of our priority setting process. Final workshop quote from parent—“Although there were not many parents involved in the final workshop I feel that the parent voice is represented in the final list of research questions. I think the healthcare professionals involved and JLA facilitators were aware that parents may feel underrepresented and therefore needed to be given particular attention.” We used the established and transparent JLA methodology to conduct this PSP. All the original research submissions and the indicative summary questions (40 in total) are available on the JLA website (1).

The number of survey responses differed to other JLA PSPs, in that we were unable to achieve an equal balance between responses from healthcare professionals and nonhealthcare professionals. Considerable efforts were employed to ensure that all patient and parent groups were able to access and respond to our national surveys. These strategies included targeting social media platforms for chronic and long-term illnesses led by parent/carer groups specifically for parents/carers. It became apparent this was a protected space away from healthcare professionals, and we were unable to engage. Furthermore, the demand on parents whose child is on PICU is high, which limited the ability of parents/carers accessing the surveys. This was illustrated in the consensus workshop when a parent whose infant was on PICU had to leave sessions throughout the day to meet with healthcare professionals.

The main limiting factor of this PSP was the overall response rate, especially from parents/carers. Although we ensured parent survey responses were heard by performing a weighted calculation on survey answers, we must highlight this issue and the potential impact on the top 10 research priorities. Another limiting factor was COVID—unfortunately, our PSP was launched at the peak of the first wave meaning many healthcare professionals were unable to respond to the scoping and interim survey due to clinical workloads. However, this also provided a unique perspective on questions posed that were

related to the management of children with COVID in intensive care specifically relating to the management of obese ventilated children and the effectiveness of vitamin D supplementation to optimize respiratory function.

Considering these obstacles outlined, it is possible that the research priorities reported still underrepresent those of parents/carers and patients. However, we are encouraged to see the broad and varied range of research uncertainties posed and those selected for the top 10—with topics ranging from postintensive care nutritional management to nutritional interventions to manage sepsis and reduce the risk of hospital acquired infections.

CONCLUSIONS

We report the research priorities around PICU Nutrition in the United Kingdom. The PSP highlighted obstacles accessing this cohort of patients and families due to the nature of the acute clinical environment. The priorities highlight uncertainties in energy requirements in ventilated neonates, nutritional supplementation of probiotics to manage and prevent sepsis, the impact of postintensive care syndrome, and when to commence parenteral (IV) nutrition. The challenge now is to refine research questions, source funding, and deliver answers to these research priorities in PICU nutrition.

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We would like to dedicate this James Lind Alliance National Institute of Health Research priority setting partnership (PSP) to Mr. Mistry and Mrs. Contractor's beautiful daughter Anoushka Rohini Mistry who passed away on the May 7, 2021, at the age of 8 years old. Mrs. Contractor is a passionate and wonderful advocate for nutrition, who eloquently stated, “it is my belief that nutrition should be at the heart of any PICU admission not just for the nutritional support but also the nourishment mothers can give their children - Food is an expression of love.”

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