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Original Article

Feed modification for increased energy and protein density as nutrition therapy in critically ill children: A protocol for a scoping review

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SUMMARY

Background and aims: Meeting the nutritional requirements of critically ill infants and young children with breastmilk or formula alone is often challenging due to disease-related increased requirements and fluid restriction. 'Feed modification' is a nutrition therapy strategy to increase energy and protein density, and includes fortification of expressed breast milk, preparation of standard powdered formula at an increased concentration and utilisation of concentrated ready-to-feed liquid formulas. However, despite anecdotal evidence suggesting frequent and varied use internationally, the evidence for feed modification is unclear and has not been reviewed systematically. This article describes the methods for a scoping review to collate the key definitions, concepts, methods and evidence for use of modified feeds for increased energy and protein density as nutrition therapy in critically ill children.

Methods: A scoping review will be completed, including searches of MEDLINE, Embase, Emtree and CINAHL databases. Grey literature will be searched using ProQuest, Web of Science, Trove Australian theses, WorldCat Dissertations and Theses, ETHOS, Dart European and conference collections via Ovid. Study selection and

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data charting will be undertaken by two reviewers. Results of this review will be presented in a tabular format and include frequency counts. Literature related to use of feed modification for increased energy and protein density in children up to the age of 5 years from the year 2010 to present and in English language only will be included. This review will be the first of its kind and of interest to all areas of paediatrics utilising feed modification for increased energy and protein density.

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Background

The provision of nutrition therapy to critically ill children is considered an essential component of care [1–3]. International guidelines emphasise the importance of early nutrition assessment and tailored nutrition interventions [4–6]. Infants and young children receive nutrition via breast milk and infant formulas, and in the critical care setting these are often administered via a gastrointestinal tube due to a reduced level of consciousness or inability to swallow [7,8].

However, meeting the nutritional requirements of critically ill children with breastmilk or formula alone is often challenging. This may be due to increased nutritional requirements related to a disease process or recovery from illness, or the requirement for fluid restriction, which limits the volume which can be administered [9–13]. ‘Feed modification’ is a nutrition therapy strategy to increase energy and protein density to better meet nutritional requirements with the same volume. Modified feed options include the fortification of expressed breast milk, preparation of standard formula powders at an increased concentration, and utilisation of concentrated ready-to-feed liquid formulas [14–22]. Anecdotal evidence suggests a variety of feed modification methods are commonly utilised internationally, however this is an area of clinical practice that has not been systematically reviewed. Navigation of the literature is further complicated by the array of definitions and outcome measures used in relation to this nutrition therapy.

A scoping review is therefore proposed to broadly collate the key definitions, concepts and evidence in the literature related to feed modification for increased energy and protein density in critically ill children. It is not well understood how the use of feed modification may affect the outcomes of critically ill children, and therefore clarification of appropriate therapeutic options and identification of knowledge gaps will allow for targeted future research.

Identification of research questions

The research questions this review seeks to address in relation to the reported literature on feed modification in infants and young children for increased energy and protein density have been identified as follows:

- What definitions are used in relation to feed modification?
- What methods of feed modification are described?
- In what settings and populations has feed modification been studied?
- What are the key clinical and logistic issues when utilising feed modification?
- What outcome measures have been used in studies of feed modification?
- What are the reported benefits of specific methods of feed modification?
- What are the reported risks associated with specific methods of feed modification?
- What is the evidence for feed modification for increased energy and protein density in critically ill infants and young children?

Methods

The scoping review will be undertaken following the methodology of the Joanna Briggs Institute (JBI) Manual for Evidence Synthesis [23] and will be reported following the format outlined by the Preferred Reporting Items for Systematic Reviews and Meta-analysis Extension for Scoping Reviews (PRISMA-ScR) [24]. Frequently used terms have been defined for this review (Table 1). A preliminary search for existing scoping and systematic reviews was conducted as per JBI methodology, searching MEDLINE via Ovid, CINAHL via EBSCO, PROSPERO, Cochrane Database for Systematic Reviews and JBI Evidence Synthesis. This demonstrated no published reviews on use of modified feeds in critically ill children.

Eligibility criteria

Inclusion criteria for literature in this scoping review comprises:

- Utilisation of a non-standard feed option for the purpose of increased energy and/or protein density (with standard feed options defined as breast milk, infant formula providing approx. 280 kJ/100 ml and paediatric feeds providing approx. 420 kJ/100 ml)
- Infants and young children up to the age of 5 years
- Literature published from the year 2010 to present
- Primary research studies of any design
- Reviews
- Grey literature including, but not limited to, theses and conference abstracts
- All geographic locations
- English language only

As it is anticipated that valuable insights may be gained from other settings, studies in infants and young children cared for outside the critical care setting will be included. Data related to infants will be extracted and reported upon within the categories of preterm infants and neonates as appropriate due to the differences in nutritional requirements. Young children beyond the age of 12 months will be included, however, in the absence of an otherwise natural cut-off a pragmatic approach has been taken in the selection of an arbitrary upper age limit of 5 years. Information sources will be limited from 2010 to present to reflect current practice and acknowledge specialised product development and availability over time. English only publications will be included for feasibility purposes. Publications that do not specify the method of feed modification will be excluded.

Search strategy

The search strategy was developed in consultation with a health sciences librarian. MEDLINE via Ovid and Emcare via Ovid were searched in a limited capacity to identify a set of relevant publications

Table 1
Definitions for purpose of scoping review.

Infants and young children	All children aged up to 5 years
Feeds	Any liquid nutrition provided orally or via gastrointestinal tube (including breast milk and any other feed or formula)
Standard feeds	Expressed breast milk (EBM), standard powdered and liquid ready-to-use infant formulas (approx. 280 kJ/100 ml), standard powdered and liquid ready-to-use paediatric formulas (approx. 420 kJ/100 ml), 'growing up' or 'toddler' formulas
Modified feeds	Feeds modified for purpose of increased energy and protein density, including EBM with additives, standard infant formula prepared at higher concentration, standard formula with macronutrient module additives, and higher energy and protein density ready-to-feed products
Critical illness	Studies with participants recruited in a critical care setting or those that receive an intervention that would generally be delivered in an intensive care unit will be defined as those with critical illness

from which text words and index terms were reviewed and utilised to devise the full search strategy (see [Appendix I](#)). The databases to be searched in this review include MEDLINE via Ovid, Emcare via Ovid, Embase via Ovid, and CINAHL via EBSCO. Refer to [Appendix I](#) for the full search strategy for MEDLINE. A search of all databases will be completed on the same date. A search for grey literature will be completed using ProQuest, Web of Science, Trove Australian theses, WorldCat Dissertations and Theses, ETHOS, Dart European and conference collections via Ovid, using the terms outlined in the database search. Reference checking will be undertaken on a selected gold set of articles and clinical guidelines. Authors of primary sources will be contacted for further information as required.

Source of evidence selection

On completion of the search, records will be collated in EndNote reference manager software (Version x9, Philadelphia: Clarivate) and an author (JW) will remove any duplicates and obviously irrelevant articles using pre-specified criteria (see [Appendix II](#)). Article titles and abstracts will then be screened by two reviewers (JW and BL) against inclusion and exclusion criteria. Records will then be transferred into Covidence systematic review software (Melbourne: Veritas Health Innovation) where two reviewers (JW and BL) will re-screen titles and abstracts against inclusion and exclusion criteria. Disagreements not resolved through consensus will be decided upon by a third reviewer (ER). The rationale for exclusion of specific articles will be outlined in the final review report.

Source selection pilot testing will be undertaken on a random sample of 25 articles by the reviewers (JW, BL and ER). Discrepancies will be debated in order to identify any required eligibility criteria adjustments. Screening of the full search will commence when 75% agreement is achieved in pilot testing.

Data charting process

A data charting tool will be utilised for the data extraction process (see [Appendix III](#)). Critical appraisal of evidence sources will not be completed. The data charting tool will be pilot tested on two articles by two reviewers (JW and BL). The authorship group will review the results of the pilot testing and reach consensus on any required changes. Any tool modifications required following the commencement of the review will be noted in the final publication.

Analysis of the evidence

The results of the review will be outlined in tabular format and categorised according to identified themes and trends. Extracted data will include the type of publication, study design, population and setting, feed modification methods used, reported potential benefits and risks, and outcome measures. Frequency counts (n [%]) will be provided in addition to the tabular data.

This scoping review will provide an overview of the definitions, key concepts and evidence for use of modified feeds for increased energy and protein density in critically ill infants and young children with intended publication in a peer-reviewed scientific journal. The review will be the first of its kind and anticipated to be of interest to all areas of paediatrics utilising feed modification. Appropriate therapeutic options will be highlighted and key knowledge gaps will be identified to inform future research questions with the intention of optimising nutrition provision and potentially altering outcomes for critically ill children.

Authors contributions

Jacinta Winderlich: Conceptualisation, Methodology, Writing – Original Draft, Writing – Editing and Reviewing, Project Administration. **Bridget Little:** Conceptualisation, Methodology, Writing – Original Draft, Writing – Editing and Reviewing. **Alice Anderson:** Conceptualisation, Methodology, Writing – Original Draft, Writing – Editing and Reviewing. **Felix Oberender:** Writing – Editing and Reviewing. **Andrew Udy:** Conceptualisation, Methodology, Writing – Original Draft, Writing – Editing and Reviewing, Supervision. **Emma Ridley:** Conceptualisation, Methodology, Writing – Original Draft, Writing – Editing and Reviewing, Supervision.

All authors have read and approved the final manuscript and will contribute to the final scoping review publication.

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Conflict of interest

The authors declare no conflict of interest.

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Not applicable.

Appendices

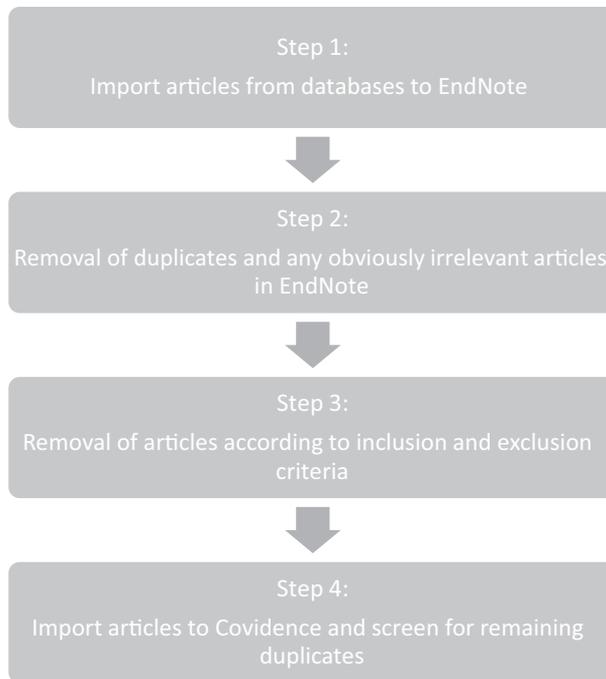
Appendix I. Search strategy

Database: Ovid MEDLINE(R) ALL <1946 to August 19, 2022>

Search Strategy:

- 1 Energy Intake/or *Enteral Nutrition/or *Nutrition Therapy/or *Nutritional Support/(34887)
 - 2 Infant, Premature, Diseases/mi [Microbiology] (850)
 - 3 (nutrition* adj 3 (therapy or program* or enteral)). tw. (23711)
 - 4 (nutrient adj 2 (deficit* or accretion)). tw. (190)
 - 5 ((energy or protein) adj 2 (intake or needs)). tw. (38381)
 - 6 (target* adj 2 (intake* or nutrition* or nutrient or fortification)). tw. (1957)
 - 7 (fluid adj 2 restrict*). tw. (2409)
 - 8 1 or 2 or 3 or 4 or 5 or 6 or 7 (87420)
 - 9 Milk, Human/or Infant Formula/or Food, Fortified/(35156)
 - 10 Nutrients/ad [Administration & Dosage] (331)
 - 11 ((feed* or formula* or milk or ebm or breast?milk) adj 2 (composition or content or concentrated or energy dense or high energy or enriched or fortification or fortified or unfortified or supplemented or supplementation or standard or non? standard or ready?to?feed or ready?to?use or speciali?ed)). tw. (20424)
 - 12 (modifi* adj (feed or formula* or ebm or milk or breastmilk)). tw. (535)
 - 13 (feed* adj 2 (choice or selection)). tw. (1083)
 - 14 ((energy or protein) adj 2 (supplement* or enriched or enteral)). tw. (8182)
 - 15 (liquid energy or fortification strategy or nutritional content). tw. (1044)
 - 16 ((energy or nutrient) adj dense). tw. (3075)
 - 17 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 (65671)
 - 18 Treatment outcome/or Weight Gain/or Length of stay/or Food Safety/or Osmolar Concentration/or Cost-Benefit Analysis/ (1355362)
 - 19 (weight adj 2 (increase* or improve* or gain)). tw. (98635)
 - 20 ((better or improved or patient or treatment or patient) adj 3 outcome*). tw. (325826)
 - 21 (growth or length of stay or LOS). tw. (1733684)
 - 22 ((reduce* or decrease* or increase* or impact*) adj 2 (stay or ventilat*)). tw. (15570)
 - 23 (cost adj 2 (product or comparison or analysis)). tw. (30234)
 - 24 (safe* or contaminat* or sterile or osmolality or osmolar). tw. (1316121)
 - 25 18 or 19 or 20 or 21 or 22 or 23 or 24 (4323497)
 - 26 8 and 17 and 25 (2018)
 - 27 limit 26 to (english and last 10 years) (985)
-

Appendix II. Screening process in EndNote and Covidence



Appendix III. Proposed data charting tool

	Evidence Source				Inclusion Criteria	Exclusion Criteria	Evidence Source Details					Details Extracted from Evidence Source					
	Author	Country	Year of publication	Citation details			Study design	Setting	Participants	Intervention/s	Definitions	Key concepts	Method/s of feed modification	Criteria for recommended use of modified feeds	Reported potential benefits of specific methods	Reported potential risks of specific methods	Outcome measures
Study 1																	
Study 2																	
Study 3																	

References

- [1] Irving SY, Albert BD, Mehta NM, Srinivasan V. Strategies to optimize enteral feeding and nutrition in the critically ill child: a narrative review. *Pediatr Med* 2022;5.
- [2] Joosten K, Van Puffelen E, Verbruggen S. Optimal nutrition in the paediatric ICU. *Curr Opin Clin Nutr Metab Care* 2016; 19(2):131–7.
- [3] Marino LV, Jotterand Chaparro C, Moullet C. Refeeding syndrome and other related issues in the paediatric intensive care unit. *Pediatr Med* 2020;3.
- [4] Tume LN, Valla FV, Joosten K, Jotterand Chaparro C, Latten L, Marino LV, et al. Nutritional support for children during critical illness: European Society of Pediatric and Neonatal Intensive Care (ESPNIC) metabolism, endocrine and nutrition section position statement and clinical recommendations. *Intensive Care Med* 2020;46(3):411–25.
- [5] Mehta NM, Skillman HE, Irving SY, Coss-Bu JA, Vermilyea S, Farrington EA, et al. Guidelines for the Provision and Assessment of Nutrition Support Therapy in the Pediatric Critically Ill Patient: Society of Critical Care Medicine and American Society for Parenteral and Enteral Nutrition. *J Parenter and Enteral Nutr* 2017;41(5):706–42.
- [6] Lee JH, Rogers E, Chor YK, Samransamruajkit R, Koh PL, Miqdady M, et al. Optimal nutrition therapy in paediatric critical care in the Asia-Pacific and Middle East: A consensus. *Asia Pac J Clin Nutr* 2016;25(4):676–96.
- [7] Briassoulis G, Ilija S, Meyer R. Enteral Nutrition in PICUs: Mission Not Impossible. *Pediatric Crit Care Med* 2016;17(1):85–7.

- [8] Mehta NM. Approach to enteral feeding in the PICU. *Nutr Clin Pract* 2009;24(3):377–87.
- [9] Joosten KFM, Kerklaan D, Verbruggen SCAT. Nutritional support and the role of the stress response in critically ill children. *Curr Opin in Clin Nutr and Metab Care* 2016;19(3):226–33.
- [10] Joosten KFM, Eveleens RD, Verbruggen SCAT. Nutritional support in the recovery phase of critically ill children. *Curr Opin in Clin Nutr and Metab Care* 2019;22(2):152–8.
- [11] Raman S, Peters MJ. Fluid management in the critically ill child. *Pediatric Nephrol* 2014;29(1):23–34.
- [12] Hulst JM, Joosten KF, Tibboel D, Van Goudoever JB. Causes and consequences of inadequate substrate supply to pediatric ICU patients. *Curr Opin in Clin Nutr and Metab Care* 2006;9(3):297–303.
- [13] Rogers EJ, Gilbertson HR, Heine RG, Henning R. Barriers to adequate nutrition in critically ill children. *Nutr* 2003;19(10):865–8.
- [14] Premkumar MH, Massieu LA, Anderson DM, Gokulakrishnan G. Human Milk Supplements: Principles, Practices, and Current Controversies. *Clin in Perinatol* 2020;47(2):355–68.
- [15] Brown JV, Embleton ND, Harding JE, McGuire W. Multi-nutrient fortification of human milk for preterm infants. *Cochrane Database of Syst Rev* 2016;2016(5).
- [16] Marino LV, Meyer R, Cooke ML. Cost comparison between powdered versus energy dense infant formula for under-nourished children in a hospital setting. *E-SPEN Journal*. 2013;8(4):e145–9.
- [17] Steele JR, Meskell RJ, Foy J, Garner AE. Determining the osmolality of over-concentrated and supplemented infant formulas. *J of Hum Nutr and Diet* 2013;26(1):32–7.
- [18] Eveleens RD, Dungen DK, Verbruggen SCAT, Hulst JM, Joosten KFM. Weight improvement with the use of protein and energy enriched nutritional formula in infants with a prolonged PICU stay. *J of Hum Nutr and Diet* 2019;32(1):3–10.
- [19] Marino LV, Eveleens RD, Morton K, Verbruggen S, Joosten KFM. Peptide nutrient-energy dense enteral feeding in critically ill infants: an observational study. *J Hum Nutr Diet* 2019;32(3):400–8.
- [20] Chen X, Zhang M, Song Y, Luo Y, Wang L, Xu Z, et al. Early high-energy feeding in infants following cardiac surgery: A randomized controlled trial. *Transl Pediatr* 2021;10(10):2439–48.
- [21] Singal A, Sahu MK, Trilok Kumar G, Kumar A. Effect of energy- and/or protein-dense enteral feeding on postoperative outcomes of infant surgical patients with congenital cardiac disease: A systematic review and meta-analysis. *Nutr in Clin Pract* 2022;37(3):555–66.
- [22] Goday PS, Lewis JD, Sang CJ, George DE, McGoogan KE, Safta AM, et al. Energy- and protein-enriched formula improves weight gain in infants with malnutrition due to cardiac and noncardiac etiologies. *J of Parenter and Enteral Nutr* 2022; 46(6):1270–82.
- [23] Aromataris E, Munn Z, editors. *JBI manual for evidence Synthesis*; 2020. JBI.
- [24] Tricco AC, Lillie E, Zarin W, O'Brien KK, Colquhoun H, Levac D, et al. PRISMA extension for scoping reviews (PRISMA-ScR): checklist and explanation. *Ann Intern Med* 2018;169(7):467–73.