

CADTH RAPID RESPONSE REPORT: REFERENCE LIST

# Pasteurized Donor Milk versus Formula for Preterm Infants: Clinical Effectiveness, Cost- Effectiveness, and Guidelines

Service Line: Rapid Response Service  
Version: 1.0  
Publication Date: October 13, 2020  
Report Length: 5 Pages

**Authors:** Diksha Kumar, Melissa Walter, Andrea Ryce

**Cite As:** *Pasteurized Donor Milk versus Formula for Preterm Infants: Clinical Effectiveness, Cost-Effectiveness, and Guidelines*. Ottawa: CADTH; 2020 Oct. (CADTH rapid response report: reference list).

**Disclaimer:** The information in this document is intended to help Canadian health care decision-makers, health care professionals, health systems leaders, and policy-makers make well-informed decisions and thereby improve the quality of health care services. While patients and others may access this document, the document is made available for informational purposes only and no representations or warranties are made with respect to its fitness for any particular purpose. The information in this document should not be used as a substitute for professional medical advice or as a substitute for the application of clinical judgment in respect of the care of a particular patient or other professional judgment in any decision-making process. The Canadian Agency for Drugs and Technologies in Health (CADTH) does not endorse any information, drugs, therapies, treatments, products, processes, or services.

While care has been taken to ensure that the information prepared by CADTH in this document is accurate, complete, and up-to-date as at the applicable date the material was first published by CADTH, CADTH does not make any guarantees to that effect. CADTH does not guarantee and is not responsible for the quality, currency, propriety, accuracy, or reasonableness of any statements, information, or conclusions contained in any third-party materials used in preparing this document. The views and opinions of third parties published in this document do not necessarily state or reflect those of CADTH.

CADTH is not responsible for any errors, omissions, injury, loss, or damage arising from or relating to the use (or misuse) of any information, statements, or conclusions contained in or implied by the contents of this document or any of the source materials.

This document may contain links to third-party websites. CADTH does not have control over the content of such sites. Use of third-party sites is governed by the third-party website owners' own terms and conditions set out for such sites. CADTH does not make any guarantee with respect to any information contained on such third-party sites and CADTH is not responsible for any injury, loss, or damage suffered as a result of using such third-party sites. CADTH has no responsibility for the collection, use, and disclosure of personal information by third-party sites.

Subject to the aforementioned limitations, the views expressed herein do not necessarily reflect the views of Health Canada, Canada's provincial or territorial governments, other CADTH funders, or any third-party supplier of information.

This document is prepared and intended for use in the context of the Canadian health care system. The use of this document outside of Canada is done so at the user's own risk.

This disclaimer and any questions or matters of any nature arising from or relating to the content or use (or misuse) of this document will be governed by and interpreted in accordance with the laws of the Province of Ontario and the laws of Canada applicable therein, and all proceedings shall be subject to the exclusive jurisdiction of the courts of the Province of Ontario, Canada.

The copyright and other intellectual property rights in this document are owned by CADTH and its licensors. These rights are protected by the Canadian *Copyright Act* and other national and international laws and agreements. Users are permitted to make copies of this document for non-commercial purposes only, provided it is not modified when reproduced and appropriate credit is given to CADTH and its licensors.

**About CADTH:** CADTH is an independent, not-for-profit organization responsible for providing Canada's health care decision-makers with objective evidence to help make informed decisions about the optimal use of drugs, medical devices, diagnostics, and procedures in our health care system.

**Funding:** CADTH receives funding from Canada's federal, provincial, and territorial governments, with the exception of Quebec.

Questions or requests for information about this report can be directed to [requests@cadth.ca](mailto:requests@cadth.ca)

## Research Questions

1. What is the comparative clinical effectiveness of pasteurized donor milk compared with formula for preterm babies of gestational age 34 weeks or earlier?
2. What is the comparative cost-effectiveness of pasteurized donor milk compared with formula for preterm babies of gestational age 34 weeks or earlier?
3. What are the evidence-based guidelines regarding the use of donor milk or formula for preterm babies of gestational age 32 to 34 weeks?

## Key Findings

One systematic review and one randomized controlled trial were identified regarding the comparative clinical effectiveness of pasteurized donor milk compared with formula for preterm babies of gestational age 34 weeks or earlier. No relevant literature was identified regarding the comparative cost-effectiveness of pasteurized donor milk compared with formula for preterm babies of gestational age 34 weeks or earlier. In addition, no relevant evidence-based guidelines were identified regarding the use of donor milk or formula for preterm babies of gestational age 32 to 34 weeks.

## Methods

### Literature Search Methods

A limited literature search was conducted by an information specialist on key resources including MEDLINE, the Cochrane Library, the University of York Centre for Reviews and Dissemination (CRD) databases, the websites of Canadian and major international health technology agencies, as well as a focused Internet search. The search strategy was comprised of both controlled vocabulary, such as the National Library of Medicine’s MeSH (Medical Subject Headings), and keywords. The main search concepts were donor milk and premature infants. Search filters were applied to limit retrieval to health technology assessments, systematic reviews, meta-analyses, or network meta-analyses, randomized controlled trials, controlled clinical trials, or any other type of clinical trial, economic studies, and guidelines. Where possible, retrieval was limited to the human population. The search was also limited to English language documents published between January 1, 2015 and October 4, 2020. Internet links were provided, where available.

### Selection Criteria

One reviewer screened literature search results (titles and abstracts) and selected publications according to the inclusion criteria presented in Table 1. Full texts of study publications were not reviewed. Open access full-text versions of evidence-based guidelines were reviewed when abstracts were not available.

**Table 1: Selection Criteria**

<b>Population</b>	Preterm infants (gestational age < 34 weeks)
<b>Intervention</b>	Pasteurized donor milk (fortified or not fortified, not mother’s own milk)
<b>Comparator</b>	Preterm formula (e.g., Similac special care, Enfamil A+ premature)
<b>Outcomes</b>	Q1: Clinical effectiveness (e.g., feed tolerance, feeds held [i.e., nothing by mouth days or Nil per Os days], weight gain, growth rate, developmental outcomes, length of neonatal care unit stay, complications [e.g., sepsis, necrotizing enterocolitis, dehydration, allergies])

	Q2: Cost-effectiveness (e.g., cost per quality life year gained, incremental cost effectiveness) Q3: Recommendations regarding the use of formula or donor milk in preterm infants between the gestational ages of 32 weeks and 34 weeks
<b>Study Designs</b>	Health technology assessments, systematic reviews, randomized controlled trials, non-randomized studies, economic evaluations, evidence-based guidelines

## Results

One systematic review<sup>1</sup> and one randomized controlled trial<sup>2</sup> were identified regarding the comparative clinical effectiveness of pasteurized donor milk compared with formula for preterm babies of gestational age 34 weeks or earlier. No relevant health technology assessments, non-randomized studies, economic evaluations, or evidence-based guidelines were identified.

Additional references of potential interest that did not meet the inclusion criteria are provided in the appendix.

### Health Technology Assessments

No literature identified.

### Systematic Reviews and Meta-Analyses

1. Buhner C, Fischer HS, Wellmann S. Nutritional interventions to reduce rates of infection, necrotizing enterocolitis and mortality in very preterm infants. *Pediatr Res.* 2020 Jan;87(2):371-377.  
[PubMed: PM31645057](#)

### Randomized Controlled Trial

2. Costa S, Maggio L, Alighieri G, Barone G, Cota F, Vento G. Tolerance of preterm formula versus pasteurized donor human milk in very preterm infants: a randomized non-inferiority trial. *Ital J Pediatr.* 2018 Aug 16;44(1):96.  
[PubMed: PM30115086](#)

### Non-Randomized Studies

No literature identified.

### Economic Evaluations

No literature identified.

### Guidelines and Recommendations

No literature identified.

## Appendix — Further Information

### Systematic Reviews and Meta-Analyses

#### *Unclear Intervention – Pasteurization not Specified*

3. Quigley M, Embleton ND, McGuire W. Formula versus donor breast milk for feeding preterm or low birth weight infants. *Cochrane Database Syst Rev*. 2019 Jul 19;7(7):CD002971.  
[PubMed: PM31322731](#)
4. Silano M, Milani GP, Fattore G, Agostoni C. Donor human milk and risk of surgical necrotizing enterocolitis: A meta-analysis. *Clin Nutr*. 2019 Jun;38(3):1061-1066.  
[PubMed: PM29566974](#)

#### Non-Randomized Study

#### *Unclear Intervention – Pasteurization not Specified*

5. Kreissl A, Sauerzapf E, Repa A, et al. Starting enteral nutrition with preterm single donor milk instead of formula affects time to full enteral feeding in very low birthweight infants. *Acta Paediatr*. 2017 Sep;106(9):1460-1467.  
[PubMed: PM28498519](#)

#### Economic Evaluation

#### *Unclear Intervention – Pasteurization not Specified*

6. Buckle A, Taylor C. Cost and cost-effectiveness of donor human milk to prevent necrotizing enterocolitis: systematic review. *Breastfeed Med*. 2017 Nov;12(9):528-536.  
[PubMed: PM28829161](#)

#### Additional Reference – Costing Study

7. Fengler J, Heckmann M, Lange A, Kramer A, Flessa S. Cost analysis showed that feeding preterm infants with donor human milk was significantly more expensive than mother's milk or formula. *Acta Paediatr*. 2020 May;109(5):959-966.  
[PubMed: PM31705551](#)