EXPLORING BEST PRACTICE INTERVENTIONS TO PROTECT, PROMOTE AND SUPPORT BREASTFEEDING

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Abstract

Across Canada (CA) and Newfoundland and Labrador (NL), most women intend to breastfeed; however in actuality rates of EBF tend to decrease drastically. The significant decrease in EBF over time suggests further intervention is needed to provide an environment that promotes breastfeeding.

Guided by the Lancet Framework "The components of an enabling environment for breastfeeding—a conceptual model" this dissertation advances the evidence base on the best practice interventions that can enable an environment that supports breastfeeding mothers. The framework outlines three determinants (Structural, Setting, and Individual) that are associated with evidence-based interventions that, if implemented, have a high likelihood of increasing EBF rates. The primary focus of this thesis is to explore the best practice interventions associated with one of three determinants: the Setting. Interventions associated with Setting include those aimed at Health System, Policy and Community.

In the first study on the *Health System*, I evaluated the efficacy of Domperidone, an off-label galactagogue prescribed to mothers by physicians with insufficient human milk production (Chapter Two). In the second study, with a *Policy* focus, I conducted a data linkage study to examine the differences in health service use (HSU) and associated costs by infant feeding mode, in an infant's first year of life (Chapter Three). Paired with this study on HSU, my third study explored mothers' perceptions of the costs associated with infant feeding, using a patient-oriented research approach (Chapter Four). In my final study, I evaluate the effectiveness of virtual lactation support for breastfeeding mothers in the *Community* (Chapter Five).

Creating an environment that protects, promotes, and supports breastfeeding involves efforts from Structural, Setting, and Individual levels. The aim of this dissertation is to investigate the best practice interventions that will allow parents to have access to a seamless system of breastfeeding support services in the transition from hospital to the home and community. Policy recommendations will support the additional efforts and funding required for an increase in access to evidence-based breastfeeding support.

Summary

The importance of exclusive breastfeeding (EBF) for the first six months and continued breastfeeding for two years or more is widely accepted due to the plethora of evidence supporting the importance of breastfeeding on child and maternal health (1). Based on the strength of the evidence, specialized global health organizations endorse these recommendations including the World Health Organization (WHO), the United Nations Children's Fund (UNICEF), Health Canada and the Canadian Pediatric Society.

Due to a number of reasons, only a very small percentage of women meet their breastfeeding goals and thus many mothers and babies do not receive the well-evidenced benefits of EBF. Across Canada (CA) and Newfoundland and Labrador (NL), the majority of women intend to breastfeed, as illustrated by initiation rates of 90% and 71.9%, respectively. However, the rates of EBF decrease drastically, and at six months of age only 32% (CA) and 13% (NL) of mothers are EBF (2). In addition to the health benefits not realized due to the reduced duration of EBF, there are economic consequences. Although limited research has been conducted in Canada on cost savings related to breastfeeding, researchers in the United States have reported if EBF to 6 months increased from 21.9 to 90%, there would be annual cost savings of $3 billion in total direct medical costs (e.g., cost of medicine, hospital overhead) with an additional cost savings of $14.2 billion associated with a reduction in premature maternal and child deaths (3).

The significant decrease in EBF over time suggests further intervention is needed to provide an environment that promotes breastfeeding. In 2016, the Lancet published a series on breastfeeding "Why invest, and what will it take to improve breastfeeding practices?" which described the types of interventions that if implemented, would likely increase EBF rates. The authors described a framework that identifies three distinct determinants of EBF. These determinants supported by a number of interventions which will be further discussed in chapter one. In brief, the three determinants are Structural (e.g., cultural norms, market content), Setting (e.g., health systems/services, family/community, workplace/employment) and Individual (e.g., mother, or infant attributes, mother-infant relationship) (1). Each determinant is associated with evidence-based interventions that, if implemented, have a high likelihood of increasing EBF rates. Examples of interventions include: social mobilization, policy, legislation, financing, counseling, support and lactation management (1). To address the determinants (i.e., Structural, Setting, and Individual), the authors recommend developing comprehensive, multi-sectorial strategies that support institutions and communities to implement the identified interventions in order to protect, promote and support breastfeeding (1).

The primary focus of this thesis is to explore the best practice interventions associated with one of three determinants: the Setting. Interventions associated with Setting include those aimed at Health System, Policy and Community. In the first study on the *Health System*, I evaluated the efficacy of Domperidone, an off-label galactagogue prescribed to mothers by physicians with insufficient human milk production (Chapter

Two). In the second study, with a *Policy* focus, I conducted a data linkage study to examine the differences in health service use (HSU) and associated costs by infant feeding mode, in an infant's first year of life (Chapter Three). Paired with this study on HSU, my third study explored mothers' perceptions of the costs associated with infant feeding, using a patient-oriented research approach (Chapter Four). In my final study, I evaluate the effectiveness of virtual lactation support compared to standard care for breastfeeding mothers in the *Community* (Chapter Five).

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Finally, my sweet Lily- who taught me more about breastfeeding than any textbook, article, or my years of research could have ever taught me.

Becoming your “mom mom” has been a dream come true.

Dedication

I would like to dedicate this thesis to the love of my life and very best friend- without his love and support, this thesis would not be possible.

To someone who now knows just as much about this topic as I do- thank you.

It is with great honour that I now get to be Dr./Mrs. Aaron.

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List of Abbreviations

BFHI, Baby Friendly Hospital Initiative;

BFRWG, Breastfeeding Research Working Group;

CI, Confidence Interval;

CMG, Case Mix Group;

CSHS, Cost of a Standard Hospital Stay;

EBF, Exclusive Breastfeeding/Exclusively Breastfed;

EFF, Exclusive Formula Feeding/Exclusively Formula Fed;

EHMV, Expressed Human Milk Volume;

ER, Emergency Room;

FiNaL Study, Feeding Infants in Newfoundland and Labrador;

GLM, Generalized linear modelling;

GNI, Gross National Income;

HSU, Healthcare Service Use;

IBCLC, International Board Certified Lactation Consultant;

ICT, Information and Communication Technologies;

IFM, Infant Feeding Mode;

KW, Kruskal-Wallis;

LBS, Live Birth System;

LST, Lives Saved Tool;

MA, Meta-analysis;

MCP, Medical Care Plan;

MCP FFS, Medical Care Plan Fee-for-Service Physician Claims;

MF, Mixed Feeding/Mixed Fed;

MTER, Meditech Module for Emergency Room Visits;

NL, Newfoundland and Labrador;

NLCHI, Newfoundland and Labrador Centre for Health Information;

NL SUPPORT, Newfoundland and Labrador Support for People and Patient Oriented Research Trials Unit;

OR, Odds Ratio

PDAD, Provincial Discharge Abstract Database;

PE, Patient Engagement;

PHAC, Public Health Agency of Canada;

POR, Patient-Oriented Research;

PROBIT, Promotion of Breastfeeding Intervention Trial;

RCT, Randomized Controlled Trial;

RoB, Risk of Bias;

RR, Relative Risk;

RIW, Resource Intensity Weight;

SD, Standard Deviation;

SRMA, Systematic Review and Meta-analysis;

TPMI, Translational Personalised Medicine Initiative;

UNICEF, United Nations International Children's Emergency Fund;

USPSTF, United States Preventive Services Task Force;

WHO, World Health Organization;

YOL, Year of Life

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Knowledge Translation

Oral Presentations

1. **A. Blackmore**, B. Howell, Z. Gao, HV. Nguyen, L.A. Allwood-Newhook, L.K. Twells. The Effectiveness of Virtual Lactation Support: A Systematic Review and Meta-Analysis. Research Reboot: Emerging from the fog, 2022. Memorial University Botanical Gardens, St. John's, NL. June 22, 2022.
2. **A. Blackmore**, H. Etchegary, K Parsons-Mercer, Z. Gao, HV. Nguyen, L.A. Allwood-Newhook, L.K. Twells. The Use of Patient Engagement to Gather Perceptions on The Cost of Infant Feeding. Research Reboot: Emerging from the fog, 2022. Memorial University Botanical Gardens, St. John's, NL. June 22, 2022.
3. **A.Blackmore**, S. Chowdhury, Z. Gao, HV Nguyen, W. Midodzi, N. Gill, B. Halfyard, L.A. Allwood-Newhook, L.K Twells. Infant Feeding Mode Predicts the Costs of Healthcare Services in One Region of Canada: a Data Linkage Pilot Study. The Baby-Friendly Initiative 2021 Virtual Symposium. October 1-7th, Organized by the Breastfeeding Committee of Canada.
4. **A.Blackmore**, S. Chowdhury, Z. Gao, HV Nguyen, W. Midodzi, N. Gill, B. Halfyard, L.A. Allwood-Newhook, L.K Twells. Infant Feeding Mode Predicts the Costs of Healthcare Services in One Region of Canada: a Data Linkage Pilot Study. Aldrich Interdisciplinary Conference, Memorial University of Newfoundland, St. John's, NL, March 21st 2021. [Accepted, Conference Postponed due to COVID-19]
5. **A. Taylor**, H. Nguyen, Z. Gao, S. Chowdhury, LA. Allwood Newhook, L. Twells. Infant feeding mode and its impact on health services use in infants during the

first year of life in the Eastern Health Region of Newfoundland and Labrador. 10th Annual international interdisciplinary conference, Maternal and Infant Nutrition and Nurture Unit (MAINN), University of Central Lancashire, Grange Over Sands, Cumbria, UK. June 10th – 12th 2019.

6. **A. Taylor**, H. Nguyen, Z. Gao, LA. Allwood Newhook, L. Twells. Differences in Self-Reported and Administrative Data on Health Care Service Use in infant's during the first year of life in the Eastern Health Region of Newfoundland and Labrador. 10th Annual international interdisciplinary conference, Maternal and Infant Nutrition and Nurture Unit (MAINN), University of Central Lancashire, Grange Over Sands, Cumbria, UK. June 10th – 12th 2019.
7. L. Twells, N. Alkusayer, W. Midodzi, **A. Taylor**, LA. Allwood Newhook. Assessing Changes in Infant Feeding Attitudes from Pre-Natal through to the Post-Partum Year. 10th Annual international interdisciplinary conference, Maternal and Infant Nutrition and Nurture Unit (MAINN), University of Central Lancashire, Grange Over Sands, Cumbria, UK. June 10th – 12th 2019
8. **A. Taylor**, H. Nguyen, Z. Gao, LA. Allwood Newhook, L. Twells. Breastfeeding and Childhood Obesity: A Cost Saving Analysis. 6th Canadian Obesity Summit, Westin Ottawa Hotel, Ottawa, ON, April 23rd-26th 2019.
9. **A. Taylor.** Investing in Healthy Mothers and Healthy Babies: A Patient Oriented Approach. Aldrich Interdisciplinary Conference, Memorial University, St. John's, NL, March 24th, 2019.

10. **A. Taylor.** Investing in Healthy Mothers and Healthy Babies: A Patient Oriented Approach. Current Controversies in Infant Feeding: Breastfeeding Symposium, Faculty of Medicine, Memorial University, St. John's, NL, October 25th 2018.
11. **A. Taylor.** Investing in Healthy Mothers and Healthy Babies: A Patient Oriented Approach. Research Rundown: Pitch Competition, 1st Place Winner, SHARE Summit, Memorial University, October 11th 2018
12. **A. Taylor**. Potential economic impact and cost savings analysis from improving breastfeeding rates in Canada. Clinical Epidemiology Seminar Series, Faculty of Medicine, Memorial University, March 21st, 2018.

Poster Presentations

1. **A.K. Taylor**, S. Chowdhury, Z. Gao, HV Nguyen, W. Midodzi, N. Gill, B. Halfyard, L.A. Allwood-Newhook, L.K Twells. Infant Feeding Mode Predicts the Costs of Healthcare Services in One Region of Canada: a Data Linkage Study. First Annual Community Health and Humanities & Clinical Epidemiology (CHH/CE) Student Research Day. Faculty of Medicine, Memorial University of Newfoundland, St. John's, NL, March 27th 2020.
2. **A.K. Taylor**, S. Chowdhury, Z. Gao, HV Nguyen, W. Midodzi, N. Gill, B. Halfyard, L.A. Allwood-Newhook, L.K Twells. Infant Feeding Mode Predicts the Costs of Healthcare Services in One Region of Canada: a Data Linkage Study. Newfoundland and Labrador Association of Students in Healthcare (NL-ASH). Faculty of Medicine, Memorial University of Newfoundland, St. John's, NL, March 20th 2020.

3. **A. Taylor,** H. Nguyen, Z. Gao, LA. Allwood Newhook, L. Twells**.** Investing in Healthy Mothers and Healthy Babies: A Patient Oriented Approach. A Plain Language Poster. NL Support SHARE Summit, Emera Innovation Exchange, Signal Hill Campus, St. John's, NL, October 10th 2019. [Plain Language]
4. **A. Taylor,** H. Nguyen, Z. Gao, LA. Allwood Newhook, L. Twells**.** Investing in Healthy Mothers and Healthy Babies: A Patient Oriented Approach. The Primary Healthcare Partnership Forum (Pri For), Emera Innovation Exchange, Signal Hill Campus, St. John's, NL, June 27-28th, 2019.
5. **A. Taylor,** H. Nguyen, Z. Gao, LA. Allwood Newhook, L. Twells**.** Investing in Healthy Mothers and Healthy Babies: A Patient Oriented Approach. Scholarship Day, Faculty of Medicine, Memorial University, St. John's, NL, June 7th, 2019.
6. **A. Taylor**, G. Logan, LA Newhook, L. Twells. Breast milk expression after Domperidone treatment in postpartum women. A Systematic Review and Meta-Analysis of Randomized Controlled Trials. Current Controversies in Infant Feeding: Breastfeeding Symposium, Faculty of Medicine, Memorial University, St. John's, NL, October 24th-26th 2018.
7. **A. Taylor,** H. Nguyen, Z. Gao, LA. Allwood Newhook, L. Twells**.**. Investing in Healthy Mothers and Healthy Babies: A Patient Oriented Approach. SHARE Summit, Memorial University, October 11th 2018
8. **A. Taylor**, G. Logan, LA Newhook, L. Twells. Breast milk expression after Domperidone treatment in postpartum women. A Systematic Review and Meta-Analysis of Randomized Controlled Trials. Scholarship Day, Faculty of Medicine, Memorial University, St. John's, NL, June 8th, 2018.

Peer Reviewed Publications & Abstracts

1. **A. Blackmore,** Etchegary H, Allwood-Newhook LA, Gao Z, Nguyen HV, Mercer-Parsons K, Twells L.The use of patient engagement to gather perceptions on the cost of infant feeding. Patient Related Outcome Measures Journal. Accepted for Publication, June 2022.
2. **A. Blackmore**, B. Howell, Z. Gao, HV. Nguyen, L.A. Allwood-Newhook, L.K. Twells. The Effectiveness of Virtual Lactation Support: A Systematic Review and Meta-Analysis. *Journal of Human Lactation*. https://doi.org/10.1177/08903344221099914
3. **A. Taylor**, S. Chowdhury, Z. Gao, HV. Nguyen, W. Midodzi, N. Gill, B. Halfyard, L.A. Allwood-Newhook, L.K. Twells. Infant Feeding Mode Predicts the Costs of Healthcare Services in One Region of Canada: A Data Linkage Pilot Study. *BMC Research Notes.* https://doi.org/10.1186/s13104-020-05228-6
4. **A. Taylor**, G. Logan, LA Newhook, L. Twells. Human milk expression after Domperidone treatment in postpartum women. A Systematic Review and Meta-Analysis of Randomized Controlled Trials. *Journal of Human Lactation*. https://doi.org/10.1177/0890334418812069
5. **A. Taylor**, H. Nguyen, Z. Gao, S. Chowdhury, LA. Allwood Newhook, L. Twells. Infant feeding mode and its impact on health services use in infants during the first year of life in the Eastern Health Region of Newfoundland and Labrador. *Maternal and Child Nutrition,* Nutrition and Nurture in Infancy and Childhood: Bio-cultural Perspectives, 10th Annual international

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6. **A. Taylor**, H. Nguyen, Z. Gao, LA. Allwood Newhook, L. Twells. Differences in Maternal Reported and Administrative Data on Health Care Service Use in infant's during the first year of life in the Eastern Health Region of Newfoundland and Labrador. *Maternal and Child Nutrition,* Nutrition and Nurture in Infancy and Childhood: Bio-cultural Perspectives, 10th Annual international interdisciplinary conference, Maternal and Infant Nutrition and Nurture Unit (MAINN), University of Central Lancashire, Grange Over Sands, Cumbria, UK. June 10th – 12th 2019.

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7. L. Twells, N. Alkusayer, W. Midodzi, **A. Taylor**, LA. Allwood Newhook. Assessing Changes in Infant Feeding Attitudes from Pre-Natal through to the Post-Partum Year. *Maternal and Child Nutrition,* Nutrition and Nurture in Infancy and Childhood: Bio-cultural Perspectives, 10th Annual international interdisciplinary conference, Maternal and Infant Nutrition and Nurture Unit (MAINN), University of Central Lancashire, Grange Over Sands, Cumbria, UK. June 10th – 12th 2019.

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Chapter 1: Introduction

1.1 Overview

This dissertation aims to explore best practice interventions that enable a supportive breastfeeding environment within the Setting determinant of the Lancet framework. It investigates a number of interventions that support breastfeeding mothers i.e., the use of galactogogues in postpartum mothers, healthcare outcomes and costs associated with infant feeding mode, mothers' perspectives on the cost surrounding infant feeding, and the use of virtual lactation care when supporting mothers postnatally.

This chapter outlines the background of my thesis research. It provides an overview of (i) global infant feeding recommendations, (ii) health benefits of breastfeeding (Infant and maternal), (iii) economic benefits of breastfeeding, (iv) trends of breastfeeding (globally, nationally and regionally), (v) reasons why EBF rates are low, (vi) supporting breastfeeding, introducing the lancet framework, and (vii) Structural, Setting, and Individual determinants of the Lancet framework. I then discuss the knowledge gap and research questions. Lastly, I outline the structure of this thesis.

1.2 Infant Feeding

1.2.1 Global Recommendations

The WHO and UNICEF breastfeeding recommendations are recognized globally and mirrored by Health Canada, the Canadian Paediatric Society, Dietitians of Canada and the Breastfeeding Committee for Canada. The WHO and UNICEF recommend that:

" .... children initiate breastfeeding within the first hour of birth and be exclusively breastfed for the first 6 months of life – meaning no other foods or liquids are provided, including water. Infants should be breastfed on demand – that is as often as the child wants, day and night. No bottles, teats or pacifiers should be used. From the age of 6 months, children should begin eating safe and adequate complementary foods while continuing to breastfeed for up to 2 years and beyond. " (4)

1.2.2 Human milk as Optimal Nutrition

Human milk is endorsed by organizations as the optimal form of infant nutrition, as it offers a unique matrix of compounds for optimal growth, health and development in a newborn child (5). There is a large and ever-growing body of literature examining the associations between infant feeding and health outcomes. Many studies have consistently shown that breastfeeding reduces infant morbidity and mortality rates and decreases the risk of chronic illnesses in childhood (6). The benefits of breastfeeding extend beyond that of infants and protect against several chronic illnesses for mothers later in life (7,8).

Due to the ethical limitations of using the randomized controlled trial (RCT) experiment to examine various infant feeding methods, the literature documented only one RCT study, namely, the Promotion of Breastfeeding Intervention Trial (PROBIT) (9). To bypass the ethical limitations of randomizing infant feeding groups, this RCT allowed for the randomization of an experimental breastfeeding promotion intervention. Within PROBIT, breastfeeding promotion was randomized across 31 hospitals in the Republic of Belarus (9). By comparing the impact of breastfeeding promotion with standard care on breastfeeding rates, the researchers demonstrated the health benefits of improved

breastfeeding rates. This was the first experimental study, a gold standard in evidence-based research, that could examine infant feeding mode and health outcomes (e.g., gastrointestinal tract infection, any respiratory tract infection). This study showed clear causal evidence of the protective effect of breastfeeding. The findings from this trial study are further supported by many observational studies, systematic reviews, and meta-analyses, as outlined below. They contribute important pragmatic data that consistently supports breastfeeding as the optimal form of infant nutrition and health.

1.2.3 Protective Effect of Breastfeeding

The guidelines provided by the World Health Organization (WHO), the United Nations Children's Fund (UNICEF) and Health Canada recommend mothers to exclusively breastfeed their infants to 6 months of age, with continued breastfeeding for up to 2 years of life (8). Breastfeeding is strongly recommended due to the documented benefits of human milk for both mother and child. Human milk decreases the incidence of mortality and morbidity related to infants' infectious diseases such as gastroenteritis, respiratory tract infections, acute otitis media, necrotizing enterocolitis, type 1 diabetes, and sudden infant death syndrome (6–8,10). In addition to immunological mechanisms of human milk, it includes a high concentration of oligosaccharides, peptides, and protective factors that protect against infections and illness (5). In addition to the benefits to an infant, some health benefits of breastfeeding have been identified for mothers. For instance, they have reduced postpartum bleeding, may return to pre-pregnancy weight at a faster rate, and are at a lower risk of developing breast and ovarian cancers (7,11,12). Based on the research surrounding the health benefits of breastfeeding, the promotion and

protection of breastfeeding has the potential to improve short- and long-term health outcomes in both mothers and infants. A table outlining a summary of evidence of the protective effect of breastfeeding is available in Appendix 1.1 (6–8,10–15).

1.2.4 Economic impact of breastfeeding

Several studies have assessed the economic value of breastfeeding and its association with lower rates of infant illness and healthcare service use (including the number and duration of hospitalizations, emergency room and physician visits). Repeated infection and hospitalizations in early life can lead to poor growth and development, and a substantial economic burden on the population and healthcare system (16).

The Lancet conducted a review using the Lives Saved Tool (LST) to estimate the impacts of increasing exclusive breastfeeding globally. The LST is a mathematical modelling tool that examines a given exposures impact on mortality rates in low- and middle-income countries. The research was conducted to examine the global impacts of suboptimal breastfeeding. The Lancet series has modeled scenarios that demonstrate how increasing EBF rates could lead to significant cost savings for individuals, healthcare system, and society through direct savings, which is associated with a decline in health care utilization from the reduction of illness; indirect savings, which emerges from the decrease in expenditures and used resources; and benefits to society by reducing the time missed at work by parents or caregivers (1,17)

Researchers examined the economic cost of lower cognition and childhood morbidity (1). The effect of breastfeeding on IQ was used to estimate the global loss in

the gross national income (GNI), where the loss associated with the suboptimal breastfeeding rates was estimated to be approximately $302 billion annually or 0.49% of world GNI (1). To show the potential effects of reduced morbidity on healthcare costs, they estimated the treatment costs of five common infectious diseases in childhood (otitis media, diarrhea, necrotising enterocolitis, pneumonia, and bronchiolitis). A 10% increase in exclusive breastfeeding up to 6 months or continued breastfeeding up to one or two years would translate into reduced treatment costs of at least $312 million in the USA, $7.8 million in the UK, $30 million in urban China, and $1.8 million in Brazil (2012 US$). Alternatively, if breastfeeding rates were to improve to 90% from the current reported national databases for USA, China, and Brazil, and to 45% for the UK would reduce treatment costs by at least $2.45 billion in the USA, $29.5 million in the UK, $223.6 million in urban China, and $6.0 million in Brazil (2012 US$) (1). Within the Lancet series, they found that if universally exclusive breastfeeding rates were 95% of infants at one month and 90% at six months, as well as 90% of infants partially breastfed between 6-23 months, up to 823,000 deaths in children under the age of five could be prevented (17).

More recently, a 2019 breastfeeding tool was developed to examine further the implications of suboptimal breastfeeding rates at a global level (18). The analysis results showed that 595,379 annual childhood deaths (6 to 59 months) from diarrhea and pneumonia and 974,956 annual cases of childhood obesity could be attributed to not breastfeeding for the duration and exclusivity that the WHO and UNICEF recommend. For women, breastfeeding is estimated to have the potential to prevent 98,243 annual

deaths from breast and ovarian cancers and type II diabetes. The authors outline how these morbidities could translate into global health system treatment costs of US$1.1 billion annually. The economic losses of premature child and women's mortality are estimated to equal US$53.7 billion in future lost earnings each year. The largest component of economic losses, however, is the cognitive losses, which are estimated to equal US$285.4 billion annually. By adding up these costs, the total global economic losses are estimated to be US$341.3 billion, or 0.70% of global GNI (18).

1.3 Trends of breastfeeding

1.3.1 Global trends

Based on the World Health Statistics, there are approximately 135 million babies born annually (19). Of these, 41% are exclusively breastfed to six months of age, while 45% are provided any human milk through continued breastfeeding up to two years of life (19). If exclusive breastfeeding rates were increased universally (from 37% in low and middle income countries, to 95% exclusively breastfeeding to 6 months), research shows the estimated global impacts would account for 823,000 preventable child deaths annually (17). The World Health Organization 2025 Global Target Exclusive breastfeeding rate is to have at least 50% of mothers exclusively breastfeeding to 6 months of age (20). The WHO released a policy brief outlining how targeted breastfeeding duration rates and exclusivity can be obtained.

1.3.2 National trends

In Canada, the breastfeeding initiation rate remains one of the highest among developed countries (17). Though the average breastfeeding initiation rate is 90%,

exclusive breastfeeding rates remain low, with 32% of mothers EBF for six months. In addition, there lies much heterogeneity in the initiation and exclusive breastfeeding rate across the Canadian provinces and territories. For instance, the highest initiation rates reported nationally are in British Columbia and Yukon, and the lowest rates are in Newfoundland and Labrador (17).

1.3.4 Provincial trends

Among the Canadian provinces, Newfoundland and Labrador (NL) has the lowest rates of breastfeeding initiation. Though higher than what is reported at a national level, 70.6% of mothers are said to initiate breastfeeding in hospital, while 20.6% exclusively breastfeed to 6 months (2). Breastfeeding initiation rates within the province have been continuously improving over the last 30 years (35.3 to 70.6%), however most women stop breastfeeding prematurely (Perinatal Program Newfoundland and Labrador, August 15, 2021). Based on the initiation rates within our province, the intent and desire to breastfeed are present; however, there is a stark drop in duration rates when examining exclusive breastfeeding rates beyond the early stages of infancy.

1.3.5 Why are rates low?

When comparing the rates of initiation and duration of exclusive breastfeeding, it is evident that many mothers do not breastfeed for their desired duration. There are many reasons why breastfeeding rates are low. The decisions and behaviours surrounding infant feeding are complex and influenced by several factors. This includes structural factors (e.g., cultural norms, societal pressures), setting factors (e.g., access to prenatal education, experiences while in hospital, lack of support or access to health professionals, maternity

leave policies) and individual characteristics (e.g., mothers' attributes, mother infant relationship) (1). The reasons reported by mothers for discontinuing breastfeeding include issues with lactation, latching and perceived milk supply (21), concerns regarding infant nutrition and weight gain, lack of confidence in their abilities to adequately nourish their infant (21), societal and cultural norms and lack of family support (22), and unsupportive work policies or hospital practices (22,23). There is a large and growing body of research on which interventions to improve breastfeeding rates, both for improving initiation and duration of breastfeeding. Successful breastfeeding practices involve support at many levels including policy, social attitudes, values, employment conditions, and health care services that support women in breastfeeding (1).

1.4 Lancet Framework

In 2016, the Lancet published a series titled "Why invest, and what will it take to improve breastfeeding practices?"(1). In this series of articles, the authors summarized evidence surrounding the protective effect of breastfeeding, the economic benefits found globally, and created a framework that outlines the types and levels of interventions needed to improve breastfeeding practices. The Lancet framework includes several levels of determinants, and associated interventions that increase EBF.

The Lancet framework examines the best practice interventions that, if implemented, would enable a supportive environment to increase rates of breastfeeding (1). It outlines three levels of Determinants that impact breastfeeding: (i) Structural, (ii) Setting and (iii) Individual (**Figure 1.1**). Numerous interventions have been identified for

these three levels for enhancing the initiation and continuation of breastfeeding. They touch on mass media interventions, legislation and policy, and individual-level intervention through support and healthcare services. Each level is outlined and further discussed below.

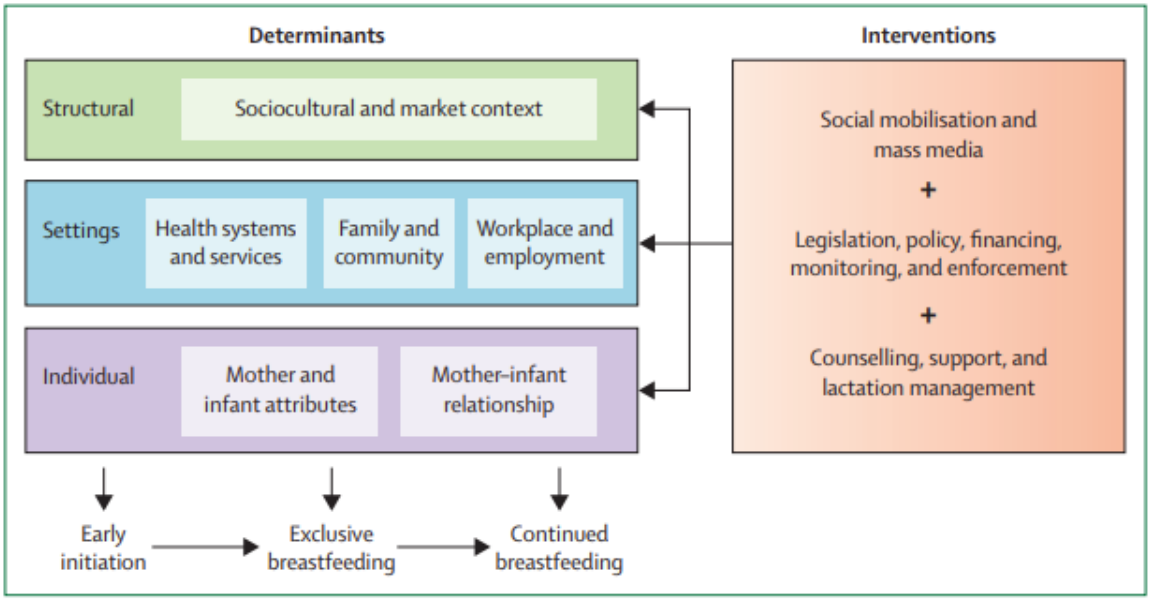

Figure 1.1 The components of an enabling environment for breastfeeding.

Reprinted from Publication The Lancet (British Edition), Vol 387 (10017), Rollins, Bhandari, N., Hajeebhoy, N., Horton, S., Lutter, C. K., Martines, J. C., Piwoz, E. G., Richter, L. M., & Victora, C. G. (2016). Why invest, and what it will take to improve breastfeeding practices? The Lancet., Page 492, Copyright (2022), with permission from Elsevier

1.4.1 Structural Determinants

The Structural determinants refer to "*social factors that affect the whole population*" (1). This broadly encompasses social norms or trends, defined as *" Common standards within a social group regarding socially acceptable or appropriate behaviour*

in particular social situations, the breach of which has social consequences" (24), which would include any beliefs about what a mother does within society, and may be unsupportive or actively undermine breastfeeding. Consequently, it is essential to foster positive societal attitudes towards breastfeeding. It is important to ensure breastfeeding promotion and educational materials are easily accessible to increase the capacity for education to all members of society. This could alter attitudes towards breastfeeding from an early age continuing into adulthood to foster breastfeeding knowledge and empowerment in our communities. This would also include providing accessible "baby-friendly spaces" including family-friendly public spaces (i.e., comfortable and precise areas devoted to breastfeeding and child care needs) (25).

Media advertisements and product availability of infant formula also influence the Structural determinant, both of which fall highly on the WHO code for the marketing of breastmilk substitutes. Globally, formula companies market aggressively to potential mothers, sending coupons or free samples to their homes or advertising within clinics or hospitals (26). The Lancet outlines how the information within the media and society is not uniformly interpreted, as pregnant mothers or women with young children are affected in more direct and personalized ways. The WHO International Code of Marketing of Breastmilk Substitutes is an intervention at the structural level which can impact legislation and policy if enforced to protect expecting mothers. The WHO code aims to protect mothers and babies of any feeding mode, to prevent the aggressive marketing practice of formula companies that often impact or prevent mothers from meeting their breastfeeding goals (27). At a Structural level, many legislations and

policies can help to enhance the environment that supports breastfeeding mothers (i.e., enforcing the WHO code, or mandating breastfeeding-friendly policies and spaces in the workplace).

1.4.2 Setting Determinants

The barriers outlined within this level can be policies and practices not supporting breastfeeding within institutions where women live and work, such as hospitals, worksites, or communities. Negative impacts of the Setting determinants can be related to a mother's hospital stay, where it may lack lactation support due to untrained staff, removing the baby from the mother after birth due to routine practices instead of increasing bonding time or skin to skin, lack of support after birth trauma, or the distribution of formula within hospital Settings (28). Many of these steps fall under the WHO Baby-Friendly Hospital Initiative (BFHI), which was launched in 1991 to ensure that all hospitals support breastfeeding. UNICEF and WHO issued a ten-step tool, the BFHI, to guide practices within healthcare facilities that provide maternity and newborn services. The ten steps outline critical management procedures and key clinical practices that must be obtained to hold the BFHI status within a healthcare facility and are outlined in Table 1.1 (29). These evidence-based procedures and practices have been found to significantly improve breastfeeding rates (29).

Table 1.1 Outlines the WHO ten steps to successful breastfeeding.

Critical management procedures:

1a	Comply fully with the *International Code of Marketing of Breast-milk Substitutes* and relevant World Health Assembly resolutions.
1b	Have a written infant feeding policy that is routinely communicated to staff and parents.
1c	Establish ongoing monitoring and data-management systems.
2	Ensure that staff have sufficient knowledge, competence and skills to support breastfeeding.
Key clinical practices:	
3	Discuss the importance and management of breastfeeding with pregnant women and their families.
4	Facilitate immediate and uninterrupted skin-to-skin contact and support mothers to initiate breastfeeding as soon as possible after birth.
5	Support mothers to initiate and maintain breastfeeding and manage common difficulties.
6	Do not provide breastfed newborns any food or fluids other than breast milk, unless medically indicated.
7	Enable mothers and their infants to remain together and to practise rooming-in 24 hours a day.
8	Support mothers to recognize and respond to their infants' cues for feeding.
9	Counsel mothers on the use and risks of feeding bottles, teats and pacifiers.
10	Coordinate discharge so that parents and their infants have timely access to ongoing support and care.

A systematic review of 58 studies showed substantial evidence that meeting the designation of the BFHI significantly improves breastfeeding rates, measured by rates of initiation, duration, and exclusive breastfeeding (30). Mothers can also experience barriers at work. Mothers report that return to work often impacts their goals relating to the duration of breastfeeding. Through policy, employers are asked to make reasonable accommodations for nursing mothers, providing them time (though not necessarily paid) and a private space (not well defined) to pump at work (31). Despite this progress,

women still have an uphill battle when considering pumping at work, facing limitations based on their career path, inability to schedule breaks, or not wanting to have uncomfortable conversations with bosses or co-workers (32). Research shows that infants who are breastfed are less likely to encounter acute or chronic illnesses and that breastfeeding provides protection against illnesses like the common cold and flu (6). Therefore, mothers who provide human milk to their babies are less likely to miss work to care for their sick children (due to decreased likelihood of illness and infection); however, there is a lack of social acceptability of breastfeeding or pumping breaks while working. For those that do plan on pumping when returning to work, there are also the economic barriers of accessing quality breast pumps and storage. Lastly, family and community support, or lack thereof can provide barriers or opportunities to breastfeeding. Similarly, to address the social norms above, the beliefs or practices of a mother's support, whether familial or within their community, may be unsupportive or undermine breastfeeding. Actively promoting, supporting, and protecting breastfeeding within society is critical to mothers breastfeeding journey. Demonstrating to policymakers the importance of hospital initiatives, safe workplaces, and enhancing the education and support within our communities is critical.

1.4.3 Individual Determinants

Lastly, the Lancet outlines the individual level and the attributes of women and their babies that influence their breastfeeding practices. Mothers' attributes that affect their likelihood of breastfeeding include factors like age, weight, education, income, marital status, maternal expectations or confidence (1). Studies show that women above

30 years old are significantly more likely to initiate and continue breastfeeding than younger women (less than 20 years old or 20-29) (33). Research also shows that high-educated women, women in the high-income class, and women who live with a partner are more likely to breastfeed (34). There are also differences in initiation rates across race and ethnicity subgroups. The Centers for Disease Control and Prevention released initiation statistics that show approximately 83% of Asian, Hispanic, Hawaiian-Pacific Islander, and Caucasian women initiate breastfeeding, compared to 71% of American Indian/Alaska Native and 66% of black women (34). Social determinants of health impact breastfeeding as well, as the inequalities associated with inaccessibility of supports related to breastfeeding (34). Additional attributes at the individual level would be related to a mother's ability to produce and express human milk (1,17). Difficulty with human milk production can be impacted by several factors, including preterm delivery, maternal-infant separation, cesarean section delivery, and other maternal factors and illnesses (35). Several interventions are used to increase human milk volume: the use of a breast pump 7-8 times a day, skin-to-skin contact, lactation counseling, and hand expression (36). These are effective tools, but some women with insufficient milk production will not respond to these methods and may need to further seek out methods to induce lactation.

In addition to the mothers' attributes, there are also the baby's attributes, such as sex, wellbeing, and temperament (1). The mothers' ability to satisfy and ensure the baby is content plays a prominent role in breastfeeding practices (1). The Lancet series outlines how it is an internalization of the influences and experiences within the structural and

Setting levels that further impact this relationship and mothers' feelings surrounding infant feeding, highlighting how ones expectations may also impact this relationship and the practicalities breastfeeding practices (1).

1.4.4 Aligning with the Lancet Framework

The primary focus of the thesis is to explore the best practice interventions that enable a supportive breastfeeding environment at the Setting level: Health System, Policy and Community. For the purpose of this thesis, I outline where the chapters of my thesis fit in the Lancet framework (Figure 1.2). I describe the importance of policy, health system and community support within the Setting Determinant and how these interventions protect, promote and support breastfeeding.

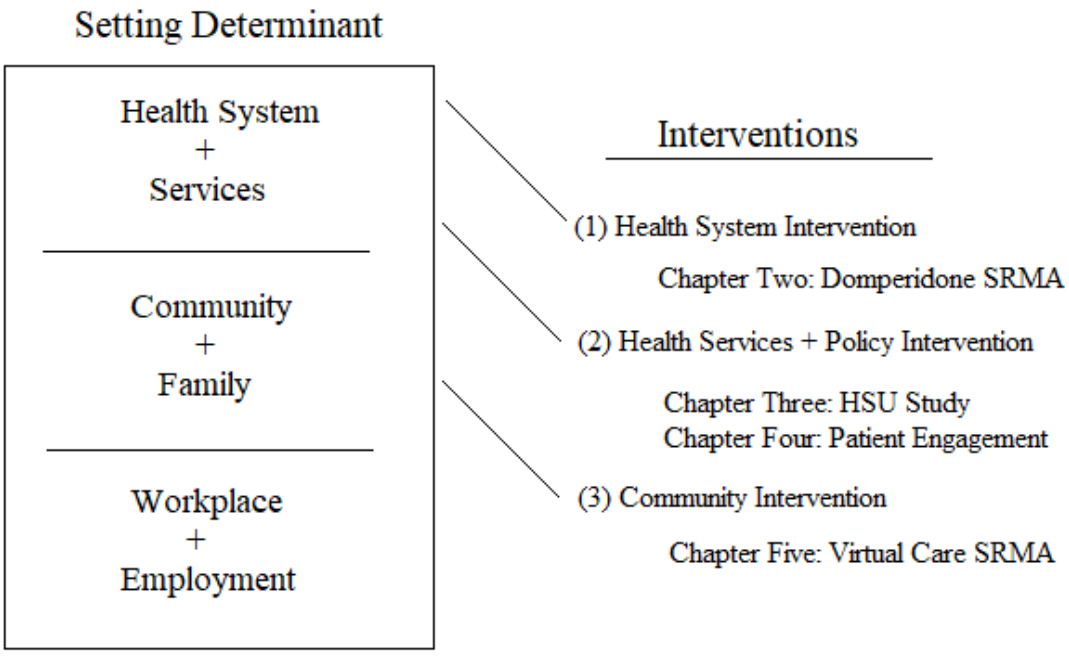

Figure 1.2 Aligning with the Lancet Framework.

1.5.1 Knowledge gap in Chapter Two: Human Milk Expression After Domperidone Treatment in Postpartum Women: A Systematic Review and Meta-Analysis of Randomized Controlled Trials

Several interventions are used to increase human milk volume: the use of a breast pump 7-8 times a day, skin to skin contact, lactation counseling, and hand expression (36). These are effective tools, but some women with insufficient milk production will not respond to these methods and may need additional methods to induce lactation. Recently there has been an increased use of medications used to induce or augment lactation in breastfeeding women called pharmacological galactagogues (37). This form of intervention is often sought out once the use of traditional non-pharmacological galactagogues has failed.

Domperidone is an anti-dopaminergic drug created to prevent nausea and vomiting but found to augment human milk production (38,39). It is believed to increase a mother's human milk production by increasing the hormone levels of prolactin in the body, and due to its inability to penetrate the blood-brain barrier results in few side effects (40,41). However, in 2004, the United States Food and Drug Administration (FDA) issued an advisory warning and block of Domperidone, citing concerns over reported cardiac arrhythmias from intravenous injections of Domperidone in cancer patients receiving chemotherapy (42,43). While Domperidone is not available for any indication in the United States due to arrhythmia concerns, it is approved in Canada and some other countries as a gastrokinetic medication, and it is widely used in practice as an off-label galactagogue (44). Currently the Academy of Breastfeeding Medicine, a credible organization that provides guidance and education regarding breastfeeding, does not

recommend any specific pharmacologic galactagogues citing insufficient evidence due to side-effects (45).

Previous systematic reviews and meta-analyses (SRMA) have been published on the effectiveness of Domperidone as a galactagogue, but these reviews do not include the latest research, and had small combined sample sizes which decreased the confidence in their meta-analyses (46,47). However, they have shown that there are minimal side effects from Domperidone as a galactagogue (46,47). More recent published randomized controlled trials (RCTs) have provided an opportunity to reevaluate this evidence, as well as an opportunity to analyze the sustained effects of Domperidone when used for greater than a week (41,48). This systematic review adds to the growing body of literature supporting the effectiveness of the use of Domperidone as a galactagogue for breastfeeding mothers.

1.5.2 Knowledge gap in Chapter Three: Infant Feeding Mode Predicts the Costs of Healthcare Services in One Region of Canada: A Data Linkage Study

Globally, studies have been conducted looking at the economic impact of suboptimal breastfeeding. Lower rates of breastfeeding initiation and exclusive breastfeeding duration have been linked to increases in annual childhood deaths related to diarrhea and pneumonia, cases of childhood obesity, and deaths related to maternal breast and ovarian cancers. The global analysis found that the morbidity and mortality rates lead to annual treatment costs of US$1.1 billion globally (18). There has been a lack of Canadian data examining the relationship between infant feeding mode and healthcare service use and costs in the literature. Studies have noted a lack of open access data

within Canada, as well as the lack of individual-level data studies within a Canadian context. At this time, we do not have sufficient valid or reliable data on measures of infant feeding in relation to healthcare use on a national level for these analyses.

In Canada, little is known about the economic impact of increasing breastfeeding rates, as few studies have examined the impact of infant feeding mode (IFM) on healthcare service use (HSU) (49–51). Two studies concluded that breastfeeding was strongly protective against hospital admission due to severe infections; however, both studies were small and focused on Indigenous populations (49,51), and neither study conducted a cost analysis related to hospital admissions, emergency room (ER) visits or physician consultations. Further studies are required to investigate total HSU costs in a Canadian context to better understand where an investment in interventions is needed to reduce the healthcare service use and unsustainable expenditures.

To examine this relationship, I conducted individual-level data analyses to ascertain health service use and the direct cost of infant feeding. While population-based data are valuable, it is also important and useful to quantify the association of infant feeding and healthcare resource cost at the individual patient level. Linking data at this level allows for exploring this relationship while controlling for known confounders (such as socioeconomic status, maternal age, education, etc.). In the current thesis, an analysis of individual-level data, allowing for the adjustment for many potential confounders, was conducted, instead of the more commonly used prevalence-based approach used globally. Linking individual-level data to physician and hospital databases enabled us to examine objective utilization to identify whether infant feeding mode is an independent predictor

of either health services use or direct healthcare costs. The ability to access health survey data representative of the provincial population and to link information to objective health services utilization data allows for the control of potential confounders and may provide a better understanding and a more reliable estimate of the healthcare utilization and its associated cost by infants during their first year of life.

1.5.3 Knowledge gap in Chapter Four: The use of patient engagement to gather perceptions on the cost of infant feeding

An area of research that would provide invaluable insight to its research outcomes using POR would be in cost analyses, specifically those examining the costs associated with breast and formula feeding. Over the last number of decades researchers have examined the value of breastfeeding and its association with lower rates of infant illness, and subsequently healthcare service use, including number and duration of hospital admissions, emergency room and physician visits (6,13). Studies have found that the protective effect of breastfeeding on a number of acute infections in infancy, and chronic illnesses in childhood, and that low breastfeeding rates increase the costs to the healthcare system (52,53). Researchers have also examined the indirect costs associated with infant feeding. These include costs that are incurred by patients or families because of their infections or illness (54). Taking all costs into consideration, researchers in the US have examined the economic impact on the healthcare system, society and the costs related to premature death, showing how suboptimal breastfeeding rates cost the US economy 14$ billion annually (3). By demonstrating the economic benefits of increasing breastfeeding rates, policymakers can make informed decisions around the development of policies and programs to invest in breastfeeding support.

While cost analyses have examined a wide scope of outcomes associated with the costs of infant feeding, there is still a gap when considering the cost of infant feeding to mothers and families. Largely, the opportunity costs associated with a mothers' time and caregiving, especially that spent breastfeeding (55). With a gap in costs related to mothers, I sought to engage mothers using the principles of patient-oriented research, to obtain their perceptions of the associated costs of infant feeding. By engaging with those with lived experience, I sought to understand their perspectives on additional costs and outcomes that could be considered in future cost analyses.

The overarching goal of POR and the development of patient engagement is to ensure research is relevant, valuable and a priority to those it impacts directly. In this paper we provide an example of using POR, specifically patient engagement methods to explore costs of infant feeding from mothers' perspectives. Using the guiding principles of POR and patient engagement, our aim was to engage with mothers, to gather their perceptions on the costs of infant feeding. By identifying and prioritizing costing outcomes of importance to mothers, our study hopes to guide future research around the costs of infant feeding, from a mothers' perspective.

1.5.4 Knowledge gap of Chapter Five: The effectiveness of virtual lactation care, a systematic review and meta-analysis

To enable mothers to establish and sustain their desired breastfeeding initiation and duration, the WHO and UNICEF recommend that pregnant women and their families be counselled about the benefits and management of breastfeeding, as well as offered antenatal breastfeeding education. These channels should be tailored to mothers' individual needs and consider their social and cultural context. The rising popularity of

technology has allowed for a shift from traditional care to technology-based modes of care (56). This may include any form of information communication technologies (ICTs), such as e-health, m-health, telehealth, transforming available care from lactation support. The use of these technologies is even more significant at the current time, given the health risks and restrictions due to the Covid-19 pandemic. E-health support, such as internet and web-based interventions, is a potential way to increase the length of EBF (56). These technologies can also enhance patients' access to supporting resources during breastfeeding, especially between visits. It may allow for "*more widespread dissemination of evidence‐based care to a broader audience in a wide array of settings and models of care than is currently possible with traditional models alone* (57)" . Pate conducted a systematic review and meta-analysis (SRMA) of breastfeeding intervention delivery methods and found that internet-based interventions were significantly effective. "The pooled results indicated that studies using e-based interventions had a moderate effect on breastfeeding (odds ratio (OR) 2.2 [1.9-2.7], d = 0.5". These findings suggest internet-based interventions may be an effective and efficient alternative to in-person interventions to support breastfeeding. To our knowledge, there are no systematic reviews (SR) exploring randomized control trials (RCT) of lactation support using various ICTs. Existing SRs exploring ICT and breastfeeding support included non-randomized trials and interventions in education and promotion technologies in the prenatal period, while our review will focus exclusively on lactation support postpartum (58,59). Existing reviews also only include studies published until Nov 2018, and the investigators of existing SRs in this area have not conducted a meta-analysis (MA) due to differences in study methodologies (i.e., study designs), breastfeeding outcomes (i.e., initiation, any

breastfeeding, EBF), intervention types (i.e., prenatal/postnatal) and intended users (i.e., mothers, partners, clinicians) (58,59). Given the increasing importance of and reliance on technologies in healthcare, it is crucial to update the existing literature on lactation support offered through virtual care. The aims of this study were twofold, namely, (1) to critically review and (2) to analyze the effectiveness of virtual lactation support for postpartum mothers' exclusive breastfeeding for up to 6 months.

1.5.5 Research questions

There are several areas in which this research adds to the current state of knowledge. The primary focus of the thesis is to explore the best practice interventions that enable a supportive breastfeeding environment at the Setting level: Health System, Policy and Community.

A combination of quantitative and patient-oriented research methods were used to answer the following research questions:

(i) What is the efficacy of Domperidone as a galactagogue compared to placebo when given to mothers with insufficient human milk production?

(ii) What are the differences in healthcare service use and its associated costs by infant feeding mode (exclusive breastfeeding, mixed feeding and formula feeding) in an infant's first year of life?

(iii) What are mothers' perceptions of the costs associated with infant feeding?

(iv) What is the effectiveness of virtual lactation support compared to standard care for postpartum mothers?

This research adds to a growing body of literature examining interventions that support breastfeeding mothers. Within the Setting determinant of the Lancet framework, I want to further explore interventions that have the ability to support mothers and increase rates of exclusive breastfeeding. The outcomes of this thesis are expected to provide evidence towards the best practice interventions that support breastfeeding by (i) exploring the efficacy of galactagogues for increasing human milk production during the postpartum period, (ii) demonstrating the healthcare costs and outcomes associated with breastfeeding and formula feeding (iii) highlighting the costs and outcomes associated with infant feeding as identified by mothers and (iv) providing evidence towards the effectiveness of virtual lactation support for postpartum mothers.

1.6 Thesis organization

This thesis is organized in a manuscript format, which includes four published articles as chapters 2-5. The chapters in this manuscript-based thesis are “stand-alone”, in that they were prepared for separate publications. However, all components have been integrated into a logical progression from chapter to chapter, presenting the publications in a unified and cohesive way. Due to this dissertation style, there is some unavoidable repetition within the introduction and methods sections. Every attempt was made to vary the language to tailor the information to the specific content of each chapter
Table 1.2 shows the published papers completed during the research and outlines the objectives of each chapter.

Papers as chapters	Objectives
Chapter 2: Human Milk Expression After Domperidone Treatment in Postpartum Women: A Systematic Review and Meta-Analysis of Randomized Controlled Trials	The aim was to update the existing literature on the efficacy of Domperidone as a galactagogue compared to placebo when given to mothers with insufficient human milk production.
Chapter 3: Infant Feeding Mode Predicts the Costs of Healthcare Services in One Region of Canada: A Data Linkage Study	The aim of this study is to evaluate differences in HSU and associated costs by IFM, in an infant's first year of life in one region of Newfoundland and Labrador, Canada.
Chapter 4: The use of patient engagement to gather perceptions on the cost of infant feeding	The objectives of our PE sessions were to identify outcomes to be included in a future cost analysis from a mother's perspective
Chapter 5: The effectiveness of virtual lactation care, a systematic review and meta-analysis	The objective of our SRMA was to evaluate the effectiveness of virtual lactation support compared to standard care for breastfeeding mothers

Chapter 2: Human Milk Expression After Domperidone Treatment in Postpartum Women: A Systematic Review and Meta-Analysis of Randomized Controlled Trials

Preface

A version of this chapter has been published in the Journal of Human Lactation. The SAGE reuse policy allows for the final published PDF to be shared in an author's dissertation or thesis (https://us.sagepub.com/en-us/nam/journal-author-archiving-policies-and-re-use). Taylor A, Logan G, Twells L, Newhook LA. Human Milk Expression After Domperidone Treatment in Postpartum Women: A Systematic Review and Meta-Analysis of Randomized Controlled Trials. *Journal of Human Lactation*. 2019;35(3):501-509. doi:10.1177/0890334418812069 As the primary author, along with Gabriela Logan, I contributed to the acquisition, analysis and interpretation of the data, drafted the manuscript, and critically revised the manuscript for final submission. Dr. Laurie Twells and Dr. Leigh Anne Newhook contributed to the conception of the study design, critically revised the final manuscript and gave final approval for submission.

Abstract

Background: Insufficient milk production is among the most cited reasons by mothers for discontinuing breastfeeding. Medications that can increase milk production, such as Domperidone, an off-label galactagogue, are often prescribed. Domperidone is

controversial as it is not approved for any purpose in the United States and is approved only for gastrokinetic

purposes in Canada and other countries.

Research Aim: The aim was to update the existing literature on the efficacy of Domperidone as a galactagogue compared to placebo when given to mothers with insufficient human milk production. The primary outcome is the change in expressed human milk volume per day from baseline.

Methods: The authors independently searched the literature from inception to May 2018. The search included any randomized controlled trials examining the efficacy of Domperidone increasing mothers' expressed human milk, measured via a human milk pump. Both authors independently assessed quality and risk of bias and extracted relevant data. Meta-analysis on expressed human milk volume per day was performed.

Results: Seven studies met the inclusion criteria for review; two were excluded from the meta-analysis due to quality grading and insufficient reporting of the outcome of interest. Five studies (N = 239) were combined in the meta-analysis. The effect size showed an increase in the mean difference of expressed human milk volume in mothers given Domperidone, 93.97 mL per day (95% CI [71.12, 116.83 mL]; random effect, T2 0.00, I2 0%).

Conclusion: This meta-analysis reports a significant improvement in expressed human milk volume per day with the use of Domperidone in mothers experiencing insufficient human milk production.

Keywords

breastfeeding, galactogogues, human milk expression, lactation, milk ejection

2.1 Introduction

Breastfeeding provides health benefits to infants that have been studied for decades (17). After giving birth there are many factors that affect a mother's decision to breastfeed, one of which can be caused by difficulties with milk supply (1,17). Difficulty with human milk production can be impacted by preterm delivery, maternal-infant separation, caesarean section delivery, and other maternal factors and illnesses (35). There are several interventions used to increase human milk volume that include: the use of a breast pump 7-8 times a day, skin to skin contact, lactation counseling, and hand expression (36). These are effective tools, but some women with insufficient milk production will not respond to these methods and may need to further seek out methods to induce lactation. Recently there has been an increased use of medications used to induce or augment lactation in breastfeeding women called pharmacological galactagogues (37). This form of intervention is often sought out once the use of traditional non-pharmacological galactagogues have failed.

Domperidone is an anti-dopaminergic drug created to prevent nausea and vomiting but found to augment human milk production (38,39). It is believed to increase a mother's human milk production by increasing the hormone levels of prolactin in the body, and due to its inability to penetrate the blood-brain barrier results in few side effects (40,41). However, in 2004, the United States Food and Drug Administration (FDA) issued an advisory warning and block of Domperidone, citing concerns over reported cardiac arrhythmias from intravenous injections of Domperidone in cancer

patients receiving chemotherapy (42,43). While Domperidone is not available for any indication in the United States due to arrhythmia concerns, it is approved in Canada and some other countries as a gastrokinetic medication, and it is widely used in practice as an off-label galactagogue (44). Currently the Academy of Breastfeeding Medicine, a credible organization that provides guidance and education regarding breastfeeding, currently does not recommend any specific pharmacologic galactagogues citing insufficient evidence due to side-effects in the galactagogues available (45).

Previous systematic reviews and meta-analyses (SRMA) have been published on the effectiveness of Domperidone as a galactagogue, but these reviews do not include the latest research, and had small combined sample sizes which decreased the confidence in their meta-analyses (46,47). However, they have shown that there are minimal side effects from Domperidone as a galactagogue (46,47). Recent published randomized controlled trials (RCTs) have provided an opportunity to reevaluate this evidence, as well as an opportunity to analyze the sustained effects of Domperidone when used for greater than a week (41,48).

2.2 Objectives

The main objective of the current study is: assess the effectiveness of Domperidone as a galactagogue in a SRMA in women with infants born either pre- or full term experiencing insufficient human milk production and to determine its impact on expressed human milk volume (EBMV). The secondary objective is to examine whether there are differences in EBMV based on the length of time using Domperidone.

2.3 Methods

This study was conducted using the guidelines of the Preferred Reporting Items for Systematic Review and Meta-Analysis Checklist (PRISMA 2009; www.prisma-statement.org) (Appendix 2.1).

2.3.1 Search Strategy

Eligibility criteria for studies included RCT study designs that examined the effect of Domperidone on human milk volume in postpartum women. For inclusion in the review, a placebo comparison group had to be available. The primary outcome was EBMV measured directly using a human milk pump, and studies that indirectly collected the EBMV were excluded.

The initial search strategy was designed with the assistance of a medical librarian. The authors independently performed a literature search of the following databases: PubMed, Embase and CINAHL. Keywords included breast feeding, milk expression, milk ejection, lactation, Domperidone and galactagogue. The expanded search string used for each electronic database can be found in Appendix 2.2. All databases were searched from inception until May 29, 2018.

Reference lists of relevant studies and systematic reviews were reviewed for any further study that the search strategy did not retrieve. Email alerts on the three main databases were also created to allow the finding of any new study published while this SRMA was conducted, and ClinicalTrials.gov was searched for any additional articles. These search methods were exhaustive and only three additional articles were found in this manner.

2.3.2 Study Selection

Results from the search strategy were combined and duplicates were removed using Endnote (version X 7.5, 2016). Titles and abstracts were screened once duplicates were removed. Title and abstract screening was done independently by two reviewers with consensus (AT, GL). The exclusion criteria were outlined as follows: nonclinical studies, reviews, study protocols, interventions not involving Domperidone, non-placebo comparators, outcomes not involving human milk volume, indirect measures of EBMV, and study duplicates that were missed in initial identification.

The screened selections were compared to examine agreement between the two reviewers (AT, GL) regarding study eligibility for full text review, and the reason for excluding ineligible studies. The two reviewers independently performed this full text screening, in which the inclusion criterion was rigidly applied. The reviewers compared studies that were included or excluded at this stage, where inter-rater agreement was 100%.

2.3.3 Data collection process & Data items

Each reviewer independently extracted relevant study data including author's name, year of publication, country of conducted study, study population, sample size, study design details (e.g. blinding level, single center vs multicenter), Domperidone and placebo dosage, duration of intervention, primary outcome, and any adverse events (Table 2.1). A data abstraction form was created for the SRMA, where both authors independently collected the pre-and post-volume data to calculate the mean difference and standard deviation for each arm of the studies. Mean difference (MD) and standard deviation (SD) was calculated, comparing the difference between baseline and final

measurements of the EBMV. Authors were contacted and asked for raw data, when study results were published in a way that limited the use in the SRMA.

2.3.4 Risk of Bias & Quality Assessment

Two independent reviewers (AT, GL) assessed the quality of the included RCT's by applying US Preventive Services Task Force (USPSTF) Quality Rating Criteria for RCTs (60). Studies that met the inclusion criteria were graded on: the quality of information provided for blinding, randomization, confounder consideration, comparable groups, reliable outcome measures, intervention definition, appropriate outcome reporting, stratification of analysis to control for confounders, and the treatment of missing variables. These quality components in the studies were graded as good, fair, low, or unclear and an overall study quality grade was given with a corresponding risk of bias from the Cochrane Risk of Bias Tool (61). Publication bias was visually assessed using a funnel plot once the MA was completed.

2.3.5 Synthesis of results

Across all studies the mean difference from pre- and post-intervention EBMV was calculated and analyzed. Methodology of calculations can be found in Appendix 2.3. Due to the outcome measures calculated across trials the analysis used continuous data. Meta-analysis of the EBMV MD was completed using Review Manager Software, RevMan 5.3 (62). The researchers used a random effects model for the meta-analysis for combining data, as although methods were judged to be similar, they were not similar enough to use a fixed-effects model. The differences across populations were due to studies being conducted in different countries, including mothers with different methods

of delivery who had given birth to either preterm or full-term infants, or mothers receiving different doses of Domperidone for different lengths of time. The random-effects model produced an overall summary statistic, and the results are presented as the MD in EBMV with its 95% Confidence Interval and SD, and the estimates of Tau and Heterogeneity.

2.3.6 Subgroup Analysis

A priori, the authors discussed the subgroup analyses that should be performed across the studies. The researchers planned to complete a subgroup analyses based on length of duration of receiving the intervention ($\leq$ 7 days, and > 7 days) and the term of the infants (premature vs full-term).

2.4 Results

2.4.1 Study Selection & Study Characteristics

The PRISMA flow diagram outlining the identification, screening, and inclusion criteria is outlined in Figure 2.1. The search strategy identified eight studies that were good candidates for inclusion. One of these studies was found by another SRMA, but the individual RCT was not accessible through our universities database and therefore was not available for evaluation. Seven studies were included in the qualitative review. The studies are summarized in Table 2.1.

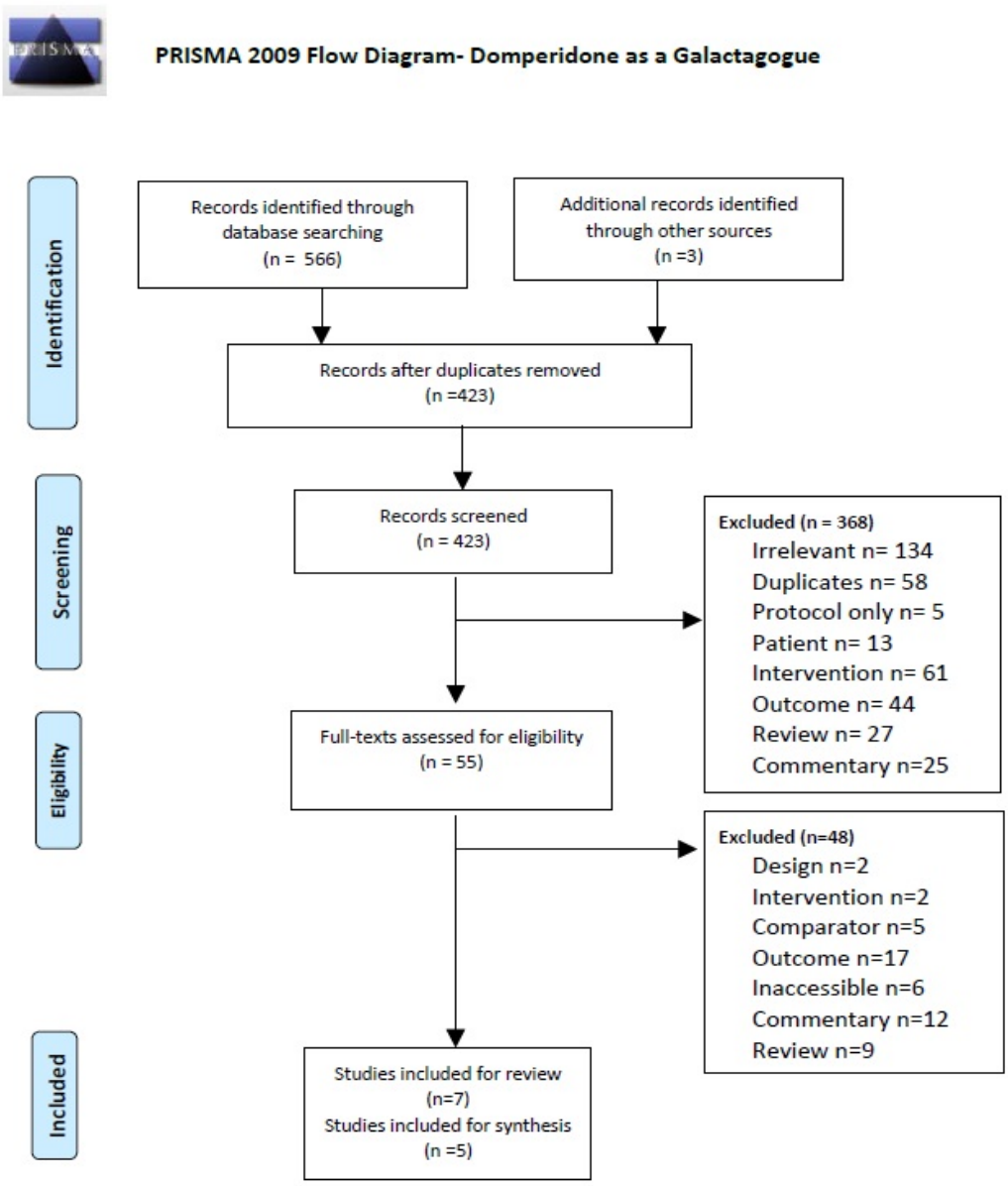

Figure 2.1 PRISMA Flow Diagram of Search Strategy and Inclusion/Exclusion Criteria of RCTs Investigating Domperidone as a Galactagogue

Table 2.1 Study characteristics of included studies for review

Study & Design & Funding Information	**Participants, Intervention / placebo (n)**	**Full Term or preterm**	**Domperidone, Dosage/ Duration**	**Primary Outcome technique**	**Results for Expressed Breast milk**	**Reported Side Effects**
De Silva et al. (2001) Double blind, RCT Canada Funded by the Research and Education Foundation of the Canadian Society of Hospital Pharmacists	6/8 (n=14)	Preterm or Vaginal 29.1 weeks Gestation	Domperidone dosage: 10 mg, 3x day 7 day duration	Mean milk production (mL/d) during 24 hours expressed Measured via breast milk pump	Domperidone: 130.4mL on day 2 To 183.5mL on day 7 (44.5% increase) Placebo: 54.7mL on day 2 to 66.1mL on day 7 (16.6% increase)	None
Campbell-Yeo et al. (2010) Blinded, RCT Canada Funded by the Canadian Nurses Foundation Nursing Care Partnership Program, IWK Health Centre, and Dalhousie University Nursing Research Fund	22/24 (n=46)	Premature, c-section, or vaginal < 31 weeks Gestation	Domperidone dosage: 10 mg, 3x day Domperidone (n=19) Placebo (n=19) 14 day duration	Mean milk production (mL/d) during 24 hours expressed Measured via breast milk pump	Breast milk volume at day 14: Domperidone = 380mL Placebo = 250mL	None

Study & Design & Funding Information	**Participants, Intervention / placebo (n)**	**Full Term or preterm**	**Domperidone, Dosage/ Duration**	**Primary Outcome technique**	**Results for Expressed Breast milk**	**Reported Side Effects**
Jantarasaengaram et al. (2012) Double Blind RCT Thailand Funded by Rajavithi Hospital	22/23 (n=45)	Full term, C-section (Single-ton)	Domperidone dosage: 10 mg, 4x day 4 day duration	Mean milk production (mL/d) from pumping both breasts for 15 minutes, 2 hours after breastfeeding, collected twice daily	Domperidone: 3.9 +/- 4.6 mL on day 1 to 191.3 +/- 139.1 mL on day 4 Placebo: 3.4 +/- 9.3 mL on day 1 to 91.4 +/- 60.3 mL on day 4	Dry mouth (31.8%)
Inam et al. (2013) Random allocation, RCT Pakistan Unable to obtain information on funding	50/50 (n=100)	Full term (Mothers delivered at term) Unclear delivery method	Domperidone dosage: 10 mg, 3x day 7 day duration	The efficacy of drug/ placebo defined as >50mL milk expressed per single expression from both breasts	Domperidone: 36 mothers (72%) showed adequate improvement, while the other 14 (28%) did not. Placebo: 11 mothers (22%) showed improvement, while 39 (78%) had no adequate improvement	None
Rai et al. (2016) RCT India Authors reported they had no source of funding	16/16 (n=32)	Pre-term infants, delivery method unclear	Domperidone dosage: dosage not specified 7 day duration	Milk output (method not specified)	Domperidone: median 186 mL/day (IQR 126.5-240) Placebo: median 70 mL/day (IQR 49.5-97)	None

Study & Design & Funding Information	**Participants, Intervention / placebo (n)**	**Full Term or preterm**	**Domperidone, Dosage/ Duration**	**Primary Outcome technique**	**Results for Expressed Breast milk**	**Reported Side Effects**
Asztalos et al. (2017) Multicenter, double masked, RCT (Intention to treat analysis) Canada Funded by the Canadian Institute of Health Research	45/45 (n=90)	Preterm (< 29 weeks gestation), Unclear delivery method	Domperidone dosage: 10 mg, 3x day Group A: 28 day duration Group B: Placebo for 14 days then Domperidone for 14 days	Mean milk volume (mL/d) during 24 hours expressed (Days 14 & 28)	More mothers achieved a 50% increase in milk volume after 14 days in Group A (77.8%) compared with Group B (57.8%), odds ratio = 2.56, 95% confidence interval [1.02, 6.25], (P = 0.04)	Cardiac, gastro, obstetrical, central nervous system, respiratory, infection Group A: 31 events Group B: 23 events
Fazilla et al. (2017) Double blind RCT Indonesia Authors did not report source of funding, however no COI were declared	25/25 (n=50)	Preterm (<37 weeks gestation) Unclear delivery method	Domperidone dosage: 10 mg, 3x day 10 day duration	Mean milk volume (mL/day) during 24 hours expressed (Days 7 & 10)	Domperidone: 181.6mL SD:80.2 Placebo: 72.4mL SD: 57.8, 95%CI: 69.36 to 148.93	None

Only five of these studies were included in the MA, as Inam et al. (2013) and Rai et al (2016) were excluded due to the quality gradings and lack of reporting mean milk volumes that could be used as a mean difference (63,64). All included studies in the qualitative synthesis were RCTs with publication dates ranging from 2001-2017. These studies were conducted in Canada, Pakistan, Indonesia, India and Thailand. Each study had sample sizes ranging from 14 to 100 participants. Five of the studies included women who had given birth to preterm infants and two included mothers with full-term infants. Five of the RCTs had Domperidone doses of 30 mg/day and one study looked at a dosage of 40 mg/day. The duration of the interventions ranged from 4 to 14 days.

2.4.2 Outcome measures

All studies investigated the volume of human milk produced by the mother. All included studies in the MA used daily mean milk volume collected over 24 hours via a human milk pump. Notably, Jantarasaengaram et al. (2012) used a slightly different method where mean human milk production (mL/d) from pumping both breasts was collected twice daily for only 15 minutes, 2 hours after breastfeeding (40).

2.4.3 Risk of bias within studies

Using the USPSTF Grading Criteria and the Cochrane Risk of Bias Tool, five of the seven studies had a low risk of bias, and two studies had an unclear risk of bias (Table 2.3). The first unclear risk of bias study, by Inam et al. (2013), had several unclear descriptions of blinding, maintenance of groups, methods of measurement and outcome data. Information regarding randomization, confounders, and intervention definition were given a fair quality rating, while the outcome was graded poor due to inability to examine

differences in baseline and final human milk volumes, or by what volumes the mothers had increased by at the end of follow-up (63). The second unclear risk of bias study by Rai et al (2016) did not provide enough information to determine any grading for the risk of bias domains (64). Da Silva et al. (2001) mentioned that randomization and blinding occurred but did not provide sufficient details to allow for replication of these methods (39). There was an unclear description of any adjustment for confounders in the analysis, but due to the quality description of the other areas for risk of bias, the full study was deemed good quality with low risk of bias. Jantarasaengaram et al. (2012) did not provide adequate information regarding the adjustment for confounders in the statistical analysis (40). The study also used a lottery system for their randomization sequence which was inadequately described. All other areas of potential biases were well controlled; thus, the study was deemed good quality with a low risk of bias. The RCT by Fazilla et al. (2017) was overall considered a good study with low risk of bias, but there were unclear explanations of the blinding process and minimal explanation of the randomization of participants (48). The final two studies by Campbell-Yeo et al. (2010) and Asztalos et al. (2017) were well reported in the publication, thus they had a low risk-of-bias and a good quality assessment (41,65). The individual quality grading criteria of each study can be found in Table 2.2, while their overall assessment of quality and risk of bias can be found in Table 2.3. The level of inter-rater agreement was 93%, where any disagreements during the process were resolved by discussion and consensus.

Table 2.2 Assessment of studies selected for inclusion in the synthesis using USPSTF quality rating criteria

Study, author & year	**Blinding of participants, personnel & outcome assessment**	**Random sequence generation & allocation concealment**	**Consideration of the confounders during selection**	**Maintenance of comparable groups**	**Equal, reliable, and valid measurement**	**Clear definition of intervention**	**Important outcome considered**	**Adjustment of confounders in analysis**	**Incomplete Outcome data**
De Silva et al. (2001)	Mentioned, not explained	Mentioned, not explained	Good	Good	Good	Good	Good	Unclear	Good
Campbell-Yeo et al. (2010)	Good	Good	Good	Good	Good	Good	Good	Good	Good
Jantarasaengaram et al. (2012)	Good	Fair	Good	Good	Good	Good	Good	Unclear	Good
Inam et al. (2013)	Unclear	Fair	Fair	Unclear	Unclear	Fair	Poor	Fair	Unclear
Rai et al. (2016)	Unclear	Unclear	Unclear	Unclear	Unclear	Unclear	Unclear	Unclear	Unclear
Asztalos et al. (2017)	Good	Good	Good	Good	Good	Good	Good	Good	Good
Fazilla et al. (2017)	Unclear	Fair	Good	Fair	Good	Good	Good	Good	Good

Table 2.3 Overall assessment of study quality (USPSTF Quality Grading Criteria) and risk of bias (Cochrane Risk of Bias Tool) for included studies

Study, author & date of publication	**Overall assessment**
De Silva et al. (2001)	Good Low Risk of Bias
Campbell-Yeo et al. (2010)	Good Low Risk of Bias
Jantarasaengaram et al. (2012)	Good Low Risk of Bias
Inam et al. (2013)	Poor Unclear Risk of Bias
Rai et al. (2016)	Poor Unclear Risk of Bias
Asztalos et al. (2017)	Good Low Risk of Bias
Fazilla et al. (2017)	Good Low Risk of Bias

2.4.4 Results of Individual Studies

Da Silva et al. (2001) included 14 mother and pre-term infant pairs (mean gestational age of 29.1 weeks).The trial examined the effect of Domperidone (10 mg, 3 times daily) compared to a placebo for seven days and its impact on human milk production in these mothers insufficient human milk supply. The treatment began for mothers in their fifth week post-delivery. The researchers found a significantly greater mean EBMV increase for Domperidone 130.4mL (day 2) to 183.5 (day 7) compared to placebo 54.7 (day 2) to 66.1 (day 7), 44.5% and 16.6% increase respectively, ($p<0.05$) (39).

Campbell-Yeo et al. (2010) included 45 mothers with pre-term infants born prior to 31 weeks gestation. Mothers self-reported that they were not producing sufficient milk supply for their infants. The trial examined the effect of Domperidone (10 mg, 3 times daily) compared to a placebo for 14 days and its impact on human milk production. The treatment began for mothers in their third week post-delivery. The researchers found a mean within subject volume increase from day 0 to 14 was 267% in the Domperidone group, and 19% in the placebo, ($p=0.005$) (65).

Jantarasaengaram et al. (2012) included 45 mothers with full term infants delivered via caesarean section. The trial examined the effect of Domperidone (10 mg, 4 times daily) compared to a placebo for four days. The researchers found a significantly greater mean human milk volume increase for Domperidone 3.9 +/- 4.6 mL (day 1) to 191.3 +/- 139.1 mL (day 4) compared to placebo 3.4 +/- 9.3 mL (day 1) to 91.4 +/- 60.3 mL (day 4), ($p <0.05$) (40).

Inam et al. (2013) included 100 mothers with full term babies. Inadequate human milk production was defined as less than 10 mL human milk per single expression from both breasts at the 6th postnatal day. The trial examined the effect of Domperidone (10 mg, 3 times daily) compared to a placebo for seven days. The researchers found that 36 mothers (72%) in the Domperidone group showed adequate improvement in human milk production, while only 11 (22%) mothers showed improvement in the placebo group. This study did not report mean human milk volume differences, or individual volumes of human milk. Authors of this study were contacted for raw data, but by the time of completing the manuscript, no response was received (63).

Rai et al. (2016) recruited 32 mothers with preterm infants who were producing insufficient milk, though the definition of insufficient milk was not provided. This RCT compared Domperidone and placebo for seven days, but did not provide the dosage of Domperidone used. Though the study found that the median milk volume was at 186.0 ml/d (IQR 126.5-240) for Domperidone at the end of the trial compared to placebo (18.7 mL/d, IQR 49.5-97) they did not specify what baseline milk volumes were before receiving intervention. Since the data was not in a format that would allow a mean difference volume calculation, the authors were contacted for their raw data. No response was received (64).

Asztalos et al. (2017) included 90 mothers who were at a higher risk of not being able to produce or maintain a supply of milk for their infants. The trial examined the effect of Domperidone (10 mg, 3 times daily) compared to a placebo. There were two groups, group A received Domperidone for a 28-day duration, and group B received the placebo for 14 days, and Domperidone for 14 days. This study took the EBMV and converted it to a dichotomous variable for any mother who achieved a 50% increase in milk volume after 14 days in group A (77.8%) compared with group B (57.8%), Odds Ratio, 2.56 [95%CI 1.02,6.25], ($p = 0.04$). Asztalos et al. (2017) did look at Domperidone use for 28 days in total, but due to the placebo group switching to Domperidone halfway through the follow-up period, the results for the total 28 days could not be utilized in this MA due to this contamination (41).

Fazilla et al. (2017) included 50 mothers with pre-term infants born prior to 37 weeks gestation. Mothers were not producing a sufficient human milk supply for their infants one week after receiving lactation counseling. The trial examined the effect of

Domperidone (10 mg, 3 times daily) for 10 days. The study found there was an increase in the mean difference of EBMV for Domperidone 181.6 mL, (SD: 80.2) compared to placebo at 72.4 mL (SD: 57.8,95%CI: 69.36 to 148.93) (48).

2.4.5 Synthesis of Results

The summary statistic of the five included RCTs is outlined in Table 2.4.

Table 2.4 Summary Statistic of Mean differences of Expressed Breast Milk Volume, Domperidone vs. Placebo.

Outcome	No. of Studies	No. of Participants	Statistical Method	Effect Size
Mean Difference in Expressed Breast Milk Volume (EBMV)	5	239	Mean Difference (IV, Random, 95% CI)	93.97 [71.12, 116.83]

The MA provides a statistically significant increase in the effect size in EBMV at 93.97 mL ([95% Confidence Interval 71.12, 116.83]; random effects, T^2 0.00, I^2 0%, $p < 0.00001$) (Figure 2.2 & Table 2.4).

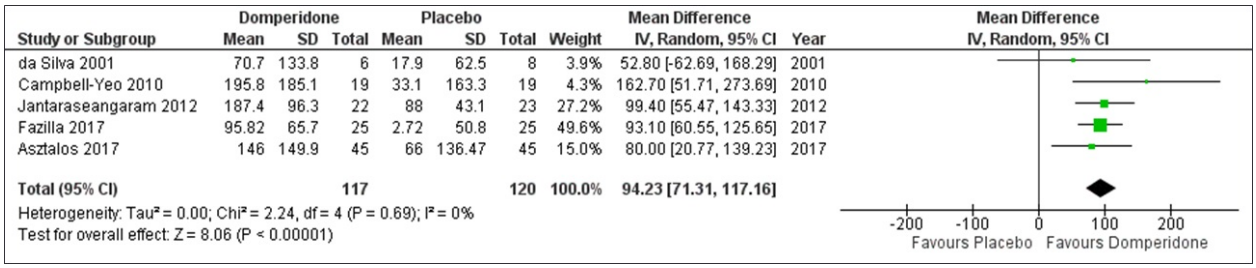

Figure 2.2 Forest Plot Examining Mean Difference of Expressed Human Milk Volume.

2.4.6 Risk of bias across studies

Publication bias was assessed by visual inspection, once a funnel plot was computed through the Revman Software (Figure 2.3). Although there are a limited number of studies included in the analysis (N=5), the funnel plot suggests there was no publication bias. With fewer studies visual interpretation of funnel plots should be interpreted with caution, as with few studies it is subjective to distinguish chance from real symmetry. No additional statistical measures (e.g., Fail Safe N, Eggers, Beggs test) were used to assess publication bias, as with a small number of studies these tests have limited statistical power.

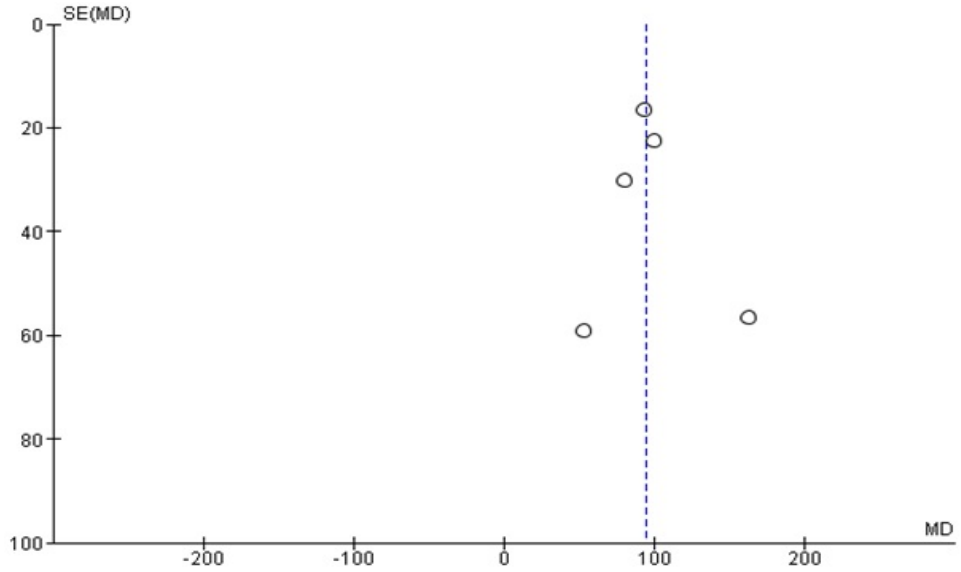

Figure 2.3 Funnel Plot of Comparison Domperidone Versus Placebo, Outcome Mean Differences of Expressed Human Milk Volume (EHMV).

2.4.7 Subgroup Analysis

Four out of the five studies in the meta-analysis examined puerperal women who gave birth to preterm infants; therefore, this SRMA was unable to conduct a subgroup

analysis based on the term of the infant. A subgroup analysis was performed based on the duration of Domperidone and efficacy in increasing human milk production. The MA provided a significant value for EBMV for both durations of Domperidone treatment (≤ 7 days and > 7 days), which are 93.51 mL ([95% Confidence Interval 52.45, 134.57]; random effects, T^2 0.00, I^2 0%, $p < 0.00001$) (Figure 2.4.1) and 94.56 mL ([95% Confidence Interval 66.93, 122.19]; random effects, T^2 0.00, I^2 0%, $p < 0.00001$) (Figure 2.4.2), respectively.

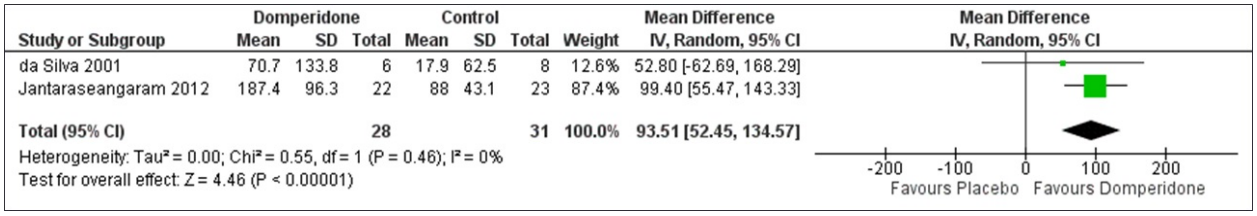

Figure 2.4.1 Forest Plot of Comparison Duration Subgroup Domperidone Duration ≤ 7 days, Outcome Mean Difference of Expressed Human Milk Volume (EHMV).

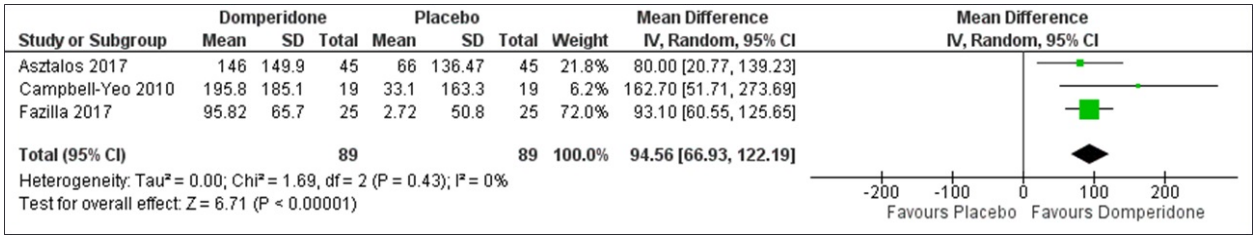

Figure 2.4.2 Forest Plot of Comparison Duration Subgroup Domperidone Duration >7 days, Outcome Mean Difference of Expressed Human Milk Volume (EHMV).

2.5 Discussion

The health community regards human milk to be important for infant nutritional needs. Mothers with an insufficient human milk supply may be less likely to breastfeed due to this barrier, unless the proper interventions are available to overcome it.

Domperidone has been used as an "off-label" galactagogue to augment human milk supply, despite warnings from the FDA regarding its safety (42). There have been two SRMAs that provide support regarding the efficacy of Domperidone as a galactagogue; however they do not include the most up to date published studies (46,47). This SRMA's objective was to reexamine the effect size of Domperidone as a galactagogue using the recently published RCTs.

All studies included in the SRMA provided evidence consistent with past research showing Domperidone effectively increases EBMV by a modest amount. In this MA the effect size of 93.97 mL per day (MD) in EBMV may be enough to help mothers supply human milk to their infants to meet their nutritional needs for the first few weeks of life. With the use of Domperidone, mothers should discuss the associated risks with a HCP and outweigh its potential benefits in assisting a mother establish milk supply.
Sub-analysis for the Domperidone groups shows there is no further EBMV increase with long-term Domperidone use, but the baseline dose of Domperidone may be necessary to maintain that modest increase from baseline level of human milk production. It is possible that increasing the dosage of Domperidone could help to increase the EBMV over time, but there have been no RCTs published to date that investigate an adaptive dose of Domperidone. Furthermore, a growing infant has an increasing need for human milk as the infant's feeding requirements also increase with age.

Despite no indication of heterogeneity among the studies, the included studies occurred in different countries, had different follow-up periods, and included different methods of infant delivery with pregnancies of viable gestations. This suggests that at the dose range of 30 mg to 40 mg, Domperidone is consistent in increasing the EBMV by the

MD effect size, regardless of the possible differences in population and study methods. It is likely that Domperidone can be used in different populations with the same effectiveness.

A previously published SRMA by Osadchy et al (2012) reached the same conclusion as this current SRMA. It also included two of the three studies that were also included in this current one, yet this current SRMA excluded one study that was included in Osadchy et al. (2012) because the included study used an indirect measure of EBMV (47). This may have been the source of the moderate heterogeneity that was found in the Osadchy et al. (2012) study. They attributed the moderate heterogeneity to the differences in the populations (full term vs preterm, vaginal vs cesarean section) and outcome measurements, but since this SRMA found no heterogeneity, and only included direct measures of EBMV, it is likely this method of measurement was causing the heterogeneity in the previous SRMA.

2.5.1 Limitations

This SRMA, though an updated study to add to the literature regarding Domperidone as a galactagogue, has limitations that need to be addressed. This review lacked a registered protocol, and the Peer Review of Electronic Search Strategies (PRESS) guidelines were not followed. Though backwards citation tracking was used to search for additional relevant articles, forward citation tracking was not explored. Notably, the most important controversy regarding Domperidone cannot be resolved at this time due to some of the RCTs in this SRMA which excluded any mother who showed signs of having a cardiovascular condition. In healthy mothers, there were very minimal

side effects reported, but Domperidone should still be used with caution in women who may be more prone to arrhythmias.

Within the included studies, mothers had self-reported insufficient milk supply. It is important to note that it is unclear whether this is actual or perceived insufficient milk production. In addition, due to including studies with preterm and full-term infants, and mothers giving birth both vaginally and through cesarean section delivery, this may provide varied challenges associated with milk production and issues with supply.

There were methodological inconsistencies between the studies as well, which should be considered when trying to generalize the results. One of the included studies used a higher dose of Domperidone compared to the other studies. It did not affect the heterogeneity and did not seem to drastically impact the effect size, but is an inconsistency in the data that should be considered. One of the studies included in the qualitative analysis was not able to provide adequate information to be included in the MA, and was of poor quality, due to the reporting of the data (63). The largest study, Aszatlos et al. (2017) included in this SRMA only contributed 14.9% to the weighting of the overall effect size, and a study that was almost half of its sample size contributed to 49.3% of the weight. These two studies were almost identical in design but had differing follow-ups. A possible reason why Aszatlos et al. (2017) contributed much less to the effect size may be because the RCT was designed initially to involve a larger sample size, but due to poor recruitment the study was concluded early with much less statistical power. This may account for why it contributed less to the effect size than expected (41). Lastly, with small sample sizes and few included studies, this limits the generalizability of findings.

2.5.2 Future Research

Cohort studies focusing on adverse events for Domperidone should be prioritized to move towards removing the restrictions for Domperidone and allowing it to be prescribed as a galactagogue instead of using it off-label as such. There could also be RCT research into higher doses of Domperidone as real-life clinical practice shows that physicians typically prescribe higher dosages to patients (37). It would also be good to see if an adequate supply of EBMV is sustained if the patient stops taking Domperidone.

2.6 Conclusions

This MA, using recently published, good quality RCTS, provided a statistically significant effect size of Domperidone on increasing human milk production in puerperal women, when taken for ≤ 7 days or > 7 days duration. The sustained effects of Domperidone have yet to be researched, nor is the EBMV continuously increasing over time. There is no clarity on the safety of Domperidone for patients with possible underlying cardiac arrhythmias.

2.7 Acknowledgments

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2.8 Conflict of Interests

The authors declare no potential conflicts of interest with respect to the research, authorship, or publication of this article.

Chapter 3: Infant Feeding Mode Predicts the Costs of Healthcare Services in One Region of Canada: A Data Linkage Pilot Study

Preface

A version of this chapter has been published in BMC Research Notes: Taylor, A., Chowdhury, S., Gao, Z., Nguyen HV., Midodzi, W., Gill, N., Halfyard, B., Newhook, LA., Twells, LK. Infant feeding mode predicts the costs of healthcare services in one region of Canada: a data linkage pilot study. *BMC Res Notes* 13, 385 (2020). https://doi.org/10.1186/s13104-020-05228-6. As the primary author, I reviewed the literature and analyzed the data. I completed the first version of the manuscript and further revised according to the suggestions of co-authors and reviewers. Dr. Laurie Twells and Dr. Leigh Anne Allwood-Newhook identified the research topic and scope. Dr. Zhiwei Gao, Dr. Hai Nguyen and Dr. William Midodzi provided statistical analysis suggestions. All authors reviewed the manuscript. All authors were involved in interpretation of the data. All authors approved the manuscript. Work previously completed on the FiNaL Study was done by Dr. Sharmeen Chowdhury, Dr. William Midodzi, Beth Halfyard, Nicole Gill, Dr. Leigh Anne Allwood-Newhook and Dr. Laurie Twells.

Abstract

Background: Few studies have examined the association between infant feeding mode (IFM) and costs related to healthcare service use (HSU) in Canada. The aim of this study

is to evaluate differences in HSU and its associated costs by IFM, in an infant's first year of life in one region of Newfoundland and Labrador, Canada.

Methods: Data from a prospective cohort study were linked to administrative databases to examine HSU during an infant's first year of life. The cohort study collected information on peri- and postnatal variables, including IFM during three stages that covered pregnancy through the first year postnatally. Consenting mothers provided their infants health insurance number for a data linkage to examine HSU by the infant. Outcomes included: hospital admissions, emergency room, family doctor and specialist visits. IFM was categorized as exclusively breastfed, mixed fed and exclusively formula fed. Descriptive statistics and multivariate analysis were performed to examine the relationship between IFM, maternal and child characteristics and costs associated with HSU.

Results: The sample included 160 mother infant dyads who consented to the data linkage. Mothers were Caucasian (95.6%), 26 years or older (95%), partnered (97.5%), living in a household with income greater than $30,000 CAN (98.1%) with a post-secondary education (97.5%). At one month 67% were exclusively breastfeeding, 20% were mixed feeding, and 13% were exclusively formula feeding. Overall, $315,235 was spent on healthcare service use for the sample of healthy full-term infants during their first year of life. Generalized linear modelling was performed to assess the effect of IFM on costs associated with HSU adjusting for confounders. When compared to exclusive breastfeeding, exclusive formula and mixed feeding were found to be significant predictors of the total costs associated with HSU during the first year of life ($p < 0.005$), driven by costs of hospital admissions.

Conclusions: Due to the human and economic burden associated with not breastfeeding, policies and programs that support and encourage breastfeeding should be a priority for governments and regional health authorities.

Keywords

Infant feeding, Breastfeeding, Healthcare Services Use, Direct Cost, Canada

3.1 Introduction

The importance of breastfeeding for infant health has been universally acknowledged and studied for decades. Human breastmilk offers a unique matrix of components for optimal growth, health and development in a newborn child (5). Studies show that breastfeeding reduces the rates of infant morbidity and mortality, as well as decreases the risk of chronic illnesses in childhood (14). Breast milk contains the immunological mechanisms that protect infants against common infections in infancy, as well as chronic diseases later in life (6,13,15). Further evidence suggests the composition of breastmilk provides protection in the early months of life against infection severe enough to require hospitalization (52).

The World Health Organization (WHO) and Health Canada recommend mothers exclusively breastfeed their infants to 6 months of age, with continued breastfeeding with complementary foods to 2 years of life and beyond (4,66) (Accessed on July 22, 2019). The recommendations by WHO are evidenced by numerous studies conducted worldwide that demonstrate the benefits of breastfeeding. There are also economic benefits associated with increased breastfeeding rates due to reduction in common infections,

resulting in a cost savings from decreased use of associated healthcare services. Previous research in developed countries has demonstrated the economic benefit of increasing breastfeeding rates (3,16,67,68). Bartick et al., examined both maternal and pediatric health outcomes, demonstrating how increasing breastfeeding rates to 90% of infants exclusively breastfed at 6 months has the potential to prevent $3 billion in direct medical costs, and $14.2 billion premature death costs, annually (3). Another study conducted in Australia estimated hospital system costs of $1-2 million annually for the treatment of common childhood infections (i.e., gastrointestinal and respiratory illness, otitis media, eczema and necrotizing enterocolitis) due to insufficient breastfeeding (67). The authors report the Australian healthcare system could save $60-120 million dollars if breastfeeding rates increased from their current rate of 10% exclusively breastfed to 90-95% (67). A study conducted in the United Kingdom estimated that approximately £26.8 million could be gained annually by avoiding the costs of treating four acute infections (i.e., gastrointestinal and lower respiratory tract infections, acute otitis media in infants, necrotizing enterocolitis in preterm babies) and breast cancer in women, if exclusive breastfeeding (EBF) rates increased to 65% at four months and 100% of babies were breastfed at hospital discharge (69).

3.2 Rationale

In Canada, little is known about the economic impact of increasing breastfeeding rates, as few studies have examined the impact of infant feeding mode (IFM) on healthcare service use (HSU) (49–51). Two studies concluded that breastfeeding was strongly protective against hospital admission due to severe infections; however, both studies were small and focused on Indigenous populations (49,51), and neither study conducted a cost analysis related to hospital admissions, emergency room (ER) visits or physician consultations. Further studies are required to investigate total HSU costs in a Canadian context to better understand where an investment in interventions is needed to reduce the use and unsustainable expenditures.

This is critical as reports have examined Canada's healthcare performance, ranking us among the lowest of 11 developed countries (70). The Commonwealth Report collects information from a variety of sources on a standardized set of metrics, based on care process, access, administrative efficiency, equity, and healthcare outcomes. Within these categories, Canada has scored poorly in care process, equity and healthcare outcomes. The primary drivers of our low ranking includes Canada's comparatively higher infant mortality rate, long wait times for the ER and specialists, lack of availability of after-hours care, unreliable coverage for healthcare claims, and the high prevalence of chronic conditions (70). With regards to healthcare expenditures, with exception of the Territories, the province of Newfoundland and Labrador (NL) reported the highest per capita healthcare expenditure in Canada, of $7,443 (71) (Accessed on July 19 2019). Per-person healthcare spending is even higher for infants, in 2014 the per-capita cost of

medical services for infants in their first year of life was $10,800 (71) (Accessed on July 19 2019).

In addition, NL has the lowest breastfeeding initiation rates (71.9%) and the lowest six-month EBF duration rates (13%) in Canada (72,73) (Accessed on February 28, 2018). Although breastfeeding initiation rates in the province have improved over the last 30 years (35.3 to 71.9%), most women stop breastfeeding before 6 months (73). With high healthcare expenditures and low breastfeeding duration rates, we sought to examine the impact of IFM on total HSU costs during an infant's first year of life in one region of Canada. We hypothesize that EBF will be associated with lower total HSU costs.

3.3 Methods

3.3.1 Design

In this retrospective cohort study, data collected from the *Feeding infants in Newfoundland and Labrador* (FiNaL) study were linked using the infant's health insurance number provided by the mother with administrative databases provided by the NL Centre for Health Information (NLCHI) to examine HSU and related costs by IFM.

3.3.1.1 Data Management

Data and information used to support this thesis has been managed by the NLCHI. NLCHI's mandate includes managing provincial health data and information assets; preparing health reports and conducting applied health research and evaluation; and protecting the privacy of individuals whose personal information or personal health information is collected, used, disclosed, stored, or disposed of by the Centre in

accordance with the Access to Information and Protection of Privacy Act, 2015 and the Personal Health Information Act (PHIA). As the custodian for key provincial health data systems, NLCHI has robust policies and procedures which govern the collection, use, and disclosure of information. They were the primary hub for record level data sharing required for this project. The NLCHI obtained extracts of the data approved for use for this investigation and provided any assistance required for data linkage. Record-level data was securely transferred using secure data transfer tools offered through the Centre.

3.3.1.1 The Feeding infants in Newfoundland and Labrador (FiNaL) Study

The FiNaL Study was conducted between August 2011 and June 2016 to evaluate maternal attitudes and infant feeding practices in NL Canada through the administration of questionnaires at three time periods (phase 1,2,3). Methods have been previously published (74,75). In brief, pregnant women in their third trimester of pregnancy (phase 1, n = 1283) were enrolled in the FiNaL Study and filled out a prenatal questionnaire. Additional questionnaires were administered postnatally at 1-3 months (phase 2, n = 658) and 6-12 months (phase 3, n = 554). Information including prenatal education, birth experience, feeding mode, psychosocial factors, socioeconomic factors, and social supports were collected at each phase. The primary focus of the FiNaL study was to assess infant feeding practices among a representative sample of pregnant women in NL. Inclusion criteria consisted of expectant mothers in their 3rd trimester of pregnancy, who were 18 years or older, English-speaking living in NL who gave birth to a full-term healthy infant. Recruitment was carried out at prenatal classes, in offices of family physicians, nurse practitioners, obstetricians and through public health nurses and via

social media outlets (i.e., Facebook) and posters. Participants were also recruited through telephone or email contact with a member of the research team in response to social media and posters placed in community Settings. The questionnaires were completed in paper form (returned in postage-paid envelopes), by telephone or on-line by using Survey-monkey. By including data collected from the FiNaL Study on maternal characteristics, we intended to control for known confounders associated with IFM and HSU (e.g., mother's age, marital status, education, household income, parity, smoking status, residence, and delivery type).

3.3.1.2 Administrative Data

The series of administrative data was created by the Health Analytics and Evaluation Services Department at the Newfoundland and Labrador Centre for Health Information (NLCHI). Individuals level record data were extracted from the Provincial Discharge Abstract Database (PDAD) for hospital admissions, NLCHI Live Birth System (LBS) for demographics and infant characteristics, MCP Fee-for-Service Physician Claims (FFS) for family doctor and specialist visits, and the ER Module of the MediTech database (Eastern Health) for ER visits.

3.3.1.2.1 LBS

The LBS contains demographic, administrative and clinical data related to all live births that occur in the province of NL, both resident and non-resident. These data are used primarily for research and information requests through the Centre for Health

Information and to provide aggregate statistical information. In addition, the Centre uses the LBS to cross reference other datasets for quality assurance and verification purposes.

3.3.1.2.2 PDAD

The PDAD contains demographic, administrative, interventional and clinical data collected at hospitals when patients are discharged from inpatient acute healthcare facilities and surgical day care services in the province. The database includes Newfoundland and Labrador residents and out-of-province patients receiving care in provincial acute care institutions. All provincially administered hospital data is then submitted to the Canadian Institute for Health Information (CIHI), where it is reviewed for its quality, and specific values calculated (e.g., resource-intensity-weight, case mix groupings and level of complexity index). Once complete the PDAD is provided to the NL Centre for Health Information where it is housed.

The database includes all discharge diagnostic codes based on the international Classification of Diseases 10 (ICD-10, ICD-10-CA (International Classification of Diseases 10-1-h Revision - Canadian Enhancement)). The ICD-10 allows for the categorization for all coding and classifying of acute or surgical day care services or cause-of death data.

3.3.1.2.3 MCP FFS

The Newfoundland and Labrador Medical Care Plan (MCP) was established in 1969 with the primary function of processing payments for fee-for-service physicians in the province. The MCP is a comprehensive plan of medical care insurance designed to

cover the cost of physician services for eligible residents of the province, where each resident of Newfoundland and Labrador is provided a lifetime unique MCP number. The MCP fee-for-service (FFS) data includes clinical and administrative information submitted by physicians who treat beneficiaries of the province's MCP for reimbursement. The MCP FFS data that is managed by the NL Centre for Health Information is an extract of the master database managed by the provincial MCP program of the Department of Health and Community Services. The MCP FFS database captures information on sex, age, diagnosis, provider's specialty (i.e., general practitioner or other specialist), service date, fee code and location of services. Potential locations of services include at home, in-patient/outpatient or office consultations, while procedures can range from diagnostic, therapeutic, radiological or surgical procedures. Fee codes are set by the Medical Care Plan Board and range from 001 (general practitioner) to 082 (medical officer of health) (Table of Codes). All information submitted is an integral part of the claims for payments for any fee-for-service specialist, and therefore is considered to be complete in terms of records represented by this database. Administrative data provided allowed for the fee for service claims for the total amount paid by physicians and specialists for visits and consults, while Resource Intensity Weights (RIW) and the Cost for a Standard Hospital Stay (CSHS) through the Canadian Institute for Health Information (CIHI) were used to cost hospitalizations, provided by the NLCHI.

3.3.1.2.4 MTER

The MediTech ER (MTER) database contains demographic, administrative and clinical data on any resident or non-resident who visits an emergency room department in

Newfoundland and Labrador. Information on triage level is collected based on medically acceptable wait times as defined by the Canadian Emergency Departments Canadian Triage and Acuity Scale (CTAS). Upon arrival to an emergency department, patients receive a triage level based on the perceived urgency of their presenting complaint. The NL medical association has outlined the five CTAS triage levels and the appropriate physician response time are: Level I, Resuscitation (e.g. cardiac arrest) requiring an immediate response from the physician; Level II, Emergent (e.g. chest pain) requiring a response within 15 minutes; Level III, Urgent (e.g. moderate asthma) requiring a response within 30 minutes; Level IV, Less Urgent (e.g. minor trauma) requiring a response within 1 hour; Level V, Non-Urgent (e.g. common cold) requiring a response within 2 hours. As secondary use data, triage levels allow for an assessment of the urgency of emergency department visits, as information regarding diagnostics and additional visit information is limited. The MTER data was provided by the regional health authorities to the Centre by Eastern Health via secure managed file transfer. Costs of the emergency room (ER) visits were provided by the NL Centre for Health Information and averaged to cost the use in 2015 Canadian dollars across the Eastern Health Authority of Newfoundland and Labrador. Costs to the emergency department include total direct operating expenses from ER primary accounts and total ER client visits from the statistical secondary account (Average=Total Direct Expenses/Total ER Client Visits).

The data linkage herein utilized data collected during Phases 1 and 3 of the FiNaL study, as well as administrative data provided by the NLCHI. The study was approved by the Health Research Ethics Authority in Newfoundland and Labrador (HREA## 2017.226). The ethical approval can be found in Appendix 3.1.

3.3.2 Sample

Mothers residing in the Eastern Health region of NL who were part of the FiNaL Study and had completed all three surveys (n=554) were invited to participate in the HSU study, provided their infant was born full term. Out of those agreeing to partake in the HSU study, 160 mothers provided their infants health insurance number for the data linkage. The sub-sample for the HSU study met the larger study inclusion criteria of the FiNaL study. Maternal and infant characteristics were chosen based on known associations with IFM and based on information provided through the FiNaL Study. This included demographic information on maternal age, income, marital status, smoking, parity, delivery method, ethnicity, and socioeconomic status.

3.3.3 Measurements

IFM was defined according to the WHO and United Nations Children's Fund (UNICEF) criteria. 'Exclusive breastfeeding (EBF)' was used when infants received only breast milk (i.e., including breastmilk that has been expressed or from a wet nurse) and nothing else, except for oral rehydration solution (ORS), medicines and vitamins and minerals when needed. 'Mixed feeding' (MF) was classified as an infant receiving breastmilk and other food or liquid including water, non-human milk, and formula. 'Exclusive formula feeding' (EFF) was classified as the IFM when infants were fed only breastmilk substitutes. The EBF rate was only valid and reliable for the first month of life. This is due to data collection within the FiNaL Study, and ensuring IFM was adequately categorized for each group.

The primary outcomes examined for HSU costs were all cause HSU during an infant's first year of life. This includes the costs associated with hospital admissions, emergency room, family doctor and specialist visits. Administrative data from the NLCHI was linked to provide a comprehensive dataset on HSU during the infant's first year of life. Costs examined reflect costs to the payer and examine direct HSU costs, over a one-year time horizon of an infant's first year of life.

3.3.4 Data analysis

3.3.4.1 Data Linkage

Deterministic linkage was used for linking the FiNaL Study and administrative data provided by the NLCHI. The infant's health insurance numbers were given a unique study identification code, which provided an easy method of linkage to the prospective cohort dataset upon return of the PDAD, FFS, LBS, and MTER datasets. Administrative datasets were structured, cleaned, and formatted to easily link data from the FiNaL Study.

3.3.4.2 Descriptive Statistics

Descriptive statistics, either frequencies for categorical variables or means (standard deviations, SD) for continuous variables were presented to compare baseline maternal characteristics and HSU outcomes associated with IFM. Both univariate and multivariate generalized linear modelling was used to compare HSU, direct medical costs, and maternal and child characteristics between the exposure of IFM. Kruskal-Wallis (KW) Tests were used to compare medians of continuous variables, and chi square tests were used to compare proportions of binary and categorical variables. KW tests were

selected as it does not require the groups to be normally distributed and is more stable to outliers. All statistical analyses were conducted using Statistical Package for Social Sciences (SPSS), IBM Version 25 software (76).

3.3.4.3 Cost Values

The total itemized cost of billable claims for visits to each healthcare professional were summed using the claims provided by the NLCHI. Means (SD), medians (interquartile ranges, IQR), min and max and total costs associated with each healthcare professional for the total group and by IFM were calculated. Costs were converted to 2015 Canadian dollars, as all resource intensity weights (RIW) provided by the NLCHI and cost per standard hospital stay (CSHS) used were for the 2015 fiscal year. The average cost of an ER visit for the EH regional health authority was provided by the NLCHI and calculated using the average of the 2014/2015 and 2015/2016 fiscal years.

3.3.4.4 Multivariate Analyses

3.3.4.4.1 Regression Models

Due to the skewed HSU costs, both base case and robustness analyses were performed in the multivariate analysis. As a base case analysis generalized linear modelling (GLM) was used, following a gamma distribution and a log link function. The robustness check used GLM following an inverse gaussian distribution and a reciprocal function, following findings from the modified park test and box cox tests. Due to the size of the sample, variables with counts less than 10 (i.e., smoking status, education, income, age, and marital status) were not included in the final model. Both the final models

included IFM, residence, parity, and delivery type as independent variables. The three additional variables; residence, parity and delivery type were controlled for in the analysis as they are known confounders of IFM.

3.3.4.4.2 Generalized Linear Modelling

We use a generalized linear model to estimate the parameters that determine positive values. Generalized linear models accommodate skewness in natural ways, give the researcher considerable modeling flexibility, and fit health care expenditures extremely well (77).

3.3.4.4.3 Distribution and Link Functions

The most common distributions and link functions for costing data is a gamma distribution with a log link function. This is the most popular approach and has been applied as a base case analysis for the generalized linear model. As for a robustness check, the park test and box-cox test will be used to identify the appropriate distribution and function for testing robustness of the results. Data and regression models were modelled using Stata for this interpretation.

3.3.4.4.4 Box-Cox Test

A Box Cox test is used to see what power function will transform the skewed dependent variable (i.e., healthcare costs) to be closest to symmetric. In brief, this approach tests which scalar power (delta) of the dependent variable results in the most symmetric distribution. The Box Cox parameters can be -1, 0 and 1, which correspond to

the reciprocal, the log, and no transformation, respectively. With this test our Box Cox theta is -0.91 (i.e., close to -1). With an estimated coefficient close to -1, this corresponds to a reciprocal transformation.

3.3.4.4.5 Park Test

To determine the distribution family, we use the modified-Park test, which empirically tests the relationship between the mean and the variance. After running a generalized linear model with a gamma distribution and log link function we computed the expected value (mean) foreach observation, conditional on the covariates. We then compute the squared error (variance) for each observation, and the test is run by taking the regression of the log of the squared error on the expected value. For modified-park test lambda can be a value close to 0, 1, 2 or 3, which would indicate a gaussian, poisson-like, gamma or inverse gaussian distributional assumption, respectively. For our sample using the modified-park test, the lambda coefficient is 5.4 and statistically significant. This corresponds to an inverse gaussian distribution.

In summary, both tests would suggest that an inverse gaussian distribution assumption and the reciprocal should be used within this analysis. Therefore, those are the parameters outlined for our generalized linear model robustness check (77).

3.3.4.5 Power Calculation

In addition, due to constraints in sample size, a power analysis was performed, which allows for an estimation of the probability of detecting a true effect between groups of a given sample size and level of confidence. Power was estimated for the generalized

linear model at an alpha level of 0.05, by IFM groupings; EBF n = 107, Mixed Fed n = 32, EFF n = 21.

3.4 Results

The FiNaL Study enrolled 1,283 expectant mothers in the third trimester living in the province of NL. From those participants, 51% (*n*=658) participated in the first postnatal survey (1-3 months postnatal, phase 2) and 43% (*n*=554) completed the second postnatal survey (6-12 months, phase 3). During phase 3 of the FiNaL Study, 362 (65.4%) mothers eligible for the HSU study were enrolled. Mothers residing in the Eastern Health region of NL who have already taken part in phase 3 of the FiNaL Study, phase 3 were invited to participate in this study and consented by providing their infants medical care plan number for the data linkage. Of them, 242 (67%) mothers consented to take part in the HSU study and returned their questionnaires on healthcare service use during the infant's first year of life, and 160 (44%) mothers provided their infants medical care plan number to be linked for the analysis. The participant recruiting process is illustrated in **Figure 3.1**.

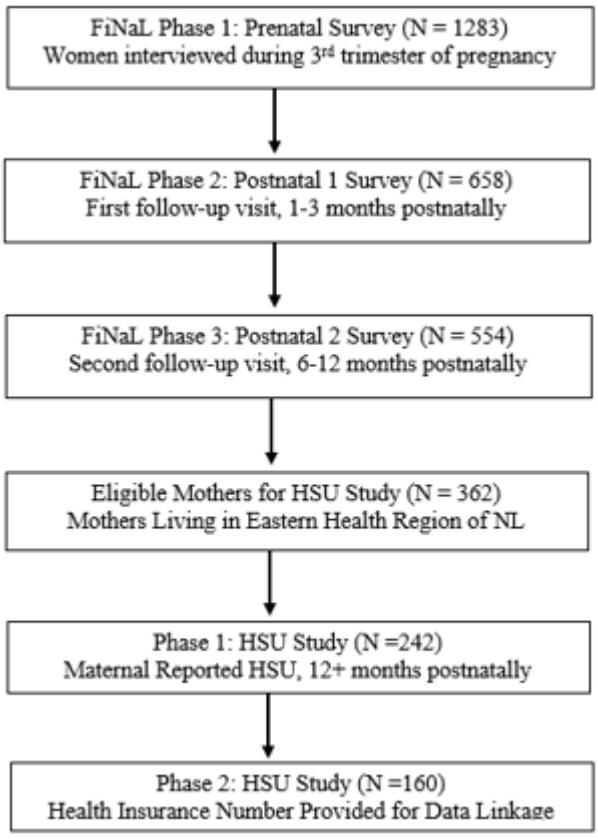

Figure 3.1 Flowchart of participant recruitment process.

Maternal characteristics are reported in **Table 3.1**. The majority of mothers were Caucasian (95.6%), 26 years of age or older (95%), partnered (97.5%), living in a household with income greater than $30,000 CAN (98.1%) and had a post-secondary education (97.5%). Based on those who did not take part in our HSU, those that were living in the Eastern Health Region and consented were more likely to be older, partnered, with higher levels of education and higher household incomes, residing in urban NL. IFM was categorized as EBF, MF or EFF. At one month 67% were EBF, 20% were MF, and 13% were EFF. The patient population consisted of births in the Eastern Health region of NL between 2012 and 2014. All infants were healthy full term (> 37

weeks gestation), 83 (51.9%) were female, and 77 (48.1%) were male. Mean birth weight was 3523.5g (SD 455.8), with the majority of infants (80%) born the appropriate size for gestational age. There were no differences when examining appropriateness of size for gestational age (appropriate, small, or large) between groups of IFM, $p > 0.05$.

Table 3.1 Maternal Characteristics (Frequency, n (%))

Characteristics	**PN1 Survey (N = 554)**	**No MCP (N= 394)**	**HSU [Admin] (N = 160)**	**P value***
Infant Feeding Mode **EBF at 1 month** **Mixed Fed** **EFF**	291 (52.5%) 165 (29.8%) 98 (17.7%)	201 (51.0%) 116 (29.4%) 77 (19.5%)	107 (66.9%) 32 (20.0%) 21 (13.1%)	**0.003**
Mother's Age (> 26 years)	494 (89.2%)	344 (86.8%)	152 (95.0%)	**0.005**
Marital Status (Married/ Partnered)	518 (93.7%)	362 (92.1%)	156 (97.5%)	**0.018**
Education Level (Post-Secondary)	510 (92.1%)	354 (89.8%)	156 (97.5%)	**0.003**
Household Income (> 30,000 CAN$)	520 (93.9%)	363 (92.1%)	157 (98.1%)	**0.008**
Parity (Primiparous)	316 (57.2%)	218 (55.6%)	98 (61.3%)	0.224

Type of Delivery (Vaginal)	403 (73.0%)	286 (73.0%)	117 (73.1%)	0.968
Dwelling Area (Urban)	253 (45.7%)	136 (44.9%)	117 (73.1%)	**0.0000**
Ethnicity: Caucasian	514 (94.5%)	362 (94.0%)	151 (95.6%)	0.478
Ethnicity: Other (i.e., Asian, Aboriginal, Afro-Canadian)	30 (5.5%)	23 (5.9%)	7 (4.4%)	
*P Value compares those that took part in the HSU study (n=160) to those that did not (n=394)				

3.4.1 Common diagnoses during infancy

In their first year of life, 81.6% of infants (*n*=133) had at least one type of infection; 29% (29) an upper respiratory tract infection, 22% (22) an ear infection, 20% (21) had the common cold, and 12% (12) had thrush. In descending order, the highest frequency of billable claims was no specific illness diagnosed at the visit (n=591, 41.2%), signs and symptoms not otherwise diagnosed as an infection or disease (n=225, 15.7%), upper respiratory tract infection (n=92, 6.4%), otitis media (n=61, 4.3%), common cold (n=49, 3.4%), disorders of eyes and ears (n=46, 3.2%), thrush (n=46, 3.2%), and atopic dermatitis (n=37, 2.6%).

3.4.2 Healthcare Service Use

Table 3.2 presents the frequency of healthcare provider visits for the total sample and by IFM. The majority (96.8%) of infants were seen by a family doctor (n = 151) within their first year of life, irrespective of feeding mode. Over half (59%) of the infants

(n=92) were seen by a specialist, which included visits to pediatricians, pediatric cardiologists, dermatologists, otolaryngologists, diagnostic radiologists and plastic surgeons. MF and EFF infants had a higher percentage of specialist visits (65.6% (n=21) and 65.0% (n=13), respectively), while 55.8% (n=58) of EBF infants visited a specialist during the first year.

Table 3.2 Healthcare Provider Visits by Infant Feeding Mode (Frequency, n (%))

	Total (n=159)	**EBF (n = 106)**	**Mixed (n= 32)**	**Formula (n=21)**
Hospitalization (n=159)	12 (7.5)	3 (2.8)	5 (15.2)	4 (19.0)
	Total (n=160)	**EBF (n = 107)**	**Mixed (n= 32)**	**Formula (n=21)**
Emergency Room (n=160)	83 (51.9)	57 (53.3)	18 (56.3)	8 (38.1)
	Total (n = 156)	**EBF (n = 104)**	**Mixed (n= 32)**	**Formula (n=20)**
Family Doctor (n=156)	151 (96.8)	100 (96.2)	32 (100.0)	19 (95.0)
Any Specialist (n=156) Includes: Pediatrician, Pediatric Cardiologist, Dermatologist, Diagnostic Radiologist, Plastic Surgeon & Otolaryngologist (ENT)	92 (59.0)	58 (55.8)	21 (65.6)	13 (65.0)

There were 12 infants hospitalized at least once during the first year of life. The length of stay (LOS) for these hospital admissions ranged from 1-7 days. Total LOS (in days) across the first year of life including time spent in hospital during the first days of

life can be found in Appendix 3.3. Most commonly, hospital admissions were related to respiratory complications (i.e., upper respiratory tract infection, croup, asthma). Descriptions of hospitalizations can be found in Appendix 3.4. EBF infants had fewer hospital admissions (2.8%) than that of MF (15.2%) and EFF (19.0%), $p < 0.05$. Half of infants (n=83, 51.9%) were brought to the ER at least once during the first year of life. More MF infants had ER visits (56.3%) than that of EBF (53.3%) and EFF infants (38.1%). MF and EBF infants had significantly more ER visits when compared to EFF infants, $p < 0.01$. In examining the triage levels for unique ER visits 43.6% were non-urgent or less urgent cases, 35.1% were urgent cases, 3.6% were emergent cases, and 17.6% had no identified triage level in the database.

3.4.3 Cost Associated

The direct healthcare expenditures of 160 healthy full-term infants during their first year of life amounted to $315,235.56. When considering costs associated with HSU post discharge from birth, the expenditures equated to $127,373.41. The highest percentage spent on HSU was for hospital admissions, 37.6%, ($47,867.56), where overall costs per infant ranged from $1430.60 – $12,664.22 when examining hospitalizations post birth, and $900.35 – $14,329.37 when including the cost of birth. This was followed by visits to the family doctor and specialists which were 30.1%, ($38,271.88) and 13.7% ($17,254.3) respectively, where costs per infant ranged from $6.40 (a single diagnostic test) – $2065.68 (a combination of visits). Costs to the ER made up 18.8% ($23,805.5), and costs per infant ranged from $147.86 – $1478.6 (**Table 3.3)**. There were no differences between infant feeding groups when comparing physician

services or ER visits, $p > 0.05$, while EFF infants had higher expenses for hospital admissions than other feeding groups (MF, EBF), $p = 0.010$. The means, medians and IQR associated with total HSU costs are described further in **Table 3.4**.

Table 3.3 Total Costs Associated with each Healthcare Provider, By Infant Feeding Mode

	Total (n = 156)	**EBF (n = 104)**	**Mixed (n= 32)**	**Formula (n=20)**
Hospitalizations (n=159)	$47,867.56	$5,132.90	$24,823.42	$17,911.24
Hospitalizations (n=159) (Including Birth)	$235,883.92	$128,434.74	$64,126.26	$43,322.92
Emergency Room (n=160)	$23,805.50	$16,264.60	$4,731.52	$2,809.34
Family Doctor & Specialist (n=156)	$55,546.18	$36,465.19	$10,949.68	$8131.31
Total Costs: **Total Costs (Including birth):**	$127,373.41 $315,235.56	$58,345.41 $181,164.53	$40,255.41 $79,807.46	$28,851.89 $54,263.57

Table 3.4 Mean (SD), Median (IQR), Min & Max of the Total Costs Associated with each Healthcare Provider, By Infant Feeding Mode

Hospitalizations	**Total (n = 156)**	**EBF (n = 104)**	**Mixed (n= 32)**	**Formula (n=20)**	**P Value**
MEAN (SD)	3988.96 (3188.99)	1710.97 (122.67)	4964.68 (4415.57)	4477.81 (2046.37)	

MEDIAN (IQR)	3040.90 (3778.43)	1781.79 (213.48)	3805.69 (6037.35)	4580.27 (3728.46)	0.141
MIN - MAX	1430.60 - 12,664.22	1569.31 - 1781.79	1430.60 - 12,664.22	2402.84 - 6347.87	
Hospitalizations (including birth)	**Total (n = 156)**	**EBF (n = 104)**	**Mixed (n= 32)**	**Formula (n=20)**	
MEAN (SD)	1483.55 (1434.19)	1211.65 (492.40)	2003.95 (2519.00)	2062.99 (1990.91)	**0.015**
MEDIAN (IQR)	1202.99 (530.25)	900.35 (481.70)	1382.06 (706.16)	1382.06 (851.18)	
MIN - MAX	900.35 - 14,329.37	900.35 - 3791.20	900.35 - 14,329.37	900.35 - 7501.69	
Emergency Room	**Total (n = 156)**	**EBF (n = 104)**	**Mixed (n= 32)**	**Formula (n=20)**	
MEAN (SD)	148.78 (220.31)	152.00 (214.42)	147.86 (246.27)	133.77 (218.83)	0.672
MEDIAN (IQR)	147.86 (147.86)	147.86 (295.72)	147.86 (147.86)	147.86 (221.79)	
MIN - MAX	147.86 -1478.6	147.86 -1478.6	147.86 -1330.74	147.86 - 739.30	
Family Doctor & Specialist	**Total (n = 156)**	**EBF (n = 104)**	**Mixed (n= 32)**	**Formula (n=20)**	
MEAN (SD)	356.07 (288.42)	350.63 (266.23)	342.18 (254.37)	406.57 (430.91)	

MEDIAN (IQR)	300.12 (307.85)	296.73 (339.74)	291.40 (307.30)	301.92 (194.61)	0.972
MIN - MAX	6.40 - 2065.68	6.40 - 1678.90	25.63 - 1244.26	54.14 - 2065.68	
*P Value compares all three groups of Infant Feeding Mode					

3.4.4 Multivariate Analysis

Prior to conducting multivariate analysis, a power calculation was conducted using SPSS. Our sample size provides a power level of 78% (alpha 0.05) to examine the primary outcome of total HSU costs. The base case analysis (Gamma Distribution with log link function) for the generalized linear regression model is presented in **Table 3.5.** IFM remained a predictor of total costs associated with HSU during an infant's first year of life, after adjustment for residence (urban vs. rural areas), delivery type (vaginal vs. caesarean section), and parity (primiparous vs. multiparous). With EBF to 1 month as our reference category, both MF and EFF were significant predictors of higher total HSU costs. No other factors were significantly associated with total costs. To further our analysis a robustness analysis (Inverse Gaussian Distribution with Reciprocal function) was run, to further examine both base cases analyses and a robust check of the results. Based on our robustness analysis the statistical significance remained the same, with infant feeding mode predictive of total HSU cost.

Table 3.5 Generalized Linear Modelling of Total Healthcare Costs During The Infant's First Year of Life

	Base Case Analysis		
	Coefficient (SE)	**95% CI**	**P Value**
Constant	7.408 (0.889)	7.234 - 7.582	0.000
Infant Feeding Mode			
EFF	0.383 (0.118)	0.152 – 0.615	0.001
MF	0.408 (0.099)	0.212 – 0.603	0.000
EBF	(Referent)	.	.
Residence			
Rural Area	0.124 (0.090)	-0.52 – 0.301	0.167
Urban Area	(Referent)	.	.
Parity			
Multiparous	0.061 (0.080)	-0.096 – 0.218	0.444
Primiparous	(Referent)	.	.
Delivery Type			
Vaginal			
Caesarean Section	-0.042 (0.088)	-0.214 – 0.130	0.629
	(Referent)	.	.
*EFF (Exclusive Formula Feeding), MF (Mixed Feeding), EBF (Exclusive Breastfeeding).			

3.5 Discussion

In the present study, 160 mother-infant dyads were enrolled in a data linkage to examine the impact of IFM on HSU and related costs during the first year of life. Overall, the majority of infants were seen by family doctors, specialists and the ER at least once during their first year. Cumulative HSU cost in the first year of life for all healthy full-term infants in one provincial region in Canada was $315, 235.56, including cost of birth. The highest percentage spent on HSU was for hospital admissions, followed by family doctor, ER and specialist visits. Higher HSU costs were associated with EFF

infants when examining hospitalizations (birth and admissions), and significant differences were found between IFM when examining the total costs associated with HSU during the first year of life.

Compared to previous studies in other countries, our findings are consistent when examining HSU costs associated with IFM. Studies have shown that infants who had early exposure to formula experienced higher volumes of visits to family doctors, infectious episodes and hospital admissions (17,53,78). These studies reveal how infants that are predominantly or exclusively breastfed have a lower risk of common childhood infections, and therefore experience fewer healthcare professional visits and consults. Similarly, our study found differences when comparing IFM, where both MF and EFF infants were predictive of higher total HSU costs. The WHO recommends EBF for 6 months for full health benefits, and our study demonstrates that even EBF to 1 month can have a significant impact on reducing the economic burden to the health systems in terms of HSU and direct costs.

Previous research in Canada on the protective effects of breastfeeding in infants has shown substantial benefits against childhood diseases (74,79) and that breastfeeding promotion programs could be a critical intervention. Estimation of healthcare services use, and related cost is necessary for developing cost-effective interventions to improve breastfeeding rates. This information could help policymakers regarding the development of educational policies and development of breastfeeding support programs. Further research is needed to determine the cost of services utilized in the first year of life extrapolated provincially and how this relates to IFM as this information provides

empirical data around the impact of not breastfeeding. Other countries have shown the impact of educational campaigns, training programs, and laws and regulations around the use of breastmilk substitutes and its impact on improving breastfeeding rates (80). An integrated provincial breastfeeding program should have the key components that include training programs, communications for health promotion at a population level, political will and legislation, advocacy, evaluation research and appropriate funding to achieve desired rates of breastfeeding.

3.5.1 Strengths and Limitations

There are several strengths of the current study. To our knowledge, this is the first time estimates of the cost of HSU by IFM of a sample of full-term healthy infants living in Canada have been conducted. Our ability to link maternal and child data allowed us to examine the specific characteristics that are associated with higher HSU costs among infant's (i.e., mother's parity, type of delivery and residence), and control for these confounders in our multivariate analysis. Though we had intended on controlling for additional confounders in our analysis, the nature of our homogenous sample led to us having a number of variables with counts less than 10, which impacted our ability to include them. The administrative database allowed for the calculation of individual level data and the direct costs associated with HSU through the claims of family doctors and specialists. Linking the databases to information collected in the FiNaL Study allowed for the examination of maternal and infant characteristics and their association with IFM. As with this type of research, there is potential for volunteer or responder bias in that those who respond are different than those who do not. Compared with respondents who were

included in the analyses, those who were excluded because residence or missing data were younger, less educated, rural residents and living in lower-income households. Evidence showed that those characteristics of mothers were associated with a shorter period of EBF in Canada (81). This might have led to an underestimation of the disease incidence and frequency of healthcare usage.

Our results are based on a relatively small sample size; however, the socio-demographic characteristics of the HSU study respondents were similar with those of the participants of the FiNaL Study, a province wide study on over 1200 expectant mothers. Notably, compared to those eligible to partake in the sub study on HSU, those who provided their infants healthcare number were more likely to be primiparous, partnered, higher education and household income mothers. We found differences among groups for the total costs of HSU, driven mainly by hospitalizations including costs of birth, however significant differences were not observed when examining the costs associated with other healthcare services (i.e., ER, Physician visits). Including cost of birth may have introduced several confounders that we were unable to control for, though delivery type was adjusted for within our multivariable analysis. In addition, the medicalization of birth may be what is driving the associated costs. In terms of not seeing a significant difference amongst other types of individual HSU (i.e., ER or Physician visits), this could be explained by either having no differences among groups, or that the study was underpowered to examine the differences of ER and physician visits. Due to challenges with collecting exposure data on feeding mode and its duration, our MF and EFF covered the first 6 months of life, but our EBF rate, as defined by the WHO was

considered valid and reliable for the first month only. The data on exposure were self-reported by mothers and therefore could result in misclassification. Based on the health insurance claims in the province of NL, the administrative databases can only collect information on fee for service physicians. Therefore, there are a proportion of family doctors and pediatricians that are salaried that we would not have healthcare service use on. The Newfoundland and Labrador Medical Association (NLMA) membership statistics concluded that for our province as a whole, 55% of physicians are fee for service, while others are salaried or receive alternative payment plans which would not be picked up in our database (82). Membership statistics for the Eastern Health Region were not available to compare the proportion of fee for service or salaried physicians. Based on these provincial rates, our results would be an underestimation of the true costs associated with healthcare service use. In addition, although we used a health systems perspective to examine the costs, not all costs were included in our analysis, such as the costs of medications.

3.6 Conclusion

NL has the lowest breastfeeding initiation and duration rates in Canada and the reasons for this are complex and related to socioeconomic, cultural, clinical, and healthcare challenges. To increase breastfeeding rates, a coordinated, multifaceted, and multi-level approach is required. There are very few studies published using Canadian data on this topic and research on healthcare services use according to infant feeding mode has never been conducted in NL. This study provides regionally relevant data that can inform future studies examining larger scale data linkages on IFM and HSU costs. In

conclusion, in one region of Canada, a pilot study found exclusive formula and mixed feeding to be significant predictors of the total costs associated with HSU during the first year of life. Recommendations for future research include examining larger samples to further investigate differences in the costs associated with HSU, as well as needing more reliable and valid measures of exposure to capture longer durations of EBF.

3.7 Acknowledgements

This project is a part of a larger research program aimed at understanding infant nutrition choices in NL and their implications. Dr. Twells and Dr. Allwood- Newhook co-chair the Breastfeeding Research Working Group (BFRWG) under the umbrella of the Baby-Friendly Council of NL. This group is a multidisciplinary team of academic researchers, health professionals (i.e., physicians, nurses, midwives, and pharmacists), students, data linkage specialists, and decision/policymakers. As well as the NL Centre for Health Information for their assistance in providing the administrative data for the analyses, which was funded through the Janeway Foundation. I would also like to acknowledge Louanne Kinsella for collecting data for the HSU subgroup, as well as all the mothers who took the time to take part in the FiNaL Study.

3.7 Conflict of Interests

The authors declare no potential conflicts of interest with respect to the research, authorship, or publication of this article.

Chapter 4: The use of patient engagement to gather perceptions on the cost of infant feeding

Preface

A version of this chapter has been accepted for publication in the Patient Related Outcome Measures Journal of the Dove Medical Press. The Dove Medical Press reuse policy allows for the final published PDF to be shared in an author's dissertation or thesis (https://www.dovepress.com/author_guidelines).

As the primary author, I contributed to the data acquisition, curation, analysis, and interpretation of the data, and drafted the manuscript. Along with myself, Dr. Laurie Twells, Dr. Leigh Anne Newhook, Dr. Zhiwei Gao and Dr. Hai Nguyen contributed to the conception of the study design, and along with Dr. Holly Etchegary, we critically revised the final manuscript. Our patient partner, Kaylah Parsons-Mercer critically revised the manuscript for its contents. All authors gave final approval for submission.

Abstract

Background: Patient-Oriented Research (POR) and Patient Engagement (PE) has highlighted the value of incorporating the ideas and priorities of patients in health research. Using the guiding principles of POR and PE, the current study conducted PE sessions to gain insight on the perceptions of mothers regarding the costs of infant feeding.

Methods: Four patient engagement sessions were held with mothers residing in Newfoundland and Labrador between November 2019 and January 2020. Mothers were

targeted through the Brighter Futures Coalition of St. John's, a not-for-profit community organization. PE sessions were designed in a two-hour format, allowing the research team to engage mothers and identify costs of infant feeding from a mothers' perspective.

Results: Through the guiding principles of patient-oriented research and patient engagement, our research team successful engaged with mothers in discussions surrounding the costs of infant feeding. The sessions allowed for an in-depth discussion surrounding monetary costs (e.g., incidentals of breast or formula feeding), the associated costs of infant feeding and the workplace (e.g., perceived productivity) and environment impacts (e.g., single use plastics). During each session, evaluations were provided to solicit feedback on whether the goals and expectations of mothers had been met, and whether they felt their opinions were heard and understood.

Conclusion: By conducting patient engagement sessions, informed by patient-oriented research guiding principles, we were able to successfully recruit and engage mothers in discussions that led to a better understanding of their perspectives on the costs of infant feeding.

Keywords: Patient Engagement, Infant Feeding, Patient Oriented Research

4.1 Introduction

Recently, there has been a move towards involving both patients and the public in health research, called Patient-Oriented Research. Patient-oriented research highlights the value of incorporating patients' ideas and priorities, improving the overall relevance and quality of research outcomes. It is defined as research that engages "...patients, their caregivers, and families as partners in the research process. Where patients are defined as an overarching term and includes those with personal experience, their caregivers, family

members and friends. This engagement helps to ensure that studies focus on patient-identified priorities, which ultimately leads to better patient outcomes…" (83).

There are various ways of addressing and incorporating patient ideas and priorities into research designs, with varying levels of patient engagement as defined by the International Association for Public Participation (IAP2) spectrum (84). The IAP2 identifies five levels of engagement: inform, consult, involve, collaborate, and empower, where the depth of patient involvement deepens with the progression across the spectrum of these levels (84,85). These levels allow for involvement to vary based on the input and decision-making patients provide (86). Patient engagement sessions allow for "meaningful collaboration", where patients have the ability to become actively engaged throughout various project stages including: governance, priority setting, research question development, and research performance (86). While there is no gold standard for patient engagement, there are several key principles that allow patients to thrive in patient-oriented research. Meaningful patient engagement is guided by: inclusiveness, support, mutual respect, flexibility, responsiveness, and accountability (85).

An area of research that would provide invaluable insight to its research outcomes using patient-oriented research would be in cost analyses, specifically those examining the costs associated with breast and formula feeding. Over the last number of decades researchers have examined the value of breastfeeding and its association with lower rates of infant illness, and subsequently healthcare service use, including number and duration of hospital admissions, emergency room and physician visits (6,13). Studies have found that based on the protective effect of breastfeeding on a number of acute infections in infancy, and chronic illnesses in childhood, low breastfeeding rates impact the costs to the

healthcare system (52,53). Researchers have also examined the indirect costs that are associated with infant feeding. This includes costs that are incurred by patients or families because of their infections or illness (54). Taking all costs into consideration, researchers in the US have examined the economic impact to the healthcare system, society and the costs related to premature death, demonstrating how suboptimal breastfeeding rates cost the US economy 14$ billion annually (3). By demonstrating the economic benefits of increasing breastfeeding rates, policymakers can make informed decisions around the development of policies and programs to invest in breastfeeding support.

While cost analyses have examined a wide scope of outcomes associated with the costs of infant feeding, there is still a gap when considering the cost of infant feeding to mothers and families. Largely, the opportunity costs associated with a mothers' time and caregiving, especially that spent breastfeeding (55). With a gap in costs related to mothers, we sought to engage mothers using the principles of patient-oriented research, to obtain their perceptions on the associated costs of infant feeding. By engaging with those with lived experience, we sought to obtain their perspectives on additional costs and outcomes that could be considered in future cost analyses.

The overarching goal of patient-oriented research and the development of patient engagement is to ensure research is relevant, valuable and a priority to those it impacts directly. In this paper we provide an example of using patient-oriented research, specifically patient engagement methods to explore costs of infant feeding from mothers' perspectives. Using the guiding principles of patient-oriented research and patient engagement, our aim was to engage with mothers, to gather their perceptions on the costs of infant feeding. By identifying and prioritizing costing outcomes of importance to

mothers, our study hopes to guide future research around the costs of infant feeding, from a mothers' perspective.

4.2 Material and methods

4.2.1 Aim

The purpose of this study was to use the principles of patient-oriented research and patient engagement, and conduct sessions to engage with mothers and gather their perceptions on the costs of infant feeding. Engaging with mothers provides an opportunity to identify additional costing outcomes that may not have been previously considered in cost analyses. By engaging with those with lived experience, our aim was to gain insight on the cost of infant feeding from a mothers' perspective.

4.2.2 Design

Patient engagement sessions were developed to engage mothers in a discussion surrounding the costs of infant feeding. Based on the International Association for Public Participation spectrum, the sessions allowed mothers to be engaged at an informed and collaborative level (84). The patient engagement sessions were designed in a two-hour format, which allowed for introductions, background information on infant feeding and studies examining the economic impact of infant feeding. A 20-minute presentation was developed which covered the introductions of the team, background information related to patient-oriented research and an overview of the research being conducted at Memorial University of Newfoundland. In order to facilitate discussion and ensure consistency across sessions, questions were developed prior to the sessions. Questions prompted the discussion of various feeding modes, and from their perspectives what outcomes should

be considered in future cost analyses. This then led to a discussion centred around a mothers' perceptions on the costs of infant feeding during their infants first year of life. Since infant feeding journeys are individual in their experiences, these sessions provided a safe avenue for discussing different views and opinions. The session facilitator (AB) kept the discussion on track and promoted an open platform for each mother to bring forth all experiences. This allowed all mothers to take part in the discussion and ensured those with similar or differing perspectives were highlighted.

4.2.3 Setting

Four sessions were held with mothers residing in Newfoundland and Labrador between November 2019 and January 2020. The largest smallest session had four mothers in attendance, while the largest had nine. Mothers were targeted through the Brighter Futures Coalition of St. John's, a not-for-profit organization made up of parents, community members and professionals from the area. Brighter Futures provides programming and services for young families to promote the growth and development of children ages 0-6. Various programs are available for different age groups so that families can be connected with children of the same age. Members of the research team attended family resource centres to provide a baby-friendly environment where patient engagement sessions could be conducted. Lunch was provided to those in attendance as a thank you for their time.

4.2.4 Data Collection

The recruitment process involved connecting with mothers and asking if they would be interested in attending a patient engagement session and partake in discussions

surrounding the costs of infant feeding. By connecting with a community organization, this study recruited a convenience sample of individuals who attend the family resource centre, who were currently pregnant, or had just given birth within the last year. By attending the patient engagement sessions, mothers provided their consent to partake in this study and provide their experiences and perspectives in identifying future research outcomes. Following written consent for audio recording, a digital recorder was placed in the centre of the room to capture the sessions. Qualitative data collection was used, where detailed notes were taken by both team members, and audio recorders were replayed at a later date to capture any additional information from the sessions. Following each session, notes were compiled regarding emerging topics. At the end of the sessions, a printed survey was circulated to mothers to collect demographic information and an evaluation of a mothers satisfaction of the session. Mothers were encouraged to complete all survey questions and make note of any comments, questions or concerns moving forward. This provided the team with an opportunity to have the session critiqued for completeness, detail, information provided, and discussion upheld.

4.2.5 Data Analysis

Written notes from the sessions and audio recordings comprise the data for analysis. Information was collected on the emerging topics based on the discussions from prompted questions. Information was written and presented as a comprehensive summary of the mothers' ideas. AB and RS discussed the written notes and comprehensive summary to the other team measures to ensure they were the key themes.

4.2.6 Ethical Approval

Ethical Approval for the current study was deemed unnecessary by The Newfoundland and Labrador Health Research Ethics Authority (Personal Communication) as the objective of the sessions was to engage with patient partners to help inform future research questions and methodology. Their provided guidelines are informed by both Involve (a government-funded entity supporting public involvement in the National Health Service in the United Kingdom) and the Canadian Institutes of Health Research Ethics Guidance.

4.3 Results

By following the guiding principles and best practices for patient-oriented research and developing patient engagement sessions, we were able to actively engage with community groups (e.g., Brighter Futures Coalition) who shared information on the engagement sessions through various means (e.g., Facebook). This organization schedules weekly gatherings for mothers to attend within their community, and members of the research team were able to hold the patient engagement sessions in these settings. During the sessions, the research team along with the mothers, explored and discussed the costs associated with infant feeding.

Four sessions were held, with 26 mothers and 18 babies (16 singleton, 1 set of twins) in attendance. On average, sessions lasted two hours each. Demographic information was captured for all but two mothers. The majority of mothers were Caucasian (n=22), married or common law (n=20), between 26 – 34 years of age (n=15), and with a university degree or diploma (n=15). All mothers were accessing care in the

Eastern Health Region of Newfoundland and Labrador (n=26). The majority of mothers were primiparous (n=20), and fifty-four percent exclusively breastfed (n=14) (breast milk only, no other food or water), while thirty-five percent used a mixed feeding method (n=9) and seven percent exclusively formula fed (n=2). Demographic information is outlined in Table 4.1.

Table 4.1. Sample Characteristics

Demographics	**N (%)**
Dwelling Area	
Urban	22 (85%)
Rural	4 (15%)
Age (Years)	
18 – 25	4 (15%)
26 – 34	15 (58%)
35+	6 (23%)
Parity	
Primiparous	20 (77%)
Multiparous	6 (23%)
Infant Feeding Mode	
Exclusive Breastfeeding	14 (54%)
Mixed Feeding	9 (35%)
Exclusive Formula Feeding	2 (7%)
Ethnicity	
Caucasian	22 (85%)
Other	4 (15%)
Level of Education	
Less than High School	1 (4%)
High School Diploma or Equivalent	4 (15%)
University Degree or Diploma	15 (58%)
Post Graduate Degree	5 (19%)
Employment Status	
Employed Full Time	15 (58%)
Employed Part time	3 (11%)
Unemployed	6 (23%)
Marital Status	
Single	4 (15%)
Married/Common Law	20 (77%)
Separated/Divorced	1 (3%)

Household Income	
< 29,999$	4 (15%)
30,000 – 59,999$	4 (15%)
60,000– 80,000$	4 (15%)
> 80,000$	11 (42%)
Prefer Not to Say	2 (7%)

There were a number of topics that arose from the patient engagement sessions, in terms of what outcomes should be considered when examining the costs incurred to mothers and families related to infant feeding. Based on the literature review around the gaps associated with the costs of infant feeding, we developed open ended questions prior to the sessions to cover topics related to general costs of feeding, workplace productivity, and environmental impacts associated infant feeding. A summary of information collected, and outcomes discussed based on prompted questions are outlined in Table 4.2.

Table 4.2. Outcomes of interest identified by mothers

Open-ended Question: "Have you ever thought about the costs of infant feeding- if so, what comes to mind?	
Costs related directly to breastfeeding	**Cost of incidentals** ● The costs surrounding materials for breastfeeding (Pumping supplies, nipple creams, prescriptions, ice packs, nipple shields, pillows, nursing bras, coolers, bottle warmers, storage bags, nursing pads) ● The costs surrounding eating more calories a day to sustain hunger while breastfeeding ● The costs surrounding certain foods and supplements for mothers who are having supply issues (Fenugreek, Blessed Thistle, Prescriptions, Mothers milk, etc.)

Costs related directly to formula feeding	**Cost of incidentals** ● The costs surrounding the price of formula (Testing different brands with different added components unsure of what to go with, liquid concentrates vs. powder formula, formula at different ages and stages) ● The costs surrounding materials for formula feeding (Instruments for heating bottles, sterilizing and cleaning bottles, materials for at home vs. while out) ● Overall mothers wished they had more information up front in prenatal classes regarding financial planning for infant feeding while on maternity leave
Costs related to either feeding method	**Cost of mothers' time** ● The amount of time spent on feeding (at the breast or with a bottle), the pressure of constant waking of mother and baby, and needing to wake baby ever 2-3 hours ● Time spent cleaning, sterilizing and preparing bottles (of breastmilk or formula), as well as storing milk (bagging, freezing, ensuring it has been consumed in time before needing to be disposed of ● Time spent finding resources (learning how to breastfeed, how to make formula, ensuring they are fed enough (how much, how often), understanding their diaper output (how much, how frequent) ● Time spent trying to figure out misinformation from multiple sources (Even differing information from healthcare providers (HCP) (i.e., family doctor, lactation consultant, public health nurse), familial advice, information online or through social media groups) **Cost of having limited access to care and support while establishing infant feeding mode** ● Limited accessibility of HCP (Public health visits limited or just by phone, family doctor appointments not as frequent or in-depth, limited public and private lactation consultants). Mothers referenced the importance and benefits of frequent contact from their public health nurses ● The lack of effectiveness of supports, (Clinics labelled as "breastfeeding clinics" vs "baby friendly or newborn clinics", lacking support for formula feeding mothers), lack of education of staff to support mothers with their desires to breastfeed or formula feed while in hospital and within the community once discharged

	● Long wait times where HCP are accessible (currently only two public lactation consultants within this health region, shortage of family doctors, mothers referenced not being able to see HCP within a timely matter and missing the window of opportunity for help/support) ● Lack of support available for various health complications (i.e., Lip and Tongue Tie) needing to pay publicly for assessments, revisions and support. Lack of access to HCP specializing in health complications; or availability of Lactation Consultants and Family Doctors regarding care for Lip/Tongue Tie
Open-ended Question "Have you ever thought about the relationship between infant feeding and workplace productivity?"	
Costs related directly to breastfeeding	● Potential of being seen as less productive in the workplace (Taking time to pump if still breastfeeding, Others noted that whether you take a sick day or not, you could be at work and unfocused if your child is home sick); ● How your career can impact the ability to continue breastfeeding when heading back to work (Thoughts about perceived productivity if they are leaving for pumping breaks- many mentioned that based on your job it just isn't possible to have a scheduled break when needed*)* ● Small Business Owners (Infant feeding takes a lot of time away from their business, where potentially breastfeeding would impact them continuing their work)
Costs related to either feeding method	● Other topics related to workplace productivity included Sick Days (Some employers state that a sick day must be used for the employee, and not be based on the needs of a child, that a doctor's note must be for the mother and not the baby) and Vacation Days (Referenced how these turn into unexpected sick days for the baby, where workplaces won't accommodate other sick days);
Open-ended Question "Have you ever thought about the relationship between infant feeding and its environmental impact?"	
Costs related directly to breastfeeding	● The waste associated with breastfeeding in terms of one-use plastics and other one-use items (i.e. storage of breastmilk (those pumping are required to use hundreds of single use bags), single use breast milk pads);

Costs related directly to formula feeding	● The waste associated with formula (premade liquid individual containers, powdered formula containers, tetra packs for “on the go” ready-made formula)

Printed evaluation forms were circulated at the end of each session. Scales were provided as a method of ranking their satisfaction with the session, as well as open-ended responses regarding their experiences and how the session could be improved. Mothers noted the session was detailed, complete and easy to understand. They stated they had enough information to actively engage in the discussions, and felt their opinions were heard and understood. Notably, there was a higher uptake in responses for scaled questions in comparison to questions that required a written response. Detailed responses to their evaluation are outlined in Table 4.3.

Table 4.3. Evaluation Survey from Patient Engagement Sessions

Survey Question Asked	**Responses**
How Detailed, Complete, Easy to Understand was the information provided?	Very Good (22) Good (2) Satisfactory (2)
Do you feel you had enough Information to take part in the discussion?	Yes (24) No (1)*
Overall, how satisfied are you that your opinions were heard and understood? (Free Text)	Very (13) Satisfied (4)
Overall, how was your experience with this session? (Free Text)	Excellent (5) Very Good/Great (3) Good (6) Very Interesting/Informative (3)

	I Loved it (1)
How could your experience have been improved? What should I do differently next time (Free Text)	N/A (6) Visual Aids (2) Recap Previous Sessions (2)

* when asked for additional information relating to this question and prompting for what information was required for the individual to more actively partake in the discussion she mentioned the language barrier impacted participation

4.4 Discussion

One of the valuable components of patient-oriented research is that through patient engagement, individuals with lived experience have the opportunity to help inform the development of future research questions. Patient engagement provides an avenue for exploring patient perspectives on a particular healthcare issue that is relevant to them. Engaging those with lived experience can provide meaningful input to the research agenda. It can be argued, that having a better understanding of their perspectives is a critical component in developing future areas of research. Due to limited research on the costs of infant feeding from a mothers' perspective, we conducted patient engagement sessions to explore the perceptions of mothers on this topic.

Using the guiding principles of patient-oriented research, patient engagement sessions were planned and successfully conducted to explore and better understand the costs of infant feeding from a mothers' perspective. The key principles of patient engagement played an important role in the success of our sessions. Our patient engagement sessions included a range of perspectives and experiences (i.e.,

inclusiveness), and mothers that felt sufficiently supported to meaningfully contribute to the discussion (i.e., support). The structure of the sessions allowed for various levels of involvement (i.e., flexibility), where mothers noted they were acknowledged and valued and were able to engage and provide input at the level of their comfort (i.e., mutual respect). During each session, evaluations were provided to solicit feedback on whether the goals and expectations of mothers had been met, and whether they felt their opinions were heard and understood (i.e., responsive).

For our research on infant feeding, engaging mothers with lived experience brought to our attention constructs that captured a more holistic view of the costs of infant feeding than may typically be considered or measured in cost analysis studies. The outcomes identified by mothers illustrate the value of using patient-oriented research in engaging those with lived experience. Overall, three broad categories were discussed, costs of infant feeding, impact on workplace productivity and environmental impact. The patient engagement sessions allowed us to explore in depth how women perceived these categories of costs, further elucidating the types of costs that would fall under these categories. For example, the costs on infant feeding included discussions on the incidentals of breast or formula feeding (e.g., nipple creams, bottles, bottle warmers), discussions around workplace productivity (e.g., perceived productivity, needing additional breaks related to feeding, time off), and discussions around environmental impacts (e.g., single use plastics, breast pads, ready-made formula). Interestingly, in the sessions there were conversations amongst mothers around the opportunity costs associated with infant feeding (e.g., cost of mothers' time (time spent feeding,

cleaning/preparing bottles, outsourcing guidance, and support), the cost of inaccessibility of healthcare providers and support when establishing infant feeding mode). In all patient engagement sessions, independent of discussions around costs, all mothers reported the need for more information, knowledge and support related to infant feeding, whether infants were breast or formula fed. Due to limited support around infant feeding, mothers discussed the additional time, effort and costs spent looking for information and support while establishing breast or formula feeding (e.g., Information on breast-pumping or preparing formula, paying for private lactation consultants). Referencing the critical role that healthcare providers can play during the stages of mothers establishing infant feeding (i.e., Lactation Consultants, Public Health Nurses, General Practitioners, and Specialists).

Topics identified by mothers that have been previously examined in cost analyses included the cost of incidentals for either feeding method, where researchers have attempted to outline the potential costs incurred by families related to breast or formula feeding (87) as well as the timing spent feeding their babies, which has been examined, but is yet to be considered in a larger global scale cost analysis (88). Mothers wished they had a higher level of the costs that may be incurred to families during their infants first year of life related to infant feeding, and how that may allow them to better prepare financially. Other researchers have also considered the importance of the timing required by families during that first year of life to promote and support their infant feeding journeys, relating to paid maternity leave (89). Researchers have examined the impact of paid parental leave on the ability to enhance population health, by providing families a greater opportunity to achieve breastfeeding initiation and longer breastfeeding durations (90).

Additional emerging topics that may not have been previously identified by mothers in this context include the importance of the workplace. Mothers outlined their concerns with perceived productivity in the workplace when returning from maternity leave, requiring time and resources for breast pumping milk, or the necessity for their own personal sick or vacation days now being used for purposes related to their infant. Mothers mentioned the impact of their career on infant feeding, and how for some it is not feasible to have planned breaks throughout their workday, or how being self-employed or a business owner can impact infant feeding journeys. These emerging topics highlighted the importance of having a work environment conducive to mothers' infant feeding journeys. This highlights the importance of workplace policies and legislation and better understanding the needs of mothers during this time (90). Policies which include access to breastfeeding friendly spaces (e.g., a clean and comfortable space if breast pumping, somewhere to store pumped milk, or to clean equipment), and if feasible, the ability to spend a scheduled work break feeding their infant (i.e., by breast pumping, or by having sufficient time to return home). Another topic that has been emerging in infant feeding research includes examining the environmental impact of formula feeding companies (91). Mothers brought to our attention the environmental impact of either feeding method. Their concerns were with their use of single-use plastics (e.g., breast pads, storage bags for breastmilk, premade liquid formula) and the waste associated with both feeding methods, which has not been considered. Conducting patient engagement sessions, as an element of patient-oriented research, allowed for much more in depth discussion on the costs of infant feeding not reported elsewhere. This

information may help to inform future cost analyses related to the economic impact of infant feeding.

We have several recommendations for future patient-oriented researchers, from our lessons learned throughout the creation planning and implementation phases of our patient engagement sessions. These lessons are those learned from our engagement sessions but would be applicable to other researchers engaging in patient-oriented research. First, linking up our research team with a community organization, was a key component to our successful patient engagement. Inserting ourselves as researchers in a community Setting led to active engagement and collaboration in a setting that was welcoming to those we wanted to engage with. We recommend that by engaging community organizations, researchers can more easily connect with and engage with those with lived experience. Second, throughout each session information on the topics discussed was compiled in various formats (audio recording, written notes, evaluation forms). This allowed the team members to better understand ideas of mothers and identify any additional outcomes to be further discussed or discussed at the following patient engagement sessions. Third, having an understanding of the needs of those you are engaging with is paramount for optimal engagement. Our sessions allowed mothers to attend with their infants, so upon the completion of a session when printed surveys were circulated, it was not as feasible for mothers to spend time completing evaluations. Specifically, the time required to fill out free-text questions, therefore in future we would consider altering the format of these surveys to better fit those in attendance (e.g., verbal discussions vs. paper format). Fourth, patient engagement requires time and resources to uphold these sessions and contact between those that have been engaged. By preparing

for the time and resources required, it ensured mothers remained informed, involved, and updated at several project stages.

This study identifies costs and outcomes to be included in a broader approach to measurement in a cost analysis from a mother's perspective. Moving forward, we hope that the use of patient-oriented research, specifically patient engagement can inform future research questions, and further expand on cost analyses on infant feeding. Future research should consider including additional outcomes in cost analyses examining the economic impact of infant feeding. In addition, future research should examine the effectiveness of infant feeding supports, prior to examining the cost effectiveness of interventions.

4.5 Limitations

Patient engagement has its limitations, based on funding, timing and recruitment. Due to the small numbers engaged throughout these sessions, there is a possible underrepresentation of individuals falling in different socio-demographics, as well as a bias that may present itself in smaller group sessions. To the nature of obtaining a convenience sample, the sessions took place with a well-educated homogenous group, which impacts its generalizability. Notably, with additional sessions there is potential for additional emerging topics and key priorities for future studies to arise. At the end of each session printed evaluations were circulated to mothers. We found additional incentives were needed regarding obtaining session feedback in this format. In future sessions we would ensure that the evaluation is in a format that is more easily complete (e.g., verbal discussion vs. printed survey).

To our knowledge this is the first study using patient engagement as a method of engaging mothers to identify costing factors related to infant feeding. These sessions allowed for a rich discussion regarding mothers' perspectives, information that would not necessarily be captured in standard surveys or cost analysis measures. It allowed for a group collaboration in describing their experiences, which then allowed us to draw emerging topics which can inform future research questions associated with the costs of infant feeding.

4.6 Conclusion

Patient-oriented research has highlighted the value of incorporating patients' ideas, priorities, and experiences in health research. By conducting PE sessions, informed by patient-oriented research guiding principles, we were able to successfully recruit and engage mothers in discussions that led to a better understanding of their perspectives on the costs of infant feeding.

4.7 Acknowledgments

We would like to thank the NL SUPPORT Unit for their guidance and support in organizing the patient engagement sessions (Kate Lambert, Kathleen Maher, Chelsey McPhee), as well as Masters Student Rosie Stanoev for attending sessions and recording minutes of the sessions. We would also like to thank the organizations that welcomed our team to engage with mothers in a community Setting- and to all of those that attended and provided their time, perspectives, and experiences.

4.8 Conflict of Interest

The author reports no conflicts of interest in this work. Funding for the patient engagement sessions were provided by the NL SUPPORT Unit through a patient engagement grant. NL Support also provides the educational funding for the lead author. The funding body had no role in the design of the study, data collection, analysis, and interpretation or in the writing of the manuscript.

Chapter 5: The effectiveness of virtual lactation support for breastfeeding mothers: a systematic review and meta-analysis

Preface

A. Blackmore, B. Howell, Z. Gao, HV. Nguyen, L.A. Allwood-Newhook, L.K. Twells. The Effectiveness of Virtual Lactation Support: A Systematic Review and Meta-Analysis. *Journal of Human Lactation*. https://doi.org/10.1177/08903344221099914

As the primary author, along with Brittany Howell, I contributed to the data acquisition, curation, analysis, and interpretation of the data, drafted the manuscript, and critically revised the manuscript for final submission. Kristen Romme assisted with the data curation, validation and drafting the manuscript. Along with myself, Dr. Laurie Twells, Dr. Leigh Anne Newhook, Dr. Zhiwei Gao and Dr. Hai Nguyen contributed to the conception of the study design, and critically revised the final manuscript. All authors gave final approval for submission.

Abstract

Background: The World Health Organization recommends lactation support to enhance the rates of exclusive breastfeeding. Access to in person lactation support may be limited

due to scarcity of resources (e.g., healthcare professionals) and geography. Advances in technology have allowed lactation supports to be offered virtually through information and communication technologies (i.e., telephone, internet, and social media).

Research Aims: The aims of this project were: 1. Conduct a systematic review of randomized controlled trials designed to test the effectiveness of virtual lactation support for postpartum mothers on rates of exclusive breastfeeding up to six months. 2. Conduct a meta-analysis of studies meeting the selection criteria for the systematic review.

Methods: MEDLINE, Embase, CINAHL, PsycINFO and Cochrane CENTRAL were searched. Keywords were breast feeding/ lactation; support or education; and information and communication technologies. Studies were included if they were (a) randomized controlled trials, (b) with a virtual lactation support intervention during the postpartum period, (c) reported on exclusive breastfeeding outcomes. Two reviewers independently assessed the risk of bias and extracted data. The prevalence of exclusive breastfeeding in each group and the total number of participants randomized for each group were entered into random-effects meta-analyses to calculate a pooled relative risk (RR) at three different time points (1, 4 and 6 months).

Results: A total of 3391 records were screened; 148 full texts were reviewed, and 19 randomized control trials met inclusion criteria. Of the 19, 16 studies were included in the meta-analysis (n =5,254). Virtual lactation support was found to be effective at increasing exclusive breastfeeding at one month (RR, 1.21 [95% CI, 1.09-1.35]; $p < 0.001$) and six months (RR, 1.87 [95% CI, 1.30-2.68]; $p < 0.001$).

Conclusion: In this meta-analysis of randomized controlled trials comparing virtual lactation support with other postnatal maternity care, virtual lactation support was

associated with increasing exclusive breastfeeding rates at one month and six months postpartum.

Keywords

Breastfeeding, lactation support, information and communication technologies

5.1 Introduction

Exclusive breastfeeding (EBF) provides the nutritional needs for optimal growth and development. It is recommended that infants be exclusively breastfed for the first six months of life, and continue breastfeeding for up to two years of age and beyond (World Health Organization, 2009). Globally, despite these recommendations, EBF rates remain low. Factors impacting breastfeeding goals and behaviours include those on a societal, environmental, and individual level (1). These are multi-factorial and can include breastfeeding supports in the community, hospital infrastructure, lack of lactation education or support, marketing of human milk substitutes, entrenched formula feeding practices, maternal perceptions of infant feeding practices, difficulty feeding, medical conditions of mother or child, and maternal attributes (i.e., maternal age, education, marital status) (1).

To enhance a mother's ability to establish and sustain breastfeeding practices, the World Health Organization (WHO) and the United Nations Children's Fund (UNICEF) have created lactation guidelines and recommendations. For example, it is recommended that expectant women and their families be counselled about the benefits of breastfeeding and offered breastfeeding education tailored to their individual needs (28). These have been shown to enhance breastfeeding practices and serve as a form of lactation support

interventions to mothers (28,56). Lactation support can be hospital-based, community-based, and delivered face to face or virtually through information and communication technologies (ICTs) (28,56).

ICTs are defined as "all communication technologies, including the internet, wireless networks, cell phones, computers, software, middleware, video-conferencing, social networking, and other media applications and services" (92). This may include any form of ICTs, such as e-health, m-health, or telehealth. The rising popularity and advances of technology have allowed the delivery of lactation support to shift from traditional in-person care to virtual delivery (56). A previously published systematic review and meta-analysis (SRMA) of interventions to increase breastfeeding reported that internet-based interventions were an effective method of increasing EBF (odds ratio (OR) 2.2 [1.9-2.7]) (57). ICTs have been found to be an efficient method of providing education and support (93), and have been found to be cost-effective, time efficient and a flexible method of delivery for healthcare interventions (28). Lactation support delivered through ICTs can include broader accessibility of supports, employing additional methods of delivery for healthcare providers, peers or other individuals who have been taught how to support breastfeeding mothers (94). As accessibility is an important aspect of healthcare, electronic services and alternatives to standard practices and traditional models of care (i.e., face to face) allow for additional avenues to support mothers (94).Expanding the use of these technologies is especially important now, given the health risks and public health restrictions due to the COVID-19 pandemic, allowing for

additional virtual resources and support while public health measures ensure limited in-person contact.

To our knowledge, there are no published systematic reviews (SR) exploring randomized control trials (RCTs) offering lactation support during the postpartum period using ICTs. Existing SRs exploring ICTs and lactation support included non-randomized trials, interventions in lactation education and promotion taking place solely in the prenatal period and have only included studies published until November 2018 (58,59). These reviews identified existing ICTs that provide lactation support (59) as well as the important characteristics required for effective internet-based lactation support (58)

Given the increasing importance of and reliance on technologies in healthcare, it is crucial to update the existing literature on lactation support offered through virtual care. The investigators of existing SRs in this area have not conducted a meta-analysis (MA) due to differences in study methodologies (i.e., study designs), breastfeeding outcomes (i.e., initiation, any breastfeeding, EBF), intervention types (i.e., prenatal/postnatal) and intended users (i.e., mothers, partners, clinicians) (58,59).

The aims of this project were twofold, (a) to conduct a systematic review of randomized controlled trials designed to test the effectiveness of virtual lactation support for postpartum mothers on rates of exclusive breastfeeding up to six months, and (b) to conduct a meta-analysis of studies meeting the selection criteria for the systematic review.

5.2 Method

5.2.1 Design

This study consisted of a SRMA to examine the effectiveness of lactation support provided by ICTs. The review is reported in accordance with the Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA 2020) guideline (Appendix 4.1). The protocol is registered (CRD42021256433) with PROSPERO. This study did not have to have institutional review board approval, nor was patient consent required, because we used published publicly available data for the systematic review.

5.2.2 Sample

Individual RCTs examining the effectiveness of any ICTs used as lactation support for mothers during the postpartum period were considered. RCTs were eligible if the researchers (a) enrolled participants who were healthy postpartum mothers (b) examined study interventions of lactation support provided through ICTs, where lactation support was defined as the provision of any form of breastfeeding support during the postpartum period; (c) included a control group; (d) reported rates of EBF, where the definition of EBF is defined at the discretion of study authors. The authors collected EBF data at a number of time points that included at one, four and six months, based on the necessity for lactation support interventions in the early stages of breastfeeding, and current global recommendations outlined as EBF to six months (8). No language restrictions or publication dates were applied in order to broaden the search and capture all studies that met our inclusion criteria. Studies in which researchers examined lactation support or education interventions for partners, clinicians, healthcare providers or community

members were excluded. Interventions implemented solely during the prenatal period were also excluded. In addition, studies examining ICTs that did not encompass some form of lactation support were excluded. The authors worked with a librarian to create a search strategy.

The search strategy yielded 4734 articles. Two authors (AB and BH) manually reviewed each of these articles using Covidence, a web-based screening and data extraction tool (95). Once duplicates were removed, there were 3391 records screened. In total, 148 articles underwent full text review and 19 studies met inclusion criteria (Figure 1). The reasons for exclusion include: additional duplicates (n=51), wrong study design (n= 24), wrong population, intervention, comparator or outcome (n =33), abstracts, protocols or those with a combination of reasons (n =21). Additional information on study exclusion can be found in Appendix 4.5. Based on reported outcomes of EBF, 16 studies were included in the MA.

5.2.3 Measurement

The primary outcome was the rate of EBF at 6 months, whereas secondary outcomes were the rate of EBF at 1 month and 4 months. EBF definitions differed based on individual RCTs, however, the most common definition, n =17 (89%) was that defined by the WHO. The WHO defines EBF as consisting of no other food or drink, not even water, except breastmilk (8). Other study definitions used include “Breast milk Only” defined as “infants receiving breast milk only at six months (i.e., breast milk being the only milk provided in the last 24 hours, not excluding solid foods)”. This variable was

reported on the basis of what mothers reported feeding their infants at various time points within the respective RCTs.

Using a standardized Excel spreadsheet, relevant information was collected to synthesize the data and information available for the individual studies. If study results or sample sizes were unclear, authors were contacted to further obtain the required data.

The tool used for evaluating the methodological quality of the included articles was the Cochrane Risk of Bias (RoB) 2 Tool (96). This includes assessment of RoB based on the randomization process, deviations from intended interventions, missing outcome data, measure of outcome, selection of reported results and overall bias. Two reviewers (AB & BH) carried out the quality assessment of each article independently. Each domain was evaluated as a low RoB, high RoB or some concern (97). A guiding document allows for the use of an algorithm for suggested judgement of risk of bias. Any differences in scoring were discussed by AB and BH and resulted in consensus.

5.2.4 Data Collection

In consultation with the research team, a medical librarian (KR) created a comprehensive search strategy which was approved by authors (AB, LT and BH). The search was developed in Ovid MEDLINE and included text words and subject heading terms related to the concepts that comprise the research question: 1) breast feeding/ lactation; 2) support or education; and 3) ICTs. The search was peer reviewed according to the PRESS Guideline (McGowan et al., 2016), and translated for the other databases.

The research team began developing the search strategy and process in April 2021, and completed the search in August 2021. The following databases were searched on June 25, 2021, from database inception to the search date: MEDLINE (Ovid), Embase.com, Cochrane CENTRAL (Wiley), CINAHL Plus (EBSCOhost), and APA PsycINFO (EBSCOhost). An RCT search filter was used in MEDLINE (98), Embase.com (99,100), and CINAHL Plus (99). We also searched ClinicalTrials.gov and the WHO International Clinical Trials Registry. The reference lists of included articles and relevant systematic reviews were manually screened for additional relevant studies. If needed, study authors were contacted to obtain the appropriate data required for the review. The full search strategy can be found in Appendix 4.2. Search results were combined in EndNote X8 citation management software (101). Duplicate citations were removed, and the remaining citations were exported to Covidence SR software (95). Two reviewers (AB & BH) completed the title, abstract and full text review independently and in duplicate. The inter-reviewer agreement was 97%, where any disagreements were resolved through discussion between AB and BH. A third author (LT) was included in the discussion if required. This rate was determined using Covidence SR software, via the full text study reporting system. Covidence generates a study report outlining the level of inter-rater agreement.

Using a standardized data extraction form, information that involved subjective interpretation or the interpretation of results (i.e., outcome data) was extracted independently by two reviewers (AB, BH). Information on study characteristics was extracted by a single reviewer (AB) followed by verification by the second reviewer

(BH). Any disagreements in extraction were examined by a third reviewer (LT) and resolved by discussion. The contents extracted from each study included study aim/question, description of the intervention and comparator, outcomes, and measurement tools (Table 1, Table 2). Authors reviewed extracted information to examine methodological congruence and the unity and consistency between study aims, measurement and analysis.

5.2.5 Data Analysis

A random-effects model was used to calculate the pooled crude and adjusted relative risks (RRs) with 95% CIs for EBF at one, four and six months. For dichotomous outcomes, we used the numbers of events and the sample sizes instead of the value of the crude RRs (Patnode et al., 2016). Two-sided P values <0.05 were considered statistically significant. The formulas we used to calculate RR and CI's can be found in Appendix 4.3. Statistical heterogeneity among pooled studies was examined using standard $\chi 2$ tests, and the proportion of total variability in point estimates was approximated using the I^2 statistic. The Cochrane Handbook outlines the interpretation of moderate, substantial and considerable heterogeneity, with higher values indicating greater heterogeneity (97). Higher levels of heterogeneity were considered. Publication bias was assessed by visual inspection of a funnel plot. The software package used for the analysis was RevMan5 (62).

5.3 Results

5.3.1 Study Characteristics

A total of 19 RCTs were included in the systematic review, of which 16 were included in the MA. The full study selection process is included in the PRISMA flowchart (Figure 5.1) and the data extracted from the included articles are in Table 5.1.

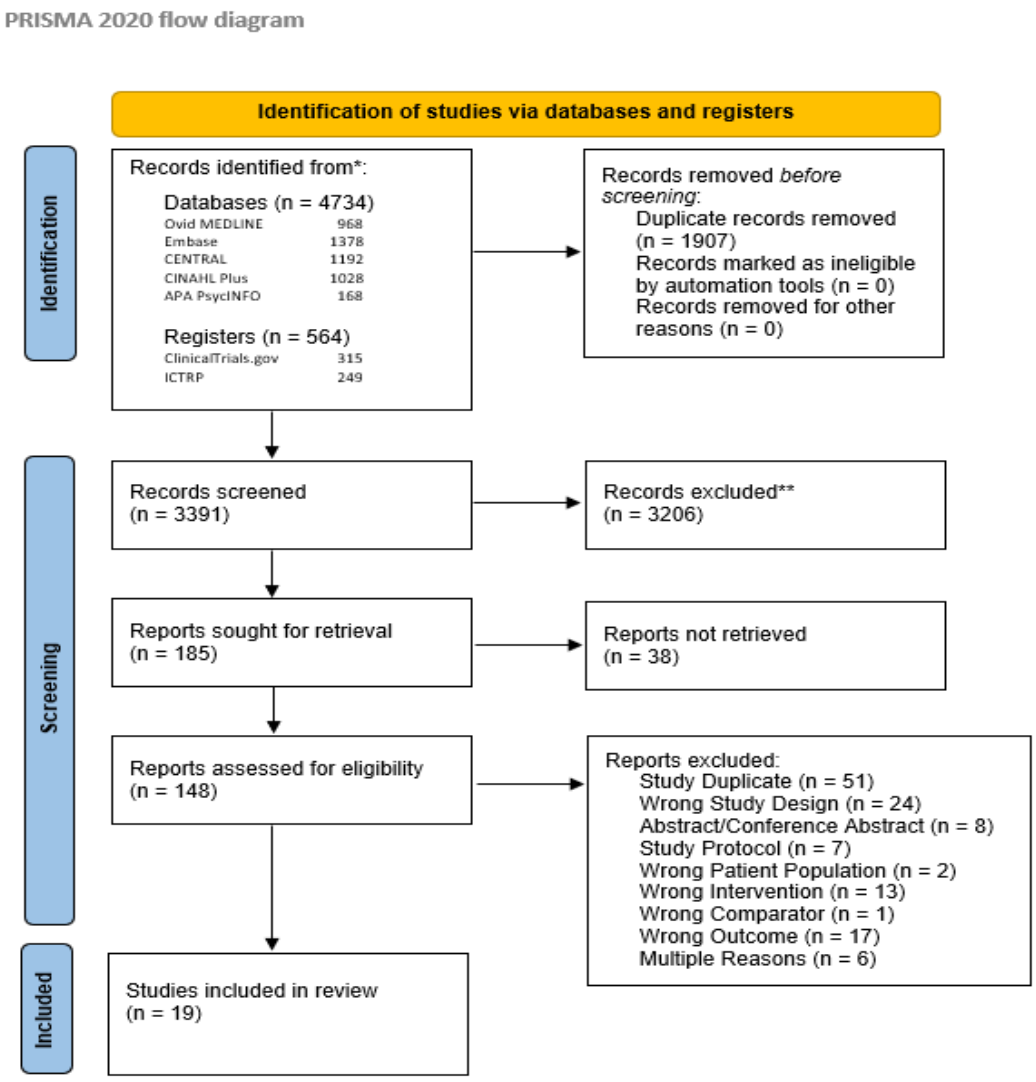

Figure 5.1 PRISMA Flow Diagram

Table 5.1. Study Characteristics of Included RCTs for Review (N = 19)

Authors (Year) Country	Study Aim	Sample Description (N)	Intervention and Control Group Description
Dennis et al. (2002) Canada	Evaluate the effect of peer (mother to mother) support on breastfeeding duration among first time breastfeeding mothers	● Primiparous breastfeeding women ● At least 16 years of age ● English speaking ● Singleton birth ≥ 37 weeks' gestation ● Resided in the surrounding region accessible by a local telephone call ● (N = 258)	**Intervention:** Conventional care plus telephone-based support (By Trained Peers), initiated within 48h after hospital discharge and subsequently thereafter) **Control:** Standard / conventional care
Wong et al. (2007) China	Assess whether a programme involving a postpartum trained peer hospital visit followed by telephone support after discharge could be an effective strategy to promote breastfeeding.	● Cantonese speaking ● Healthy mothers, and had a vaginal delivery of a full term healthy infant. ● Mothers must have planned to stay in Hong Kong for six months postpartum ● Expressed an intention to breastfeed upon admission to the postnatal unit. ● (N = 368)	**Intervention:** Trained peers visited mothers during their postpartum hospital stay. The intervention included 7 regular telephone consultations from a peers (at 24 hours, 4, 7 and 14 days, 2 months and 4 months post discharge) **Control:** No visit or any phone contacts. They would receive the usual postnatal care and breastfeeding
Hoddinott et al. (2012) Scotland	Assess the feasibility of implementing a dedicated feeding support team on a postnatal ward and pilot the potential effectiveness of team (proactive) and woman-initiated (reactive) telephone support after discharge.	● All women who potentially could be admitted to the postnatal ward after birth ● Mothers were sent written study information when they were 32-36-week pregnant. ● (N = 1,036)	**Intervention:** Proactive Telephone Support (from trained Research Team members) daily for 1 week following hospital discharge. Calls terminated at the woman's request **Control:** Reactive Telephone Support. Women could telephone or text message the feeding team at any point over the 2 weeks following discharge.

Simonetti et al. (2012) Italy	Test the effectiveness of a structured telephonic counselling on exclusive breastfeeding on healthy babies.	● Italian speaking ● Primiparous women ● Expressed their intention to breastfeed ● (N = 114)	**Intervention**: Every mother in the experimental group received telephone calls (By Midwife) during the first 6 weeks after delivery. Phone calls were at least once per week; and mothers were invited to call when necessary. **Control**: a standard counselling program, consisting of periodical visits with the physician at 1, 3 and 5 months after delivery. They were also invited to call the Midwife in case of breastfeeding problems
Tahir et al. (2013) Malaysia	Study the effectiveness of telephone lactation counselling on breastfeeding practices.	● 18 years of age or older ● Malaysian nationality ● Singleton birth ≥ 37 weeks' gestation ● Expressed intention to breastfeed ● Malaysian or English speaking ● (N = 357)	**Intervention:** Telephone calls (by Lactation Consultant) twice monthly, in addition to conventional care. It was expected every mother will receive 12 lactation counselling sessions via phone **Control:** Conventional care included breastfeeding talks during immunization, communication with during postnatal follow ups
Fu et al. (2014) China	Evaluate the effect of two postnatal professional support interventions on the duration of any and exclusive breastfeeding.	● 18 years of age or older ● Hong Kong Chinese ● Primiparous ● Expressed intention to breastfeed ● Without any major obstetric complications or serious medical problems ● (N = 724)	**Intervention:** Standard care plus weekly post-discharge breastfeeding telephone support (By a Research Nurse, Midwife or Lactation Consultant), of 20–30 minutes in duration **Control:** Standard postnatal maternity care, and standard care plus three in hospital professional breastfeeding support sessions (30-45 minutes)

Giglia et al. (2015) Australia	Evaluate the effect of a breastfeeding support Internet intervention on breastfeeding outcomes on women living in regional Western Australia	● A sample of mothers and their infants were recruited from hospitals ● Mothers were living within four regional areas of Western Australia ● Mothers were recruited during a universal home visit to new mothers within the first week postdischarge from the hospital. ● (N = 489)	**Intervention:** The Web site was developed using formative research. Mothers could post on the discussion forums, initiate conversations with group members, and contact a lactation consultant online with questions. **Control:** Usual care consisted of normal postpartum maternity services available in the community. Mothers accessed a website that redirected them to helpful parenting and infant feeding websites.
Ahmed et al. (2016) USA	Determine whether an interactive web-based monitoring system during the first month after hospital discharge increased breastfeeding rates.	● English speaking ● 18 years of age or older ● Expressed intention to breastfeed ● No serious medical condition ● Basic knowledge of how to use the Internet, and access electronic ● (N = 141)	**Intervention:** Access to an online, interactive, automated-web based response breastfeeding monitoring system and prompted to record breastfeeding output data for 30 days **Control:** Usual care consisted of standard hospital protocol
Maslowsky et al. (2016) Ecuador	Evaluate the effects of a mobile phone-based intervention on postnatal maternal health behavior and maternal and infant health in a middle-income country.	● 15 years of age or older ● Spanish speaking ● Newborn had not been admitted to the neonatal intensive care unit. ● (N = 178)	**Intervention:** Mothers received a two-part intervention. (1) Educational info administered by the nurse via phone within 48 h of hospital discharge (2) Nurse on-call during the first 30 days of the newborn's life. The nurse was available via phone from 8 am to 5 pm, Monday to Friday. **Control:** Standard care, consisting of brief discharge instructions delivered by a nurse at the time of hospital or clinic discharge.

Ericson et al. (2018) Sweden	Evaluate the effectiveness of proactive telephone support provided to breastfeeding mothers of preterm infants after discharge from neonatal intensive care units (NICU).	• Mothers with preterm infants, gestational age <37 weeks • Infants had been admitted to one of the NICUs for at least 48 hours • Mothers' breastfed or expressed breast milk. • (N = 493)	**Intervention:** Daily telephone call to the mother initiated by a member of the breastfeeding support team (BST), that is proactive support, from day 1-14 after discharge, including weekends. Mothers could call someone in the BST during the same period (reactive support). **Control:** Mothers could phone the BST from day 1-14 after discharge 08.00–16.00 every day, including weekends.
Patel et al. (2018) India	Evaluate the effectiveness of text messages and counselling using cell phones as they are ubiquitous, even in the lower socioeconomic strata of the urban population.	• Participating hospitals had to have annual deliveries of above 5000 and catered to women belonging to poor socioeconomic background. • Women in their third trimester (32–36 weeks), registered for antenatal clinics, planning to deliver at the same hospital and willing to give follow up till 6 months of infant age • (N = 1,037)	**Intervention:** Cell phone counselling (CPC) + Baby Friendly Hospital Re-training. CPC was provided by certified lactation counsellors weekly, starting in the third trimester of pregnancy until a week after the infant was 6 months old. Women received a text message daily. **Control:** Usual care consisted of routine healthcare services and Baby Friendly Hospital Initiative re-training
Chaves et al. (2019) Brazil	Evaluate the effect of telephone educational intervention on maternal self-efficacy, duration and exclusivity of breastfeeding	• Singleton full-term gestation • Expressed intention to breastfeed • Having at least one telephone number for contact. • (N = 132)	**Intervention:** Women received an educational intervention by telephone. Phone calls lasted seven minutes, on average, made by an experienced nurse/lactation educator. They used a form that followed the principles of the Motivational Interview. **Control:** Standard care, women received only the

			routine guidelines of the child-friendly hospital.
Cavalcanti et al. (2019) Brazil	Evaluate the effectiveness of a participatory intervention promoted by health professionals on the duration of EBF during the first six months of the child's life using an online social network	● Mothers gave birth between August 2016 and February 2017 ● Over 18 years of age ● Knew how to read and write ● Used the online social network Facebook ● Were discharged from the hospital together with their child. ● (N = 251)	**Intervention:** After hospital discharge mothers were followed for 6 months in a closed group of the online social network. The women were tagged in a post of the group, corresponding to a topic of the booklet, once each week. Each tag in the group generated an automatic and immediate notification, enabling communication in real time. **Control:** All mother's in the received the same booklet after birth while they were still in the maternity ward
Uscher-Pines et al. (2019) USA	Evaluate the feasibility and impact of telelactation via personal electronic devices on breastfeeding duration and exclusivity among rural women	● 18 years of age or older ● English speaking ● Singleton baby, $\geq$ 35 weeks gestation ● Had initiated breastfeeding and planned to continue after hospital discharge. ● (N = 203)	**Intervention:** The Pacify Health's telelactation application was used. Mothers could request unlimited, on-demand video calls with IBCLCs through the app for as long as they desired. The app aimed to provide video calls within seconds of a visit request. **Control:** While in the hospital, both control and telelactation arm participants received access to the standard support offered by various healthcare professionals (nurses, obstetricians, and pediatricians) who cared for them during their hospital stay.
Forster et al. (2019) Australia	Determine whether proactive telephone-based peer support during the postnatal period increases the proportion of infants	● Primiparous ● Admitted as public patients to the postnatal units of the participating hospitals ● English speaking	**Intervention:** Proactive telephone-based support from a peer volunteer. Peers made an initial telephone call to the new mother 24-48 h after hospital discharge, with a follow-up call 3-4 days after the initial call.

	being breastfed at six months of age.	● Expressed intention to breastfeed ● (N = 1,152)	Subsequent calls were to be made each week for the first twelve weeks after birth, then 3-4 weekly between 3-6 months. **Control:** The standard postpartum hospital stay at all sites was up to 48-72 hours. Each site provides access to breastfeeding services by lactation consultants if needed. Women were offered 1-2 postnatal visits in the home from a midwife within the first week after discharge, after which a Maternal and Child Health Nurse (MCHN) service was provided in the community
Lewkowitz et al. (2020) USA	Determine whether a novel smart-phone application "Breastfeeding Friend" increases breastfeeding rates for low-income, first-time mothers	● Primiparous ● Approximately 36 weeks gestation ● Expressed intention to breastfeed ● (N = 170)	**Intervention**: Interactive advice via a smart phone application on common breastfeeding challenges, educational content (breastfeeding, pumping, infant behavior, diet, exercise), and hyperlinks to videos and resources **Control**: A control app was used containing only digital versions of conventional breastfeeding support handouts provided at routine third-trimester prenatal care visits.
Puharic et al. (2020) Croatia	Test the effect of an educational intervention in the form of a breastfeeding booklet and proactive telephone calls during the prenatal and postnatal period, on EBF rates at 3 and 6 months.	● Primiparous ● Attended their primary care obstetrician between 20 to 32 weeks of pregnancy ● Croatian speaking ● Residing within the territory of the Republic of Croatia for at least a year ● (N =400)	**Intervention:** A breastfeeding booklet and a general pregnancy booklet, followed by four proactive telephone calls (By a Registered Nurse) – one in pregnancy and three after delivery, at 2, 6 and 10 weeks. **Control:** Standard care, mothers did not receive any

			written materials or phone calls before or after birth
Wu et al. (2020) China	Assess the effectiveness of using WeChat to improve breastfeeding practices	● Pregnant women, 11-37 weeks gestation, with a singleton fetus ● 18 years of age or older ● No known illness that limits breastfeeding ● Mandarin speaking ● Ability to use WeChat through their smartphone and had access to the internet. ● (N = 344)	**Intervention:** The intervention consisted of a development application "WeChat". Within the application there was a special modules, this was designed for BF promotion, education and provided key breastfeeding knowledge. Tailored automated messages were sent 3x weekly **Control:** Used the WeChat application, but were not given access to the Ke Xue Wei Yang module
Ogaji et al. (2021) Nigeria	Evaluate the impact of mobile phone-based breastfeeding support on the rate and duration of EBF at a baby-friendly hospital in Nigeria	● Mothers who delivered in the hospital ● Residents in Port Harcourt metropolis ● Expressed intention to breastfeed ● (N = 75)	**Intervention:** Mobile phone-based advisory support service from the same paediatrician. Mothers were contacted on the 7th and 14th day of the first month and subsequently on the infant monthly birthdays, until they were 6 months old. **Control:** Standard care during visits to the post-natal clinic, infant nutrition clinic and routine immunization unit.

Note. All included studies in this review are randomized controlled trials. N = Sample Size of participants randomized in each RCT; RCT = Randomized Controlled Trial

The three studies excluded from the MA were excluded due to varying follow-up periods that did not align with the current study's primary or secondary outcomes and therefore could not be included in the MA.

In total 5,729 participants were randomized in the 19 RCTs, 2,867 to the intervention groups (range 32 to 503) and 2,862 to the comparator groups (range 26 to 515). Sample sizes ranged from 58 to 1,016. The most common intervention examined was lactation support provided via telephone (N=13/19). Studies were published between 2002 and 2021, and were conducted in 13 different countries (Australia, Brazil, Canada, China, Croatia, Ecuador, India, Italy, Malaysia, Scotland, Sweden, USA, and Nigeria). Of the 19 studies, 17 reported EBF defined by the WHO (e.g., breastmilk only, no other foods or liquids). Two of the 19 studies examined ICTs that began during late pregnancy and followed mothers postnatally, while the others were solely during the postpartum period. Study results were presented as Relative Risks, Odds Ratios, Mean Differences or Percent Rate Comparisons. The variables and instruments used to measure each variable are presented in Table 5.2.

Table 5.2. Study Characteristics including outcome measurement, definition and measurement tool (N = 19)

1st Author (Year) Country	Intervention Type	Outcome Measured	Outcome Definition	Measurement Tool	Validity	Reliability
Dennis (2002) Canada	Telephone	Any and EBF at 1,2 & 3 mos	Unclear	Maternal self-report	Content Validity	Questionnaires pre-tested
Wong (2007) China	Telephone	EBF 5 days, 3 & 6 mos.	WHO	Maternal self-report	Face Validity	None Reported
Hoddinott (2012) Scotland	Telephone	EBF at 6-8 weeks	WHO	Maternal self-report via telephone survey	Content Validity	WHO Procedures
Simonetti (2012) Italy	Telephone	EBF at 1,3 & 5 mos	WHO	Maternal self-report	Content Validity	None Reported
Tahir (2013) Malaysia	Telephone	EBF at 1,4 & 6 mos	WHO	Maternal self-report via telephone survey	Face Validity	Pre-tested with target population
Fu (2014) China	Telephone	Any and EBF at 1,2,3 & 6 mos	WHO	Maternal self-report via telephone survey	Content Validity	WHO Procedures
Giglia (2015) Australia	Website, Email and Video chat	EBF at 6 mos	WHO	Maternal self-report	Content Validity	WHO Procedures
Ahmed (2016) USA	Web-based monitoring	EBF at 1,2 & 3 mos	WHO	Maternal self-report via telephone questionnaire	Content Validity	None Reported
Maslowsky (2016) Ecuador	Telephone	EBF at 3 mos	WHO	Maternal self-report via telephone	Face Validity	None Reported

Ericson (2018) Sweden	Telephone	EBF at 8 weeks	WHO	Maternal self-report	Face Validity	None Reported
Patel (2018) India	Telephone	EBF at 24h, 6, 10, & 14wks & 6 mos	WHO	Maternal self-report via telephone survey	Content Validity	WHO procedures
Chaves (2019) Brazil	Telephone	EBF at 1,4 mos	WHO	Maternal self-report	Content Validity	Cronbach's alpha of 0.74
Cavalcanti (2019) Brazil	Online Social Network (Facebook)	EBF at 1, 2, 3, 4, 5 & 6 mos	WHO	Maternal self-report interview	Face Validity	None Reported
Forster (2019) Australia	Telephone	Any BF at 6 mos	Human milk only	Maternal self-report	Face Validity	None Reported
Uscher-Pines (2019) USA	Application	EBF at 4 mos	WHO	Maternal self-report via in person survey	Content Validity	CDC Survey Procedures
Lewkowitz (2020) USA	Smart phone Application	EBF at 2d, 6 wks & 6 mos	WHO	Maternal self-report survey	Content Validity	CDC Survey Procedures
Puharic (2020) Croatia	Telephone + Booklet	EBF at 3 & 6 mos	WHO	Maternal self-report via postal infant feeding survey	Face Validity	None Reported
Wu (2020) China	Direct Messaging Application	EBF at 0-1, 2-3, & 4-5 mos	WHO	Maternal self report survey	Content Validity	WHO Procedures
Ogaji (2021) Nigeria	Telephone	Exclusive breastfeeding at 1, 2, 3, 4, 5 and 6 mos	WHO	Maternal self-report during 6th month home visit	Content Validity	WHO Procedures

Note: EBF = Exclusive breastfeeding. EBF is that defined by the World Health Organization. The WHO defines EBF as consisting of no other food or drink, not even water, except breastmilk.

Study follow-up durations ranged from one to six months. Nineteen studies were included in the SR; 16 were included in the MA. Those not included in the MA reported findings outside those identified for inclusion criteria and included outcomes at 6 weeks, RR 1.73 [95% CI 0.88 – 3.37] (102), two months, RR 0.98 [95% CI 0.80 – 1.20] (103) and three months, RR 1.30 [95% CI 1.07 – 1.59] (104). Of the 16 studies included in the MA, four reported EBF outcomes at all three timeframes (105–108). At one month, seven studies reported significant results favouring virtual lactation support (N=7/9). RRs ranged from 1.13 [95% CI 1.01 – 1.26] - 1.80 [95% CI 1.29 – 2.51] (105,107–112). At four months one RCT found significant increases in EBF (N = 1/6), RR 2.14 [95% CI 1.62 – 2.83] (105). At six months investigators of most studies found no increase in EBF due to virtual lactation support (n=7/10). For those investigators who reported significant increases in EBF at six months, RRs ranged from 4.67 [95% CI 2.45 – 8.89] to 19.55 [95% CI 7.39 – 51.70] (105,113,114). Summary statistics for each time frame are outlined in Table 5.3

Table 5.3. Meta-Analysis Comparing Intervention and Control Groups

Outcome	*n* (%)	Intervention Group		Control Group		Pooled RR [95% CI]	*p*
		Events	Total	Events	Total		
EBF at 1 month	8 (42.1)	802	1182	657	1175	1.21 [95% CI, 1.09 - 1.35]	< 0.001
EBF at 4 months	6 (31.6)	347	640	297	654	1.18 [95% CI, 0.94 - 1.49]	0.150
EBF at 6 months	10 (52.6)	966	2017	579	2039	1.87 [95% CI, 1.30 - 2.68]	< 0.001

Note. EBF = Exclusive Breastfeeding.

5.3.2 Synthesis of Results

In total, the 16 RCTs included 5,254 participants (2630 in intervention groups, and 2624 in control groups) with sample sizes ranging from 77 to 1016. The results of the random-effects MA are presented in Figures 5.2.1, 5.2.2, and 5.2.3 (i.e., three time periods) as forest plots. The forest plot summary scores favour the intervention group (i.e., virtual lactation support) at one month and six months ($p<.05$) but not at four months. The characteristics of the included studies are summarized in Table 5.1 and 5.2.

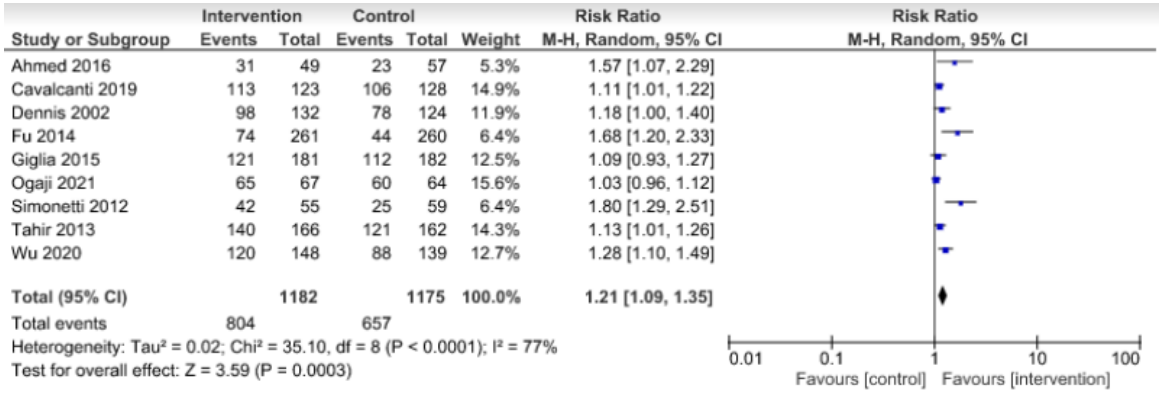

Figure 5.2.1 Forest Plot Examining Pooled RR for Exclusive Breastfeeding at 1 Month

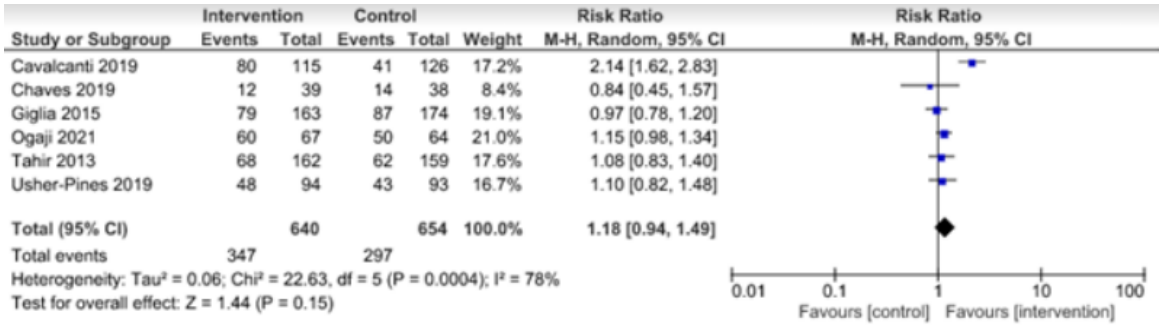

Figure 5.2.2 Forest Plot Examining Pooled RR for Exclusive Breastfeeding at 4 Months

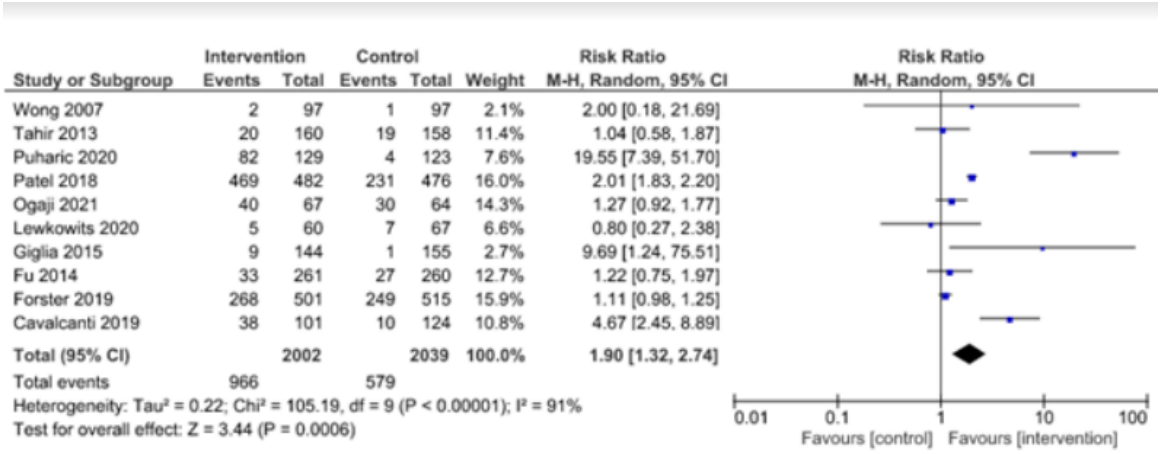

Figure 5.2.3 Forest Plot Examining Pooled RR for Exclusive Breastfeeding at 6 Months

5.3.2.1 EBF at six months

At six months, ten studies were included in the MA. The pooled estimate was significant (RR, 1.87 [95% CI, 1.30-2.68]; T^2 0.21, I^2 91%, $p < 0.001$) (Figure 5.2.3). Interventions included telephone calls (n=7), social media (n= 1), smartphone application (n= 1) and a combination of internet, e-mail, and web-conferencing (n=1). Contact was made with mothers weekly, bimonthly, monthly or through reactive intervention care. The majority of investigators (6/10) reported sustained contact with mothers for the entirety of the six-month period.

5.3.2.2 EBF at four months

At four months, six studies were included in the MA. The summary score was not in favor of virtual lactation support (RR, 1.18 [95% CI, 0.94 – 1.49]; T^2 0.06, I^2 78%, $p = 0.150$) (Figure 5.2.2). Interventions were delivered via telephone (n=3), social media (n=1), phone application (n=1) and a combination of internet, e-mail, and web-conferencing (n=1). Frequency of contact with mothers was reported as weekly

(n=1), bimonthly (n=2), through reaction intervention care (n=1), or was unreported (n= 2). At four months, five of the six RCTs reported no difference in EBF due to virtual lactation support. One RCT reported a significant finding, RR 2.14, [95% CI, 1.62 – 2.83] and also reported the highest frequency of contact compared to other studies (105).

5.3.2.3 EBF at one month

At one month, the summary score illustrates virtual lactation support increased rates of EBF by 20% (RR, 1.21 [95% CI, 1.09 – 1.35]; T^2 0.02, I^2 77%, p = < 0.001) (Figure 5.2.1). For the 9 studies included at one month, intervention types included follow up telephone calls (n=5), text messaging (n=1), internet/social media (n= 2) and a combination of internet, e-mail, and web-conferencing (n=1). Contact was made at varying time periods: weekly, bi-monthly, three times a week, or via reactive care (i.e., mothers initiating the intervention themselves). Larger RRs were reported in studies with a higher frequency of contact (109,111,112,115).

5.3.3 Sensitivity Analyses

A formal sensitivity analysis on RoB was not performed, as studies were categorized with a higher RoB due to lack of available information reported, therefore study authors would not want to break down pooled analyses based on RoB assessment. However, at six months, studies assessed as having a higher RoB and contributing significantly to the weight of the summary statistic were removed to determine the impact on summary score results. Based on our RoB assessment, 4/10 studies were assessed as having some concern or a high RoB. Of these four studies, two contributed a substantial amount of weight to the overall outcome; 32.1% (113,116). To determine the impact of

these two studies on the overall study results, we reran the MA removing these two studies. The summary score results remained significant, in favour of the intervention.

5.3.4 Risk of Bias within Studies

The RoB assessment for the included studies is presented in Table 5.4. Using the Cochrane RoB tool, 10/19 studies were assessed as having a low RoB, while four were assessed as having a high RoB and five studies were assessed as having some concerns with bias. Most high RoB studies lacked the necessary information to provide a RoB judgment. Primarily, a lack of information provided in the study and concerns were observed related to intervention assignment, appropriateness of outcome, missing outcome data, and selective reporting. The individual quality grading criteria of each study can be found in Appendix 4.4. The level of interrater agreement was 97% which was calculated based on percent agreement between raters (AB and BH). Each individual quality rating for the ROB-2 was reviewed, and an overall score was given based on the number of ratings in agreement.

Table 5.4. Quality rating of included studies based on the Revised Cochrane risk-of-bias tool for randomized trials (RoB 2)

Authors (Year)	Randomization Process	Deviation from Intended Interventions		Missing Outcome Data	Measurement of Outcome Data	Selection of Reported Result	Overall Bias
		Assignment	Adherence				
Dennis et al. (2002)	L	L	L	L	L	L	L
Wong et al. (2007)	H	H	L	L	SC	SC	H
Hoddinott et al. (2012)	L	SC	L	L	L	L	SC
Simonetti et al. (2012)	L	L	L	L	L	L	L
Tahir et al. (2013)	L	L	L	L	L	L	L
Fu et al. (2014)	L	L	L	L	L	L	L
Giglia et al. (2015)	SC	L	L	L	L	SC	H
Ahmed et al. (2016)	L	L	L	L	L	L	L
Maslowsky et al. (2016)	L	L	L	SC	L	SC	H

Ericson et al. (2018)	L	L	L	L	L	L	L
Patel et al. (2018)	L	H	SC	L	L	L	H
Chaves et al. (2019)	L	L	L	L	L	L	L
Cavalcanti et al. (2019)	L	L	L	L	L	L	SC
Forster et al. (2019)	L	L	L	L	SC	L	SC
Uscher-Pines et al. (2019)	L	L	L	L	L	L	L
Lewkowitz et al. (2020)	L	L	L	L	L	L	L
Puharic et al. (2020)	L	L	L	L	L	L	L
Wu et al. (2020)	L	L	L	SC	L	L	SC
Ogaji et al. (2021)	L	L	L	SC	L	L	SC

Note. Cochrane Risk of Bias Tool for Randomized Controlled Trials (RoB 2.0) was used. Scoring of L = Low risk; H = High risk; SC = Some concern was used by Higgins et al. (2016)

5.4 Discussion

With the increasing importance of and reliance on technologies in patient care and support and the inconsistencies in reporting of results, we sought to examine the association between virtual lactation support interventions and rates of EBF during the postpartum period through a MA. Several types of virtual care interventions were evaluated in the included studies (e.g., telephone, smartphone application, text messaging, internet), and were delivered by various providers (e.g., IBCLC, nurse, midwife, peer, automated system, researcher). Increased EBF rates were reported in a number of studies, however there were inconsistencies in study results (i.e., favoring the intervention, or showing no difference). Our primary finding is virtual lactation support significantly increased EBF rates to 6 months.

There are several findings to highlight. First, at six months, those receiving virtual lactation support were twice as likely to be EBF. Independent of decreasing rates of EBF in all studies over time, at six months the intervention compared to the control was effective at increasing EBF. Frequency of contact by a lactation support person appears to make a difference in rates of EBF, however it is unclear at this time as authors were unable to perform a subgroup analysis examining intervention frequency. There were four RCTs that reported outcome data at all three time points, with varying findings (105–108). In studies with findings favoring virtual care, contact was made with mothers on a weekly basis by an intervention researcher or IBCLC (105,106). In studies showing no significance, there was limited contact and follow up by a healthcare professional (monthly, and bimonthly) (107,108). Second, at one-month, early intervention with

virtual lactation supports increased rates of EBF by 20%. Third, although at four months, the overall summary score demonstrated increased EBF rates, the result was not significant. This may be explained by a fewer number of studies reporting outcome data at four months and reduced sample sizes in both the intervention and comparator groups. Of the ten studies included in the MA at 6 months, two contributed a significant amount of weight to the analysis (113,116). Both studies were assessed at having some concern or a high RoB. To determine the impact of these studies on the overall summary score, they were removed from the analysis. We therefore have comfort that our findings at six months are valid.

The three MAs exhibited a high level of heterogeneity for EBF outcomes. Due to the small number of studies meeting inclusion criteria, a high level of heterogeneity was anticipated (e.g, small number of studies at each time point, variability in type of intervention). Due to variability in intervention characteristics (type, duration, frequency of contact, and provider) it is clinical heterogeneity that is driving force for the high rate of statistical heterogeneity. Examination of the forest plots show that this is quantitative as opposed to qualitative heterogeneity. Despite the statistical heterogeneity, the results are similar from study to study, and study results were pooled regardless of heterogeneity.

The MA at six months provides evidence that is supported by published research on the effectiveness of ehealth lactation support for mothers (57), and further expand on previous SRs on virtual care interventions (58,59). Pate et al. (2009) found that mothers receiving internet-based lactation support were twice as likely to EBF (57). Almohanna (2020) identified the characteristics of successful internet-based interventions and

reported that interactions with mothers and the personalization of content were key factors in supporting breastfeeding women (58). Similarly, we found that studies with regular and sustained contact resulted in significant increases in rates of EBF. In a 2017 Cochrane review of support for breastfeeding mothers, study authors reported any form of extra support regardless of intervention or provider showed a decrease in early cessation of any breastfeeding (117). These findings highlight consistency of contact may matter more than the level of expertise in relation to continued duration of EBF.

Overall, our findings provide evidence that virtual lactation support compared to standard care increased the likelihood of EBF to six months. These findings may be relevant in the context of the COVID-19 pandemic where health care system have been faced with challenges regarding access to care. By demonstrating the effectiveness of virtual lactation support, scarce resources may be used more effectively to deliver support to breastfeeding mothers.

For future research, from a policy perspective a cost effectiveness analysis of virtual lactation support is needed to inform decision-making and resource prioritization and allocation. Most jurisdictions are challenged with meeting the recommendation of EBF to six months. Based on our current research demonstrating that virtual lactation support provided on a regular basis increase EBF up to six months, future studies could focus on the expansion of and development of virtual interventions to include additional functions such as real time web conferencing and or the use of facetime. Providing real time support to breastfeeding mothers with the addition of visual aids may result in greater rates of EBF to six months (58).

5.5 Limitations

This study has some limitations. There was some variability in the interventions delivered within these studies, which contributed to the level of statistical heterogeneity reported. The studies varied based on type of lactation support delivery (telephone, text messaging, smartphone application, internet, mixed media), frequency (weekly, bimonthly, monthly), intervention length (2-26 weeks), and provider (IBCLC, midwife, nurse, physician, peer, researcher, automated technology). Overall, the study results were presented in a number of different formats, however by collecting the prevalence of EBF in each group, it mitigated these differences. In most cases authors were reached and appropriate data and sample sizes obtained directly from the research team where needed. In addition, two groups of investigators measured EBF through the 24-hour recall method (i.e., mothers asked over the phone what type of milk their infant was currently receiving in the last 24 hours) which can overestimate the number of mothers exclusively breastfeeding (111,115). Due to the limited number of studies per outcome, no additional statistical measures (e.g., Fail Safe N) were used to assess publication bias. This is because when there are fewer studies, the power of the tests is too low to distinguish chance from real asymmetry, and additional tests have limited statistical power (97). The study authors had anticipated being able conduct subgroup analyses based on intervention delivery type, duration or frequency of contact. However, due to the lack of reporting of these details within the included RCT's a subgroup analysis was not performed. An additional limitation is the exclusion of unpublished data and gray literature, which might have introduced selection bias to this analysis.

5.6 Conclusions

This meta-analysis provides evidence that virtual lactation support compared to other postnatal maternity care increases exclusive breastfeeding up to six months. Our findings support an increased allocation of resources towards virtual lactation support for breastfeeding mothers.

5.7 Acknowledgments

I would like to acknowledge the Janeway Foundation for providing graduate student education funding for this research.

5.8 Conflict of Interest

The authors declare no potential conflicts of interest with respect to the research, authorship, or publication of this article.

Chapter 6: Summary

This chapter summarizes and discusses the main findings of this thesis. It provides study implications and policy recommendations based on my research findings, followed by recommendations for areas of future research.

6.1 Summary and Discussion

This dissertation aimed to explore the best practice interventions that enable a supportive breastfeeding environment within the Setting determinant of the Lancet Framework. It covers various topics and has generated four peer-reviewed, published manuscripts: 1) a systematic review and meta-analysis on the efficacy of Domperidone use as a galactagogue for mothers with insufficient human milk production; 2) a data linkage study examining the differences in healthcare service use and costs by infant feeding mode in an infant's first year of life; 3) a patient engagement study exploring the perceptions of mothers on the costs of infant feeding; and, 4) a systematic review and meta-analysis of the effectiveness of virtual lactation support for postpartum mothers.

In Chapter 2, I conducted an updated review of literature on the efficacy of Domperidone as a galactagogue compared to placebo when given to mothers with insufficient human milk production. A systematic review and meta-analysis were performed to synthesize and quantify the efficacy of Domperidone for women with infants born either pre- or full term experiencing insufficient human milk production and

to determine its impact on expressed human milk volume (EBMV). A total of 423 unique citations were screened initially, and seven studies met the inclusion criteria for review; two were excluded from the meta-analysis due to quality grading and insufficient reporting of the outcome of interest. Five studies with a total sample size of 239 were combined in the meta-analysis (MA). Using recently published, good quality RCTs, as defined by the US Preventive Services Task Force (USPSTF) Quality Rating Criteria, we found a significant increase in the effect size in EBMV at 93.97 mL (95% CI 71.12-116.83; random effects, T^2 0.00, I^2 0%, $p < 0.00001$). There was a significant effect size of Domperidone on increasing human milk production in puerperal women, when taken for ≤ 7 days or > 7 days duration. All studies included in the SRMA provided evidence consistent with past research showing Domperidone effectively increases EBMV by a modest amount. In this MA the effect size of 93.97 mL (MD) in EBMV may be enough to help mothers supply human milk to their infants to meet their nutritional needs for the first few weeks of life. Sub-analysis for the Domperidone groups shows there is no further EBMV increase with long-term Domperidone use, but the baseline dose of Domperidone may be necessary to maintain that modest increase from baseline level of human milk production. It is possible that increasing the dosage of Domperidone could help to increase the EBMV over time, but there have been no RCTs published to date that investigate an adaptive dose of Domperidone. Furthermore, a growing infant has an increasing need for human milk as the infant's feeding requirements also increase with age. Despite no indication of heterogeneity among the studies, the included studies occurred in different countries, had different follow-up periods, and included different methods of infant delivery with pregnancies of viable gestations. This suggests that at the

dose range of 30 mg to 40 mg, Domperidone is consistent in increasing the EBMV by the MD effect size, regardless of the possible differences in population and study methods. It is likely that Domperidone can be used in different populations with the same effectiveness. The sustained effects of Domperidone on EBMV overtime are yet to be researched. There is no clarity on the safety of Domperidone for patients with possible underlying cardiac arrhythmias.

In Chapter 3, I examined the relationship between infant feeding mode (IFM) and healthcare service use costs (HSU) during an infant's first year of life. Data on 160 infants collected from the *Feeding infants in Newfoundland and Labrador* (FiNaL) prospective cohort study were linked using the infant's health insurance number provided by the mother with administrative databases provided by the NL Centre for Health Information (NLCHI) to examine HSU and related costs by IFM. Overall, the majority of infants were seen by family doctors, specialists and the emergency room (ER) at least once during their first year. Cumulative HSU cost (including cost of birth) in the first year of life for all healthy full-term infants in one provincial region in Canada was $315,235. The highest percentage spent on HSU was for hospital admissions, followed by family doctor, ER and specialist visits. Higher HSU costs were associated with EFF infants when examining hospitalizations (birth and admissions), and significant differences were found between IFM when examining the total costs associated with HSU during the first year of life. Previous research in Canada on the effects of breastfeeding in infants has shown substantial protective benefits against childhood diseases (74,79) and that breastfeeding promotion programs are a critical intervention. Estimation of healthcare services use and

related cost is necessary for developing cost-effective interventions to improve breastfeeding rates. This information could help policymakers develop educational policies and breastfeeding support programs. An integrated provincial breastfeeding program should include training programs, communications for health promotion at a population level, political will and legislation, advocacy, evaluation research and appropriate funding to achieve desired rates of breastfeeding.

In Chapter 4, I used the guiding principles of patient-oriented research (POR) to conduct patient engagement sessions and gain insights on the perceptions of mothers on the cost associated with infant feeding. Patient Engagement (PE) sessions were designed in a two-hour format, which allowed for introductions, presentations of background information on infant feeding and a brief review of the literature examining the economic impact of infant feeding. A total of 26 mothers and 18 infants (16 singleton, 1 set of twins) were engaged during our PE sessions. The majority of mothers were Caucasian, married or common law, between 26 – 34 years of age, with a university degree or diploma, and accessing care in the Eastern Health region of Newfoundland and Labrador. Using the guiding principles of POR, PE sessions were planned and successfully conducted to explore and better understand the costs of infant feeding from a mothers' perspective. Following the principles of patient engagement helped to ensure the success of our sessions. Our PE sessions included a range of perspectives and experiences (i.e., inclusiveness), and mothers that felt sufficiently supported to meaningfully contribute to the discussion (i.e., support). The structure of the sessions allowed us to include various levels of involvement (i.e., flexibility), where mothers noted they were acknowledged and

valued and were able to engage and provide input at the level of their comfort (i.e., mutual respect). During each session, evaluations were provided to solicit feedback on whether the goals and expectations of mothers had been met, and whether they felt their opinions were heard and understood (i.e., responsive). Engaging mothers with lived experience brought to our attention constructs that captured a more holistic view of the costs of infant feeding than may typically be considered or measured in cost analysis studies. The outcomes identified by mothers illustrate the value of using POR in engaging those with lived experience. The three broad categories that were discussed included costs of infant feeding, impact on workplace productivity and environmental impact. The PE sessions allowed us to explore in depth how women perceived these categories of costs, further elucidating the types of costs that would fall under these categories. For example, the costs on infant feeding included discussions on the incidentals of breast or formula feeding (e.g., nipple creams, bottles, bottle warmers), discussions around workplace productivity (e.g., perceived productivity, needing additional breaks related to feeding, time off), and discussions around environmental impacts (e.g., single use plastics, breast pads, ready-made formula). Interestingly, in the sessions there were conversations amongst mothers around the opportunity costs associated with infant feeding (e.g., cost of mothers' time (time spent feeding, cleaning/preparing bottles, outsourcing guidance, and support), the cost of inaccessibility of healthcare providers and support when establishing infant feeding mode). In all PE sessions, independent of discussions around costs, all mothers reported the need for more information, knowledge and support related to infant feeding, whether infants were breast or formula fed. Due to limited support around infant feeding, mothers discussed the additional time, effort and costs spent looking for

information and support while establishing breast or formula feeding (e.g., Information on breast-pumping or preparing formula, paying for private lactation consultants). Referencing the critical role that healthcare providers can play during the stages of mothers establishing infant feeding (i.e., Lactation Consultants, Public Health Nurses, General Practitioners, and specialists). POR has highlighted the value of incorporating patients' ideas, priorities, and experiences in health research. By conducting PE sessions, informed by patient-oriented research guiding principles, we were able to successfully recruit and engage mothers in discussions that led to a better understanding of their perspectives on the costs of infant feeding.

In chapter 5, I evaluated the effectiveness of virtual lactation support for postpartum mothers. The aims of this project were twofold. The first aim was to conduct a systematic review of randomized controlled trials designed to test the efficacy of virtual lactation support for postpartum mothers on rates of exclusive breastfeeding up to six months, and the second aim was to conduct a meta-analysis of studies meeting the selection criteria for the systematic review. A total of 3391 records were screened; 148 full texts were reviewed, and 19 randomized control trials met inclusion criteria. Of the 19, 16 studies were included in the meta-analysis (n =5,254). Virtual lactation support was found to be effective at increasing EBF at one month (RR, 1.21 [95% CI, 1.09-1.35]; $p < 0.001$) and six months (RR, 1.87 [95% CI, 1.30-2.68]; $p < 0.001$). In this meta-analysis of randomized controlled trials RCT's comparing virtual lactation support with other postnatal maternity care, virtual lactation support was associated with increasing EBF rates at one month and six months postpartum. Several types of virtual

care interventions were evaluated in the included studies (e.g., telephone, smartphone application, text messaging, internet), and were delivered by various providers (e.g., IBCLC, nurse, midwife, peer, automated system, researcher). The MA at six months provides evidence supported by published research on the effectiveness of ehealth lactation support for mothers (57), and further expands on previous SRs on virtual care interventions (58,59). Pate et al. (2009) found that mothers receiving internet-based lactation support were twice as likely to EBF (57). Almohanna (2020) identified the characteristics of successful internet-based interventions and reported that interactions with mothers and the personalization of content were key factors in supporting breastfeeding women (58). Similarly, we found studies with regular and sustained contact resulted in significant increases in rates of EBF. In a 2017 Cochrane review of support for breastfeeding mothers, study authors reported any form of extra support regardless of type of intervention or type of provider showed a decrease in early cessation of any breastfeeding (117). These findings support that consistency of contact may be more important the level of expertise in relation to continued duration of EBF. Overall, our findings provide evidence that virtual lactation support compared to standard care increased the likelihood of EBF to six months. In the context of the COVID-19 pandemic and its impact on health care systems and ability to access health care providers, these findings may be relevant. By demonstrating the effectiveness of virtual lactation support, scarce resources may be used more effectively to deliver support to breastfeeding mothers.

6.2 Implications of Study Findings

The body of evidence on the health and economic benefits of breastfeeding continues to increase. Implementing evidence-based interventions to support EBF have the potential to protect, promote and support breastfeeding and will increase rates of EBF. This doctoral research adds to the body of literature by examining best practice interventions to support breastfeeding through Policy, Health System and Community level interventions.

6.2.1 Policy Recommendations

Creating an environment that protects, promotes and supports breastfeeding involves a multi-dimensional approach, encompassing efforts from Structural, Setting and Individual levels. A number of policy recommendations directed at the Setting determinant follow from my research findings. Parents within our communities should have access to a seamless system of breastfeeding support services as they transition from hospital to home and to community. Based on the series of interconnected journal articles within this thesis, I have summarized interventions needed to improve breastfeeding practices within our province.

6.2.2 System Level

There are several ways in which the government of Newfoundland and Labrador can enhance an environment that enables breastfeeding at a system level. Policies should be put in place to ensure all maternity healthcare services comply with the WHO Code of regulating the marketing of breastmilk substitutes, as well as achieve the Baby Friendly Hospital Initiative designation. By enhancing the hospital environment, mothers are more

likely to receive the critical support and best-practice health care when starting their breastfeeding journey.

Within our health systems, if properly trained and knowledgeable in the management of breastfeeding, healthcare professionals can enhance and support the establishment and continuation of breastfeeding. As outlined in Chapter Two, a challenge sometimes faced by mothers is difficulties with milk supply. Several interventions can be used to increase human milk volume (e.g., hand expression, breast pump, feeding on demand) and our SRMA further demonstrates the efficacy of a pharmacological galactagogue (e.g., Domperidone). Further training in these interventions can help with exclusive and continued breastfeeding if challenges with milk production occur. Importantly, within the maternity healthcare services, healthcare professionals should be highly trained to explore the reasoning for challenges with milk production and provide education and support towards establishing milk supply prior to starting pharmaceuticals. Overall, to properly support families, healthcare providers must be available to assist with infant feeding during the early hours of birth and have the knowledge and skills to support continued breastfeeding. Notably, where resources are scarce and limited, and mothers may not have access to additional resources associated with establishing supply and breastfeeding practices, the accessibility and availability of Domperidone may be what helps kickstart a mother's breastfeeding journey, providing them with an increase in supply and the ability to continue onward and establish breastfeeding.

In Chapter Three, a pilot study in one region of Canada, showed that exclusive formula feeding, and mixed feeding were found to be significant predictors of the total

healthcare service use costs during an infant's first year of life. This pilot study allowed for the exploration of the feasibility of examining the association of infant feeding mode and the costs associated with healthcare use in this local population. By exploring the available data future studies with larger sample sizes and longer exposure data can further explore this relationship. By demonstrating the associated healthcare use and costs associated with not breastfeeding, development of policies and programs that support and encourage breastfeeding should be a priority. This includes better understanding and increasing women's options for care during labour and delivery (i.e., birthing centres, increasing availability of midwifery-led care, skin to skin options following cesarean section).

In Chapter Four, through the patient engagement sessions that followed the healthcare service use study, mothers were engaged to discuss their perceptions on the costs of infant feeding. The aim of this study was to outline outcomes that could be considered in future costing studies including a mother's perspective, however it continued to highlight the disparities in our system. Outlining the need for enhanced support in existing programs, and the necessity for more education surrounding infant feeding. This can be achieved by continuing to allocate resources and support both financially and through hired personnel (i.e., The Baby Friendly-Council of Newfoundland and Labrador).

Chapter Five provided evidence that virtual lactation support increases the likelihood of exclusive breastfeeding to 6 months. By demonstrating the effectiveness of virtual lactation support, scarce resources within healthcare and community settings may

be used more effectively to deliver support to breastfeeding mothers. With an increase in and reliance on technology in healthcare, this would provide an additional avenue to provide greater accessibility of support. From a policy perspective, future research would include a cost effectiveness analysis of virtual lactation support to inform decision making around the policies for resource prioritization and allocation.

Lastly, public awareness and social acceptability of breastfeeding in public can also support breastfeeding within our health system, workplaces and community and should be encouraged at a system level through established policies (i.e., through advertisements, social media, promoting baby-friendly spaces for parents).

Higher rates of exclusive breastfeeding can be achieved by investing in best practice interventions, and improving policies and programs that promote, protect and support breastfeeding. Investing in breastfeeding promotion interventions will allow for investment in improved health outcomes, healthcare prevention, and supported communities.

6.3 Strengths and Limitations

6.3.1 Strengths

Various methods were used to investigate a number of interventions that support breastfeeding mothers. Following the Lancet Framework and exploring interventions that can enable the Setting determinants to support breastfeeding were critical in guiding the research in this dissertation. By using meta-analyses, data linkage cost analysis and patient-oriented research, a wide scope of methodology provided a rich evidence-base for

furthering research on the best practice interventions. The strengths of each study will be described below, with further details in the respective chapters.

There are several strengths to the meta-analyses conducted in this thesis. Both were conducted with a narrow focus of the research question, with a clear inclusion and exclusion criteria. Strong search strategies were built with the help of medical research librarians, which allowed for transparent and comprehensive search strategies. Multiple reviewers were used during the project stages of both reviews, where study selection, data abstraction, risk of bias assessment and data synthesis were all completed independently by two reviewers at all stages to minimize bias. Lastly, the PRISMA reporting guidelines were used throughout both analyses, which ensure consistency in reporting, demonstrate quality of the review and allows for replication of methodology.

Strengths of the data linkage healthcare service use study include the following. To my knowledge, this was the first estimate of healthcare service use costs associated with infant feeding mode of a sample of full-term healthy infants living in Canada. By linking HSU data to specific characteristics collected from the *Feeding Infants in Newfoundland and Labrador* (FiNaL) prospective cohort study we were able to control for various covariates in the analysis (i.e., mother's parity, type of delivery, residence). In addition, using administrative data allowed for the calculation of individual level costs and the direct costs associated with HSU through the claims of family doctors and specialists. This pilot study, also allowed for an assessment of the feasibility of collecting data in a Canadian context and estimate variability in outcomes to help determine sample size required for future larger provincial studies.

There are also several strengths associated with the use of patient-oriented research, and the patient engagement sessions that were conducted to assess the perceptions of mothers. Connecting the research team with a community organization was a key component to our successful patient engagement. Engaging as researchers in a community Setting led to active engagement and collaboration in a Setting that was welcoming to those in attendance. Throughout each session, information on the topics discussed was compiled in various formats (audio recording, written notes, evaluation forms). This allowed the team members to better understand mothers' responses and identify any additional outcomes to be further discussed during patient engagement sessions. Lastly, by preparing for the time and resources required to uphold patient engagement sessions, the team ensured mothers remained informed, involved, and updated at several project stages.

6.3.2 Limitations

Several limitations have been identified. The limitations of each study will be described below, with further details in the respective chapters.

The SRMA on the use of Domperidone as a galactagogue has limitations. This review lacked a registered protocol, and the Peer Review of Electronic Search Strategies (PRESS) guidelines were not followed. Though backwards citation tracking was used to search for additional relevant articles, forward citation tracking was not explored In healthy mothers described in these studies, there were very minimal side effects reported; importantly as stated by Health Canada, Domperidone should not be used in women at risk for arrhythmias. Only two studies reported on the side effects of Domperidone, only

one of which reported on cardiac events. Within the included studies, mothers had self-reported insufficient milk supply. It is important to note that it is unclear whether this is actual or perceived insufficient milk production. In addition, due to including studies with preterm and full-term infants, and mothers giving birth both vaginally and through caesarean section delivery, this may provide varied challenges associated with milk production and issues with supply. There were some methodological inconsistencies between the studies, which should be considered when generalizing the study results. One of the included studies used a higher dose of Domperidone compared to the other studies. It did not affect the heterogeneity and did not seem to significantly impact the effect size but is an inconsistency in the data that should be considered. Lastly, with small sample sizes and few included studies, this limits the generalizability of findings.

The data linkage healthcare service use study also had limitations. Our results are based on a relatively small sample size (n = 163), where the subsample of the FiNaL Study had a selection bias of primiparous, Caucasian, higher education, and household income mothers, which impacts its generalizability. We found differences among groups for the total costs of HSU, driven mainly by hospitalizations including costs of birth, however significant differences were not observed when examining the costs associated with other healthcare services (i.e., ER, Physician visits). Including cost of birth may have introduced several confounders that we were unable to control for, though delivery type was adjusted for within our multivariable analysis. In addition, the medicalization of birth may be what is driving the associated costs. In terms of not seeing a significant difference amongst other types of individual HSU (i.e., ER or Physician visits), this could be

explained by either having no differences among groups, or that the study was underpowered to examine the differences of ER and physician visits.. Due to challenges with collecting exposure data on feeding mode and its duration, our mixed feeding and exclusive formula feeding covered the first 6 months of life, but our exclusive breastfeeding rate was considered valid and reliable for the first month only. The data on exposure were self-reported by mothers and therefore could result in misclassification. Based on the health insurance claims in the province of Newfoundland and Labrador, the administrative databases can only collect information on fee-for-service physicians. There are a proportion of family doctors and pediatricians that are salaried that we did not have HSU on, therefore this an underestimate of the use and cost experienced in this region. In addition, although we used a health systems perspective to examine the costs, not all costs were included (i.e., medications).

The conducted patient engagement sessions have their limitations, based on funding, timing and recruitment. Due to the small numbers engaged throughout these sessions, there is a possible underrepresentation of individuals falling in different socio-demographics, as well as a bias that may present itself in smaller group sessions. To the nature of obtaining a convenience sample, the sessions took place with a well-educated homogenous group, which impacts its generalizability. Notably, with additional sessions there is potential for additional emerging topics and key priorities for future studies to arise. At the end of each session printed evaluations were circulated to mothers. We found additional incentives were needed regarding obtaining session

feedback in this format. In future sessions we would ensure that the evaluation is in a format that is more easily complete (e.g., verbal discussion vs. printed survey).

Lastly, the SRMA on the effectiveness of virtual lactation support has limitations. There was some variability in the interventions delivered within these studies, which contributed to the level of statistical heterogeneity reported. The studies varied based on type of lactation support delivery, frequency, intervention length, and provider. Overall, the study results were presented in a number of different formats; however, by collecting the prevalence of exclusive breastfeeding in each group, it may have mitigated these differences. Definitions of exclusive breastfeeding did vary among reviewed articles. In most cases authors were reached and appropriate data and sample sizes obtained directly from the research team. In addition, two groups of investigators measured exclusive breastfeeding through the 24-hr recall method, which can overestimate the number of participants exclusively breastfeeding. Due to the limited number of studies per outcome, no additional statistical measures (e.g., Fail Safe N) were used to assess publication bias. The study authors had anticipated being able conduct subgroup analyses based on intervention delivery type, duration, or frequency of contact. However, due to the lack of reporting of these details within the included RCT's a subgroup analysis was not performed. An additional limitation was the exclusion of unpublished data and gray literature, which might have introduced selection bias to this analysis.

6.4 Areas of future research

My dissertation has further identified several research questions for future studies. These are described below. Additional broader research questions are outlined at the end.

6.4.1 Human Milk Expression After Domperidone Treatment in Postpartum Women: A Systematic Review and Meta-Analysis of Randomized Controlled Trials

Current research supports the effectiveness of Domperidone as a galactagogue, in increasing human milk production in puerperal women, when taken for ≤ 7 days or > 7 days duration. There is a need for more studies evaluating the safety of Domperidone, as well as those examining higher dosages. Phase 2 and 3 clinical trials focusing on adverse events of Domperidone should be prioritized to provide more information about the safety and side effects of this drug. By further exploring its safety, it could warrant a move towards removing the restrictions for Domperidone, allowing it to be prescribed as a galactagogue instead of using it off-label. Additional Phase 2 clinical trials on dose ranging are needed, as real-life clinical practice shows that physicians typically prescribe higher doses to patients (37). Additional research is warranted to examine if an adequate supply of EBMV is sustained if the patient stops taking Domperidone.

6.4.2 Infant Feeding Mode Predicts the Costs of Healthcare Services in One Region of Canada: a Data Linkage Study

Expanded research is needed in the Canadian context to examine the association between infant feeding mode and healthcare service use and costs. Future research should examine larger samples to further investigate differences in the costs associated with HSU and use more reliable and valid measures of exposure to capture longer durations of EBF. Additionally, including other perspectives (population health and economic perspectives)

than the healthcare system perspective would provide further insights into the benefits associated with increasing exclusive breastfeeding initiation and duration.

6.4.3 The use of PE to gather perceptions on the cost of infant feeding

The intent of this PE initiative was to further outline research questions and outcomes to be considered in future cost analyses performed using a mothers' perspective. Various topics and emerging themes were outlined through PE sessions. This includes cost of incidentals; cost of wait times, access to care and available supports; cost of returning to work, and workplace productivity; and cost surrounding the environmental impact of infant feeding. The PE sessions demonstrate how a broader approach to measurement should be considered when undergoing a cost analysis from a mother's perspective. Future research should consider conducting a cost analysis from a mothers' perspective, which would provide a greater scope of costs incurred by mothers and families, by including outcomes that are of importance to them.

6.4.4 The effectiveness of virtual lactation support for breastfeeding mothers: a systematic review and meta-analysis of randomized controlled trials

This review aimed at examining the effectiveness of virtual lactation support. For future research, from a policy perspective a cost effectiveness analysis of virtual lactation support is needed to inform decision-making and resource prioritization and allocation. Most jurisdictions are challenged with meeting the recommendation of EBF to six months. Based on our current research demonstrating that virtual lactation support provided on a regular basis increases EBF to six months, future studies could focus on the

expansion of and development of virtual interventions to include additional functions such as real time web conferencing and or the use of facetime. Providing real time support to breastfeeding mothers with the addition of visual aids may result in greater rates of EBF to six months.

6.4.5 General Areas for Future Research

While I have outlined recommendations for future research that are specific to each study, there are other research questions that can be addressed in future studies. From a policy standpoint, it is important to further examine costs associated with healthcare service use, and a larger scale provincial linkage study is warranted to look at longer term breastfeeding and health outcomes in the Canadian context. In addition, there are various additional interventions (e.g., pre and post-natal education, 1-on-1 lactation support) that could be examined from a cost effectiveness perspective, allowing policy makers to consider the reallocation of costs for enhanced health outcomes.

6.5 Conclusion

My thesis has used diverse research methods, including systematic reviews and meta-analyses, cost analyses, and patient-oriented research to pool evidence on the interventions that can enable an environment that supports breastfeeding. These studies provided evidence on the efficacy of Domperidone as a galactagogue for breastfeeding mothers, the effectiveness of virtual lactation support for postpartum mothers, and the costs surrounding infant feeding mode and healthcare service use, from a healthcare and maternal perspective. The patient engagement research also provides guidance to future

research examining the costs of infant feeding from a mother's perspective. Each chapter of this thesis is associated with evidence-based interventions that have the potential to support breastfeeding and will increase rates of EBF. Comprehensive, multi-sector strategies that support breastfeeding mothers require policies and practices that promote, protect and support breastfeeding at the Structural, Setting and Individual levels.

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Appendix 1.1: Summary of evidence table associated with the health benefits of breastfeeding

Mother/ Infant	Outcome Examined	Studies of Evidence	Lactation Status/ (Disease Onset)	Risk Measure	Disease risk change associated with breastfeeding compared with formula feeding [95% CI]
Infant	Gastroenteritis	Duijts et al., 2010	EBF 4m, continued BF to 6 m (Before 1st year)	Adjusted Odds Ratio	0.41 [CI: 0.26-0.64]
Infant	Upper and Lower RTI	Duijts et al., 2010	EBF 4m, continued BF to 6 m	Adjusted Odds Ratio	0.65 [CI: 0.51-0.83] 0.50 [CI: 0.32-0.79]
	Lower Respiratory Tract Infection (requiring hospitalization)	Ip et al., 2007(AHRQ report)	EBF less than 4m	Risk Reduction	72% RR in hospitalization
Infant	Acute Otitis Media	Ip et al., 2007(AHRQ report)	Ever BF vs FF EBF vs EFF	Pooled adjusted Odds Ratio	0.77 [CI: 0.64 – 0.91] 0.50 [CI: 0.36 – 0.70]
Infant	Leukemia	Amitay & Keinan‐Boker 2015	Any BF less than 6m	Odds Ratio	0.82 [CI: 0.73 – 0.93]

	(Acute lymphoblastic leukemia)		(before 20th year)		
Infant	Childhood Obesity	Grummer Strawn, Yan or Horta (SRMAs)	Any BF 6-12m	Pooled adjusted odds ratio	0.70 [CI: 0.50 - 0.99]
			Any BF 12m +		0.49 [CI: 0.25 - 0.95]
			(Prior to 5th year)		
Infant	Necrotizing Enterocolitis	Colaizy et al.,2016	Partial BF prior 3m	Adjusted Odds Ratio	500-1000g or 1000-1500g
			EBF to 3m		0.72 [CI: 0.43 - 1.21]
			(before child turn 36 weeks post menstrual gestational age)		0.083 [CI: 0.0106 - 0.65]
Infant	Sudden Infant Death Syndrome	Thompson 2017	<2m was not protective	Adjudted Odds Ratio	2-4m 0.60 [CI: 0.44 – 0.82]
			>2m and beyond was protective		4-6m 0.40 [CI: 0.26 – 0.63]
			(Death before 1 y)		>6 m 0.36 [CI: 0.22 - 0.61]
Infant	Type 2 Diabetes	Horta et al., 2019	Ever BF vs FF	Pooled Odds Ratio	0.67 [CI: 0.56 - 0.80]
Infant	Chrohns/ Ulcerative Colitis	Klement et al.,2004	Disease onset had to occur before child turned 20 years. Incidence between ages 18–20 years was equal to ages 15-17years	Pooled Odds Ratio	0.45 [CI: 0.26 - 0.79] (Chrons) 0.56 [CI: 0.38 - 0.81] (UC)

Mother	Breast Cancer	Unar Munguia 2017	Per Year (Any BF) (maximum of 48 months of lifetime lactation)	Risk Reduction	0.72 [CI: 0.58 - 0.90]
					0.72 [CI: 0.58 - 0.90]
Mother	Ovarian Cancer	Danforth et al.,2007	Risk reduction limited to a maximum of 18m of lifetime lactation. Disease onset had to occur before mother turned 51	Relative Risk	>18m lactation 0.66 [CI: 0.46 - 0.96]
					12–17 months lifetime any lactation 0.82 [CI: 0.54 - 1.24]
					7–11 months lifetime any lactation 0.76 [CI: 0.52 - 1.11]
					1–6 months lifetime any lactation 0.96 [CI: 0.76 - 1.21]
					Never lactated 1.0 (Referent)
Mother	Type 2 Diabetes	Stuebe et al,2005	limited to a maximum of 24 months of lifetime lactation. Disease onset was limited to 15 years after mothers last birth	Hazard Ratio	>23 months lifetime any Lactation 0.53 [CI: 0.40 - 0.70]
					11–23 months lifetime any Lactation 0.76 [CI: 0.59 - 0.98]
					>6–11 months lifetime any Lactation 0.76 [CI: 0.58 - 0.99]
					3–6 months lifetime any Lactation 0.78 [CI: 0.57 - 1.06]
					0–3 months lifetime any Lactation 1.03 [CI: 0.80 - 1.35]

					Never lactated 1.0 (Referent)
Mother	Hypertension	Stuebe et al.,2011	Limited to maximum of 4 births	Hazard Ratio	12 months or more of any lactation per birth 1.0 (Referent)
					9 to less than 12 months of any lactation per birth 1.07 [CI: 0.99 - 1.17]
					6 to less than 9 months of any lactation per birth 1.09 [CI: 1.02 -1.18]
					More than 3 to less than 6 months of any lactation per birth 1.19 [CI: 1.11 - 1.28]
					More than 0 to 3 months of any lactation per birth 1.21 [CI: 1.12 - 1.30]
					Never lactated 1.22 [CI: 1.13 - 1.32]
Mother	MI (Myocardial Infarction)	Stuebe et al. 2009	limited to a maximum of 24 months of lifetime lactation. Disease onset was limited to 30 years after mothers last birth	Hazard Ratio	>23 months lifetime any lactation 0.66 [CI: 0.49 - 0.89]
					11–23 months lifetime any lactaion 0.89 [CI: 0.71 - 1.1]
					>6–11 months lifetime any lactation 0.96 [CI: 0.76 - 1.21]

					3–6 months lifetime any lactation 0.98 [CI: 0.8 - 1.21]
					0–3 months lifetime any lactation 0.94 [CI: 0.79 - 1.12]
					Never lactated 1.0 (Referent)

Appendix 2.1: PRISMA (2009) Checklist

Section/topic	#	Checklist item	Reported on page #
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	2.0
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	2.0
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	2.1
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	2.2
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	NA
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	2.3.1
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	Appendix
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	2.3.1
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	2.3.2

Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	2.3.3
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	2.3.3
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	2.3.4
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	2.3.5
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis.	2.3.5

Section/topic	#	Checklist item	Reported on page #
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	2.3.4
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	2.3.6
RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	Figure 2.1
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	Table 2.1
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	2.4.3
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	2.4.4
Synthesis of results	2	Present results of each meta-analysis done, including confidence intervals and measures of	2.4.5

	1	consistency.	
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	2.4.6
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	2.4.7
DISCUSSION			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	2.5
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	2.5.1
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	2.6
FUNDING			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	2.7

From: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 6(7): e1000097. doi:10.1371/journal.pmed1000097

For more information, visit: **www.prisma-statement.org**.

Appendix 2.2: Expanded Search Strings (Pubmed, Embase & CINAHL)

The Pubmed search strategy included the following terms: ("milk, human"[Mesh] OR "Milk Ejection"[Mesh] OR "Breast Feeding"[Mesh] OR breastfeeding OR "breast milk" OR "breast milk expression" OR "mother's milk" OR "breast milk production" OR lactation OR "Lactation"[Mesh] OR "milk ejection" OR "milk expression") AND ("Domperidone"[Mesh] OR domperidon* OR "Galactagogues"[Mesh] OR galactagogue*).

This search strategy produced 177 articles.

The Embase search strategy included the following terms: ('breast feeding'/exp OR 'milk ejection'/exp OR 'lactation'/exp OR 'breast milk'/exp OR breastfeeding OR 'breast feeding' OR 'breast milk' OR 'mothers milk' OR lactation OR 'milk ejection' OR 'milk expression') AND ('Domperidone'/exp OR Domperidone OR 'galactagogue'/exp OR galactagogue*).

This search strategy produced 344 articles.

Lastly, CINAHL included the following terms: ("human milk" OR "milk ejection" OR "breast feeding" OR "breastfeeding" OR "breast milk" OR "breast milk expression" OR "mother's milk" OR "breast milk production" OR lactation OR "milk ejection" OR "milk expression" OR (MH "Breast Feeding") OR (MH "Milk Expression") OR (MH "Milk, Human") OR (MH "Lactation")) AND ("Domperidone" OR domperidon* OR "Galactagogues" OR galactagogue*). This search strategy produced 73 articles.

Appendix 2.3: Formulas used to calculate and impute Mean Difference (MD) and Standard Deviation (SD)

Formula Used to Calculate Mean Difference

$$Mpost - Mpre$$

M pre: Mean Expressed Breast Milk Volume (baseline)

M post: Mean Expressed Breast Milk Volume (final)

Formula Used to Impute Standard Deviation

$$\sqrt{\frac{(\frac{SDpre}{Npre})^2 + (\frac{SDpost}{Npost})^2}{2}} \times \sqrt{Npost}$$

SD pre: The baseline standard deviation

N: corresponding number of participants (baseline)

SD post: The final standard deviation

N: corresponding number of participants (final)

Appendix 3.1: Ethics approval letter

Ethics Office

Suite 200, Eastern Trust Building
95 Bonaventure Avenue
St. John's, NL
A1B 2X5

October 27, 2017

Faculty of Medicine
Discipline of Epidemiology

Dear Miss Taylor:

Researcher Portal File # 20180871
Reference # 2017.226

RE: "Infant feeding and its impact on health care services use in infants for the first year of life in the Eastern Health Region of Newfoundland and Labrador"

Your application received a delegated review by a sub-committee of the Health Research Ethics Board (HREB). ***Full approval*** of this research study is granted for one year effective **October 26, 2017**.

This is your ethics approval only. Organizational approval may also be required. It is your responsibility to seek the necessary organizational approval from the Regional Health Authority (RHA) or other organization as appropriate. You can refer to the HREA website for further guidance on organizational approvals.

This is to confirm that the HREB reviewed and approved or acknowledged the following documents (as indicated):

- Application, approved,
- Letter of request
- List of variables

This approval will lapse on October 26, 2018 . It is your responsibility to ensure that the Ethics Renewal form is submitted prior to the renewal date; you may not receive a reminder. The Ethics Renewal form can be found on the Researcher Portal as an Event form.

If you do not return the completed Ethics Renewal form prior to date of renewal:

- ***You will no longer have ethics approval***
- *You will be required to stop research activity immediately*
- *You may not be permitted to restart the study until you reapply for and receive approval to undertake the study again*
- *Lapse in ethics approval **may result in interruption or termination of funding*** **You are solely responsible for providing a copy of this letter**, along with your approved HREB application form; **to Research Grant and Contract Services** should your research depend on funding administered through that office.

Modifications of the protocol/consent are not permitted without prior approval from the HREB. **Implementing changes without HREB approval may result in your ethics approval being revoked, meaning your research must stop**. Request for modification to the protocol/consent must be outlined on an amendment form (available on the Researcher Portal website as an Event form) and submitted to the HREB for review.

The HREB operates according to the Tri-Council Policy Statement: Ethical Conduct for Research Involving Humans (TCPS2), the Health Research Ethics Authority Act (HREA Act) and applicable laws and regulations.

You are responsible for the ethical conduct of this research, notwithstanding the approval of the HREB.

We wish you every success with your study.

Sincerely,

Ms. Patricia Grainger (Chair, Non-Clinical Trials Health Research Ethics Board) Dr. Joy Maddigan (Vice-Chair, Non-Clinical Trials Health Research Ethics Board)

CC: Dr. Laurie Twells
Dr. Leigh Anne Newhook

Appendix 3.2: NLCHI Data Sharing Approval from Secondary Use Committee

Newfoundland & Labrador Centre for Health Information

June 5, 2018

Alicia Taylor
Faculty of Medicine
Memorial University

Dear Ms. Taylor:

RE: Infant Feeding and its impact on health care services use in infants for the first year of life in Eastern Health Region of Newfoundland and Labrador
Our Reference *IM140211*

This is to advise you that the Chair of the Centre's Secondary Uses Committee (SUC) has reviewed your amendment application to request de-identified Record-Level Information for Secondary Use. Having consulted with the SUC chair, I authorize the release of the requested data.

The approval of your application and use of the requested data is conditional upon the following:

- The data received must be used only for the purposes of this request. Any future uses and/or disclosures of the data provided must have HREB approval as well as approval from the Centre;
- Members of the research team accessing the released data must not attempt to re-identify the subjects of the released data;
- Cell counts or statistics based on cell counts less than 5 are not published;
- The data must be stored on a Memorial University asset and must not be placed on a personal device;
- All members of the research team must comply with Memorial University's policies and procedures for privacy, security and data storage, and have signed an Oath of Confidentiality;

Newfoundland and Labrador Centre for Health Information
www.nlchi.nl.ca
70 O'Leary Avenue, St. John's, NL A1B 2C7
t. 709 752 6000 f. 709 752 6011 e. contact@nlchi.nl.ca

- At the end of the data retention period data must be disposed of by ensuring the drives on the device are appropriately sanitized (securely deleted or destroyed) prior to the disposal or repurposing of the system or any storage components;

- If there are changes with the research study and/or research team then the Centre must be notified. Any amendments or updated ethics approval(s) will be supplied to the Centre accordingly;

- Transfer of all record-level data to and from the Centre will be completed using the Centre's Managed File Transfer System (MFT);

- The Centre reserves the right to conduct an audit review of requestors who have been disclosed record-level data.

Please sign below and return to acknowledge you accept the above conditions of approval.

Sincerely,

Gillian Sweeney
Vice President, Clinical Information Programs and Quality
NL Centre for Health Information
Cc: Donna Roche, Chair, Secondary Uses Committee
Cc: Laurie Twells, Supervisor
Cc: Leigh Ann Newhook, Co-Supervisor

Newfoundland and Labrador Centre for Health Information
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Appendix 3.3: Number of Unique Visits to Healthcare Providers and the Associated Costs by Infant Feeding Mode (Counts)

	Total (n=159)	EBF (n = 106)	Mixed (n= 32)	Formula (n=21)
Hospitalizations				
Total L.O.S (days) Mean (SD)	31 2.58 (2.43)	6 2.0 (1.0)	9 1.8 (0.84)	16 4.0 (2.16)
Total L.O.S (days) including birth Mean (SD)	386 2.42 (1.28)	227 2.14 (0.97)	95 2.96 (1.18)	64 3.04 (2.11)
	Total (n=160)	**EBF (n = 107)**	**Mixed (n= 32)**	**Formula (n=21)**
Emergency Room Visit	161	110	32	19
Triage Level of ER Visits				
Emergent (Within 15min)	6	-	-	-
Urgent (Within 30min)	58	39	14	5
Less Urgent (Within 60 min)	59	46	8	5
Non-Urgent (in 120 min)	13	6	-	-
No Triage Level Listed	25	15	5	5
	Total (n=156)	**EBF (n = 104)**	**Mixed (n= 32)**	**Formula (n=20)**
Family Doctor	1101	711	237	153
Any Specialist	220	130	54	36
Pediatrician	46	30	7	9
Pediatric Cardiologist	15	10	-	-
Dermatologist	18	4	7	7
Diagnostic Radiologist	117	74	30	13
Otolaryngologist (ENT)	20	12	-	-

Appendix 3.4: Description of Hospitalizations During the First Year of Life

Hospitalization	LOS	Case Mix Group	Description	Admit Category
1	4	Major Respiratory Complication	Bronchiolitis Resp Syncytial Infection	Urgent/Emergent
2	1	Hernia Repair	Undescended testicle	Elective
3	5	Upper/Lower RTI	Bronchiolitis Resp Syncytial Infection	Urgent/Emergent
4	3	Upper/Lower RTI	Bronchiolitis Unspecified	Urgent/Emergent
5	4	Fever	Fever	Urgent/Emergent
6	1	Fever	Fever	Urgent/Emergent
7	1	Other Resp	Dyspnoea	Urgent/Emergent
8	1	Other Resp	Dyspnoea	Urgent/Emergent
9	2	Asthma	Asthma Unspecified	Urgent/Emergent
10	2	Gastrointestinal Hemorrhage	Haematemesis	Urgent/Emergent
11	1	Croup	Croup – Acute obstructive laryngitis	Urgent/Emergent
12	1	Hand Intervention	Upper Limb (Accessory Finger)	Elective
13	2	Jaundice	Jaundice unspecified	Urgent/Emergent
14	2	Short Gestation	Unspecified	Urgent/Emergent
15	2	Jaundice	Jaundice unspecified	Urgent/Emergent

Appendix 4.1 PRISMA (2020) Checklist

Section and Topic	Item #	Checklist item	Location where item is reported
TITLE			
Title	1	Identify the report as a systematic review.	5.0
ABSTRACT			
Abstract	2	See the PRISMA 2020 for Abstracts checklist.	5.0
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of existing knowledge.	5.1
Objectives	4	Provide an explicit statement of the objective(s) or question(s) the review addresses.	5.1
METHODS			
Eligibility criteria	5	Specify the inclusion and exclusion criteria for the review and how studies were grouped for the syntheses.	5.2.2
Information sources	6	Specify all databases, registers, websites, organisations, reference lists and other sources searched or consulted to identify studies. Specify the date when each source was last searched or consulted.	5.2.2
Search strategy	7	Present the full search strategies for all databases, registers and websites, including any filters and limits used.	Appendix
Selection process	8	Specify the methods used to decide whether a study met the inclusion criteria of the review, including how many reviewers screened each record and each report retrieved, whether they worked independently, and if applicable, details of automation tools used in the process.	5.2.3/4
Data collection process	9	Specify the methods used to collect data from reports, including how many reviewers collected data from each report, whether they worked independently, any processes for obtaining or confirming data from study investigators, and if applicable, details of automation tools used in the process.	5.2.3
Data items	10a	List and define all outcomes for which data were sought. Specify whether all results that were compatible with each outcome domain in each study were sought (e.g. for all measures, time points, analyses), and if not, the methods used to decide which results to collect.	5.2.3
	10b	List and define all other variables for which data were sought (e.g. participant and intervention characteristics, funding sources). Describe any assumptions made about any missing or unclear information.	5.2.3
Study risk of bias assessment	11	Specify the methods used to assess risk of bias in the included studies, including details of the tool(s) used, how many reviewers assessed each study and whether they worked independently, and if	5.2.3

Section and Topic	Item #	Checklist item	Location where item is reported
		applicable, details of automation tools used in the process.	
Effect measures	12	Specify for each outcome the effect measure(s) (e.g. risk ratio, mean difference) used in the synthesis or presentation of results.	5.2.5
Synthesis methods	13a	Describe the processes used to decide which studies were eligible for each synthesis (e.g., tabulating the study intervention characteristics and comparing against the planned groups for each synthesis (item #5)).	5.2.4/5
	13b	Describe any methods required to prepare the data for presentation or synthesis, such as handling of missing summary statistics, or data conversions.	5.2.4/5
	13c	Describe any methods used to tabulate or visually display results of individual studies and syntheses.	5.2.4/5
	13d	Describe any methods used to synthesize results and provide a rationale for the choice(s). If meta-analysis was performed, describe the model(s), method(s) to identify the presence and extent of statistical heterogeneity, and software package(s) used.	5.2.4/5
	13e	Describe any methods used to explore possible causes of heterogeneity among study results (e.g. subgroup analysis, meta-regression).	5.3.3
	13f	Describe any sensitivity analyses conducted to assess robustness of the synthesized results.	5.5
Reporting bias assessment	14	Describe any methods used to assess risk of bias due to missing results in a synthesis (arising from reporting biases).	5.2.3
Certainty assessment	15	Describe any methods used to assess certainty (or confidence) in the body of evidence for an outcome.	5.2.3
RESULTS			
Study selection	16a	Describe the results of the search and selection process, from the number of records identified in the search to the number of studies included in the review, ideally using a flow diagram.	5.3
	16b	Cite studies that might appear to meet the inclusion criteria, but which were excluded, and explain why they were excluded.	Appendix
Study characteristics	17	Cite each included study and present its characteristics.	Table 5.1
Risk of bias in studies	18	Present assessments of risk of bias for each included study.	Table 5.4/ Appendix
Results of individual studies	19	For all outcomes, present, for each study: (a) summary statistics for each group (where appropriate) and (b) an effect estimate and its precision (e.g. confidence/credible interval), ideally using structured tables or plots.	Figures
Results of syntheses	20a	For each synthesis, briefly summarise the characteristics and risk of bias among contributing studies.	5.3.2
	20b	Present results of all statistical syntheses conducted. If meta-analysis was done, present for each the	5.3.2

Section and Topic	Item #	Checklist item	Location where item is reported
		summary estimate and its precision (e.g. confidence/credible interval) and measures of statistical heterogeneity. If comparing groups, describe the direction of the effect.	
	20c	Present results of all investigations of possible causes of heterogeneity among study results.	5.4
	20d	Present results of all sensitivity analyses conducted to assess the robustness of the synthesized results.	5.3.3
Reporting biases	21	Present assessments of risk of bias due to missing results (arising from reporting biases) for each synthesis assessed.	5.3.4
Certainty of evidence	22	Present assessments of certainty (or confidence) in the body of evidence for each outcome assessed.	5.3.3
DISCUSSION			
Discussion	23a	Provide a general interpretation of the results in the context of other evidence.	5.4
	23b	Discuss any limitations of the evidence included in the review.	5.4
	23c	Discuss any limitations of the review processes used.	5.4
	23d	Discuss implications of the results for practice, policy, and future research.	5.4
OTHER INFORMATION			
Registration and protocol	24a	Provide registration information for the review, including register name and registration number, or state that the review was not registered.	See publication
	24b	Indicate where the review protocol can be accessed, or state that a protocol was not prepared.	See publication
	24c	Describe and explain any amendments to information provided at registration or in the protocol.	NA
Support	25	Describe sources of financial or non-financial support for the review, and the role of the funders or sponsors in the review.	See publication
Competing interests	26	Declare any competing interests of review authors.	5.8
Availability of data, code and other materials	27	Report which of the following are publicly available and where they can be found: template data collection forms; data extracted from included studies; data used for all analyses; analytic code; any other materials used in the review.	See publication

From: Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ 2021;372:n71. doi: 10.1136/bmj.n71

Appendix 4.2 Search Strategy

Ovid MEDLINE(R) ALL <1946 to June 24, 2021>

Date Searched: June 25, 2021

1	exp Breast Feeding/
2	(breast feed* or breastfeed* or breast fed or breastfed or breast milk feed* or breastmilk feed* or breast milk fed or breastmilk fed).tw,kf
3	(chest feed* or chestfeed* or chest fed or chestfed).tw,kf
4	exp Lactation/
5	lactation.tw,kf
6	or/1-5 [BREASTFEEDING]
7	telelactation.tw,kf
8	Education, Distance/
9	Computer-Assisted Instruction/
10	exp Educational Technology/
11	Distance Counseling/
12	or/8-11 [DISTANCE EDUCATION]
13	6 and 12 [BREASTFEEDING & DISTANCE EDUCATION]
14	Health Education/
15	exp Consumer Health Information/
16	Health Promotion/
17	exp Patient Education as Topic/
18	ed.fs
19	exp Social Support/
20	Self-Help Groups/
21	Consultants/
22	Counselors/
23	Counseling/
24	(educat* or teach* or instruct* or train* or promot* or support* or counsel* or consult*).tw,kf
25	or/14-24 [HEALTH EDUCATION / SUPPORT]
26	exp Telemedicine/
27	exp Telecommunications/
28	exp Software/
29	exp Internet/
30	(tele* or technolog* or ict* or electronic* or "e health" or ehealth or "m health" or mhealth).tw,kf
31	(virtual* or digital* or remote or computer* or software or video* or audiovisual* or audio visual*).tw,kf
32	(internet* or online or "on line" or website* or web site* or web based or world wide web).tw,kf
33	(app or apps or facebook or social media or social network*).tw,kf

34 (smartphone* or phone* or iphone* or android or ipad* or tablet* or mobile or text messag* or text based or sms).tw,kf
35 or/26-34 [ICTs]
36 6 and 25 and 35
37 7 or 13 or 36
38 ((randomized controlled trial or controlled clinical trial).pt. or randomi?ed.ab. or placebo.ab. or randomly.ab. or trial.ab. or groups.ab.) not (exp animals/ not humans.sh)
39 37 and 38

Note: Line 38 is a one-line version of the Cochrane Highly Sensitive Search Strategy for identifying randomized trials in MEDLINE: sensitivity-maximizing version (2008 revision); Ovid format

Lefebvre C, Glanville J, Briscoe S, Littlewood A, Marshall C, Metzendorf M-I, Noel-Storr A, Rader T, Shokraneh F, Thomas J, Wieland LS. (2021). Technical Supplement to Chapter 4: Searching for and selecting studies. In: Higgins JPT, Thomas J, Chandler J, Cumpston MS, Li T, Page MJ, Welch VA (eds). *Cochrane Handbook for Systematic Reviews of Interventions* Version 6.2 (updated February 2021). Cochrane, 2021. Available from: www.training.cochrane.org/handbook.

Embase.com
Date Searched: June 25, 2021

#1 'breast feeding'/exp
#2 'breast feed*':ti,ab,kw OR breastfeed*:ti,ab,kw OR 'breast fed':ti,ab,kw OR breastfed:ti,ab,kw OR 'breast milk feed*':ti,ab,kw OR 'breastmilk feed*':ti,ab,kw OR 'breast milk fed':ti,ab,kw OR 'breastmilk fed':ti,ab,kw
#3 'chest feed*':ti,ab,kw OR chestfeed*:ti,ab,kw OR 'chest fed':ti,ab,kw OR chestfed:ti,ab,kw
#4 'lactation'/de
#5 lactation:ti,ab,kw
#6 #1 OR #2 OR #3 OR #4 OR #5
#7 telelactation:ti,ab,kw
#8 'distance learning'/exp
#9 'virtual learning environment'/de
#10 'educational technology'/de
#11 'e-counseling'/de
#12 'online support group'/de
#13 'teleconsultation'/exp
#14 'video consultation'/de
#15 #8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14
#16 #6 AND #15
#17 'breast feeding education'/de
#18 'health education'/de
#19 'consumer health information'/de
#20 'health promotion'/exp
#21 'patient education'/de

#22 'social support'/de

#23 'social care'/de

#24 'support group'/de

#25 'consultation'/exp

#26 'counselor'/de

#27 'counseling'/de

#28 'parent counseling'/de

#29 educat*:ti,ab,kw OR teach*:ti,ab,kw OR instruct*:ti,ab,kw OR train*:ti,ab,kw OR promot*:ti,ab,kw OR support*:ti,ab,kw OR counsel*:ti,ab,kw OR consult*:ti,ab,kw

#30 #17 OR #18 OR #19 OR #20 OR #21 OR #22 OR #23 OR #24 OR #25 OR #26 OR #27 OR #28 OR #29

#31 'telemedicine'/de

#32 'telecommunication'/de

#33 'teleconference'/de

#34 'telehealth'/de

#35 'computer'/exp

#36 'software'/exp

#37 'internet'/de

#38 'web-based intervention'/de

#39 'web conferencing'/de

#40 'videoconferencing'/de

#41 'mobile phone'/exp

#42 'tablet computer'/de

#43 'social media'/de

#44 'text messaging'/de

#45 'webcast'/de

#46 'webinar'/de

#47 'wireless communication'/de

#48 tele*:ti,ab,kw OR technolog*:ti,ab,kw OR ict*:ti,ab,kw OR electronic*:ti,ab,kw OR 'e health':ti,ab,kw OR ehealth:ti,ab,kw OR 'm health':ti,ab,kw OR mhealth:ti,ab,kw

#49 virtual*:ti,ab,kw OR digital*:ti,ab,kw OR remote:ti,ab,kw OR computer*:ti,ab,kw OR software:ti,ab,kw OR video*:ti,ab,kw OR audiovisual*:ti,ab,kw OR 'audio visual*':ti,ab,kw

#50 internet*:ti,ab,kw OR online:ti,ab,kw OR 'on line':ti,ab,kw OR website*:ti,ab,kw OR 'web site*':ti,ab,kw OR 'web based':ti,ab,kw OR 'world wide web':ti,ab,kw

#51 app:ti,ab,kw OR apps:ti,ab,kw OR facebook:ti,ab,kw OR 'social media':ti,ab,kw OR 'social network*':ti,ab,kw

#52 smartphone*:ti,ab,kw OR phone*:ti,ab,kw OR iphone*:ti,ab,kw OR android:ti,ab,kw OR ipad*:ti,ab,kw OR tablet*:ti,ab,kw OR mobile:ti,ab,kw OR 'text messag*':ti,ab,kw OR 'text based':ti,ab,kw OR sms:ti,ab,kw

#53 #31 OR #32 OR #33 OR #34 OR #35 OR #36 OR #37 OR #38 OR #39 OR #40 OR #41 OR #42 OR #43 OR #44 OR #45 OR #46 OR #47 OR #48 OR #49 OR #50 OR #51 OR #52

#54 #6 AND #30 AND #53

#55 #7 OR #16 OR #54

#56 'randomized controlled trial'/de

#57 'controlled clinical trial'/de

#58 random*:ti,ab OR random*:tt

#59 'randomization'/de

#60 'intermethod comparison'/de

#61 placebo:ti,ab OR placebo:tt

#62 compare:ti OR compare:tt OR compared:ti OR compared:tt OR comparison:ti OR comparison:tt

#63 (evaluated:ab OR evaluate:ab OR evaluating:ab OR assessed:ab OR assess:ab) AND (compare:ab OR compared:ab OR comparing:ab OR comparison:ab)

#64 ((open NEXT/1 label):ti,ab) OR ((open NEXT/1 label):tt)

#65 (((double OR single OR doubly OR singly) NEXT/1 (blind OR blinded OR blindly)):ti,ab) OR (((double OR single OR doubly OR singly) NEXT/1 (blind OR blinded OR blindly)):tt)

#66 'double blind procedure'/de

#67 ((parallel NEXT/1 group*):ti,ab) OR ((parallel NEXT/1 group*):tt)

#68 crossover:ti,ab OR crossover:tt OR 'cross over':ti,ab OR 'cross over':tt

#69 (((assign* OR match OR matched OR allocation) NEAR/6 (alternate OR group OR groups OR intervention OR interventions OR patient OR patients OR subject OR subjects OR participant OR participants)):ti,ab) OR (((assign* OR match OR matched OR allocation) NEAR/6 (alternate OR group OR groups OR intervention OR interventions OR patient OR patients OR subject OR subjects OR participant OR participants)):tt)

#70 assigned:ti,ab OR assigned:tt OR allocated:ti,ab OR allocated:tt

#71 ((controlled NEAR/8 (study OR design OR trial)):ti,ab) OR ((controlled NEAR/8 (study OR design OR trial)):tt)

#72 volunteer:ti,ab OR volunteer:tt OR volunteers:ti,ab OR volunteers:tt

#73 'human experiment'/de

#74 trial:ti OR trial:tt

#75 #56 OR #57 OR #58 OR #59 OR #60 OR #61 OR #62 OR #63 OR #64 OR #65 OR #66 OR #67 OR #68 OR #69 OR #70 OR #71 OR #72 OR #73 OR #74

#76 ((random* NEXT/1 sampl* NEAR/8 ('cross section*' OR questionnaire* OR survey OR surveys OR database OR databases)):ti,ab) NOT ('comparative study'/de OR 'controlled study'/de OR 'randomised controlled':ti,ab OR 'randomized controlled':ti,ab OR 'randomly assigned':ti,ab) OR (((random* NEXT/1 sampl* NEAR/8 ('cross section*' OR questionnaire* OR survey OR surveys OR database OR databases)):tt) NOT ('comparative study'/de OR 'controlled study'/de OR 'randomised controlled':tt OR 'randomized controlled':tt OR 'randomly assigned':tt))

#77 cross-sectional study' NOT ('randomized controlled trial'/de OR 'controlled clinical study'/de OR 'controlled study'/de OR 'randomised controlled':ti,ab OR 'randomized controlled':ti,ab OR 'control group':ti,ab OR 'control groups':ti,ab) OR ('cross-sectional study' NOT ('randomized controlled trial'/de OR 'controlled clinical study'/de OR 'controlled study'/de OR 'randomised controlled':tt OR 'randomized controlled':tt OR 'control group':tt OR 'control groups':tt))

#78 'case control*':ti,ab AND random*:ti,ab NOT ('randomised controlled':ti,ab OR 'randomized controlled':ti,ab) OR ('case control*':tt AND random*:tt NOT ('randomised controlled':tt OR 'randomized controlled':tt))

#79 ('systematic review':ti OR 'systematic review':tt) NOT (trial:ti OR trial:tt OR study:ti OR study:tt)

#80 nonrandom*:ti,ab NOT random*:ti,ab OR (nonrandom*:tt NOT random*:tt)

#81 'random field*':ti,ab OR 'random field*':tt

#82 (('random cluster' NEAR/4 sampl*):ti,ab) OR (('random cluster' NEAR/4 sampl*):tt)

#83 review:ab AND review:it NOT (trial:ti OR trial:tt)

#84 'we searched':ab AND (review:ti OR review:tt OR review:it)

#85 'update review':ab

#86 (databases NEAR/5 searched):ab

#87 (rat:ti OR rat:tt OR rats:ti OR rats:tt OR mouse:ti OR mouse:tt OR mice:ti OR mice:tt OR swine:ti OR swine:tt OR porcine:ti OR porcine:tt OR murine:ti OR murine:tt OR sheep:ti OR sheep:tt OR lambs:ti OR lambs:tt OR pigs:ti OR pigs:tt OR piglets:ti OR piglets:tt OR rabbit:ti OR rabbit:tt OR rabbits:ti OR rabbits:tt OR cat:ti OR cat:tt OR cats:ti OR cats:tt OR dog:ti OR dog:tt OR dogs:ti OR dogs:tt OR cattle:ti OR cattle:tt OR bovine:ti OR bovine:tt OR monkey:ti OR monkey:tt OR monkeys:ti OR monkeys:tt OR trout:ti OR trout:tt OR marmoset*:ti OR marmoset*:tt) AND 'animal experiment'/de

#88 'animal experiment'/de NOT ('human experiment'/de OR 'human'/de)

#89 #76 OR #77 OR #78 OR #79 OR #80 OR #81 OR #82 OR #83 OR #84 OR #85 OR #86 OR #87 OR #88

#90 #75 NOT #89

#91 #55 AND #90

Note: Lines #56-#90 are a modified version of the Cochrane RCT filter for Embase.com. The filter provided at https://drive.google.com/file/d/10JU-2vicvIc83_PghgelfqY5aQnYd-hB/view was modified to run the translated title field separately from the title and abstract fields.

Glanville, J., Foxlee, R., Wisniewski, S., Noel‐Storr, A., Edwards, M., & Dooley, G. (2019b). Translating the Cochrane EMBASE RCT filter from the Ovid interface to Embase.com: A case study. Health Information & Libraries Journal, 36(3), 264–277. https://doi.org/10.1111/hir.12269

Corrigendum. (2020). Health Information & Libraries Journal, 37(4), 351–351. https://doi.org/10.1111/hir.12333

Cochrane CENTRAL Register of Controlled Trials (Wiley)
Issue 6 of 12, June 2021
Date Searched: June 25, 2021

#1 [mh "Breast Feeding"]

#2 ((breast NEXT feed*) OR breastfeed* OR "breast fed" OR breastfed OR ("breast milk" NEXT feed*) OR (breastmilk NEXT feed*) OR "breast milk fed" OR "breastmilk fed"):ti,ab,kw

#3 ((chest NEXT feed*) OR chestfeed* OR "chest fed" OR chestfed):ti,ab,kw

#4 [mh ^Lactation]

#5 lactation:ti,ab,kw

#6 #1 OR #2 OR #3 OR #4 OR #5

#7 telelactation:ti,ab,kw

#8 [mh ^"Education, Distance"]

#9 [mh ^"Computer-Assisted Instruction"]

#10 [mh "Educational Technology"]

#11 [mh ^"Distance Counseling"]

#12 #8 OR #9 OR #10 OR #11

#13 #6 AND #12

#14 [mh ^"Health Education"]
#15 [mh "Consumer Health Information"]
#16 [mh ^"Health Promotion"]
#17 [mh "Patient Education as Topic"]
#18 [mh /ED]
#19 [mh "Social Support"]
#20 [mh ^"Self-Help Groups"]
#21 [mh ^Consultants]
#22 [mh ^Counselors]
#23 [mh ^Counseling]
#24 (educat* OR teach* OR instruct* OR train* OR promot* OR support* OR counsel* OR consult*):ti,ab,kw
#25 #14 OR #15 OR #16 OR #17 OR #18 OR #19 OR #20 OR #21 OR #22 OR #23 OR #24
#26 [mh Telemedicine]
#27 [mh Telecommunications]
#28 [mh Software]
#29 [mh Internet]
#30 (tele* OR technolog* OR ict* OR electronic* OR (e NEXT health) OR ehealth OR (m NEXT health) OR mhealth):ti,ab,kw
#31 (virtual* OR digital* OR remote OR computer* OR software OR video* OR audiovisual* OR (audio NEXT visual*)):ti,ab,kw
#32 (internet* OR online OR "on line" OR website* OR (web NEXT site*) OR "web based" OR "world wide web"):ti,ab,kw
#33 (app OR apps OR facebook OR "social media" OR (social NEXT network*)):ti,ab,kw
#34 (smartphone* OR phone* OR iphone* OR android OR ipad* OR tablet* OR mobile OR (text NEXT messag*) OR "text based" OR sms):ti,ab,kw
#35 #26 OR #27 OR #28 OR #29 OR #30 OR #31 OR #32 OR #33 OR #34
#36 #6 AND #25 AND #35
#37 #7 OR #13 OR #36 in Trials

CINHAL Plus with Full Text (EBSCOhost)
Date Searched: June 25, 2021

S1	(MH "Breast Feeding+") OR (MH "Lactation")
S2	TI ("breast feed*" OR breastfeed* OR "breast fed" OR breastfed OR "breast milk feed*" OR "breastmilk feed*" OR "breast milk fed" OR "breastmilk fed" OR "chest feed*" OR chestfeed* OR "chest fed" OR chestfed OR lactation) OR AB ("breast feed*" OR breastfeed* OR "breast fed" OR breastfed OR "breast milk feed*" OR "breastmilk feed*" OR "breast milk fed" OR "breastmilk fed" OR "chest feed*" OR chestfeed* OR "chest fed" OR chestfed OR lactation)
S3	S1 OR S2
S4	TI telelactation OR AB telelactation
S5	(MH "Online Education") OR (MH "Educational Technology") OR (MH "Remote Consultation")
S6	S3 AND S5

S7	(MH "Breast Feeding Promotion") OR (MH "Health Education") OR (MH "Consumer Health Information") OR (MH "Health Promotion") OR (MH "Patient Education") OR (MW "ED") OR (MH "Support, Psychosocial") OR (MH "Support Groups") OR (MH "Referral and Consultation") OR (MH "Consultants+") OR (MH "Counselors") OR (MH "Counseling")
S8	TI (educat* OR teach* OR instruct* OR train* OR promot* OR support* OR counsel* OR consult*) OR AB (educat* OR teach* OR instruct* OR train* OR promot* OR support* OR counsel* OR consult*)
S9	S7 OR S8
S10	(MH "Telemedicine") OR (MH "Telehealth") OR (MH "Communications Media") OR (MH "Telecommunications") OR (MH "Teleconferencing") OR (MH "Computers and Computerization+") OR (MH "Software+") OR (MH "Internet") OR (MH "Internet-Based Intervention") OR (MH "Videoconferencing") OR (MH "Cellular Phone+") OR (MH "Computers, Portable+") OR (MH "Mobile Applications") OR (MH "Social Media+") OR (MH "Text Messaging") OR (MH "Webcasts") OR (MH "Webinars") OR (MH "Electronic Bulletin Boards") OR (MH "Wireless Communications")
S11	TI (tele* OR technolog* OR ict* OR electronic* OR "e health" OR ehealth OR "m health" OR mhealth OR virtual* OR digital* OR remote OR computer* OR software OR video* OR audiovisual* OR "audio visual*" OR internet* OR online OR "on line" OR website* OR "web site*" OR "web based" OR "world wide web" OR app OR apps OR facebook OR "social media" OR "social network*" OR smartphone* OR phone* OR iphone* OR android OR ipad* OR tablet* OR mobile OR "text messag*" OR "text based" OR sms) OR AB (tele* OR technolog* OR ict* OR electronic* OR "e health" OR ehealth OR "m health" OR mhealth OR virtual* OR digital* OR remote OR computer* OR software OR video* OR audiovisual* OR "audio visual*" OR internet* OR online OR "on line" OR website* OR "web site*" OR "web based" OR "world wide web" OR app OR apps OR facebook OR "social media" OR "social network*" OR smartphone* OR phone* OR iphone* OR android OR ipad* OR tablet* OR mobile OR "text messag*" OR "text based" OR sms)
S12	S10 OR S11
S13	S3 AND S9 AND S12
S14	S4 OR S6 OR S13
S15	(MH "Randomized Controlled Trials") OR (MH "Double-Blind Studies") OR (MH "Single-Blind Studies") OR (MH "Random Assignment") OR (MH "Pretest-Posttest Design") OR (MH "Cluster Sample") OR TI (randomised OR randomized) OR AB (random*) OR TI (trial) OR ((MH "Sample Size") AND AB (assigned OR allocated OR control)) OR (MH "Placebos") OR (PT "Randomized Controlled Trial") OR AB (control W5 group) OR (MH "Crossover Design") OR (MH "Comparative Studies") OR AB (cluster W3 RCT)
S16	(MH "Animals+") OR (MH "Animal Studies") OR TI (animal model*)
S17	(MH "Human")
S18	S16 NOT S17
S19	S15 NOT S18
S20	S14 AND S19

Note: Lines S15-S19 are the Cochrane CINAHL Plus filter (modified to use fewer lines).

Glanville, J., Dooley, G., Wisniewski, S., Foxlee, R., & Noel-Storr, A. (2019a). Development of a search filter to identify reports of controlled clinical trials within CINAHL Plus. Health Information & Libraries Journal, 36(1), 73–90. https://doi.org/10.1111/hir.12251

APA PsycINFO (EBSCOhost)
Date Searched: June 25, 2021

S1	DE "Breast Feeding" OR DE "Lactation"
S2	TI ("breast feed*" OR breastfeed* OR "breast fed" OR breastfed OR "breast milk feed*" OR "breastmilk feed*" OR "breast milk fed" OR "breastmilk fed" OR "chest feed*" OR chestfeed* OR "chest fed" OR chestfed OR lactation) OR AB ("breast feed*" OR breastfeed* OR "breast fed" OR breastfed OR "breast milk feed*" OR "breastmilk feed*" OR "breast milk fed" OR "breastmilk fed" OR "chest feed*" OR chestfeed* OR "chest fed" OR chestfed OR lactation) OR KW ("breast feed*" OR breastfeed* OR "breast fed" OR breastfed OR "breast milk feed*" OR "breastmilk feed*" OR "breast milk fed" OR "breastmilk fed" OR "chest feed*" OR chestfeed* OR "chest fed" OR chestfed OR lactation)
S3	S1 OR S2
S4	TI telelactation OR AB telelactation OR KW telelactation
S5	DE "Distance Education" OR DE "Electronic Learning" OR DE "Asynchronous Learning" OR DE "Mobile Learning" OR DE "Digital Game-Based Learning" OR DE "Virtual Classrooms" OR DE "Computer Assisted Instruction" OR DE "Computer Supported Collaborative Learning" OR DE "Online Therapy" OR DE "Teleconsultation" OR DE Televised Instruction" OR DE "Videotape Instruction" OR DE "Audiovisual Instruction" OR DE "Online Social Networks"
S6	S3 AND S5
S7	DE "Health Education" OR DE "Health Promotion" OR DE "Client Education" OR DE "Social Support" OR DE "Support Groups" OR DE "Professional Consultation" OR DE "Counselors" OR DE "Counseling"
S8	TI (educat* OR teach* OR instruct* OR train* OR promot* OR support* OR counsel* OR consult*) OR AB (educat* OR teach* OR instruct* OR train* OR promot* OR support* OR counsel* OR consult*) OR KW (educat* OR teach* OR instruct* OR train* OR promot* OR support* OR counsel* OR consult*)
S9	S7 OR S8
S10	DE "Telemedicine" OR DE "Telecommunications Media" OR DE "Information and Communication Technology" OR DE "Digital Technology" OR DE "Computer Mediated Communication" OR DE "Communications Media" OR DE "Audiovisual Communications Media" OR DE "Teleconferencing" OR DE "Computers" OR DE "Microcomputers" OR DE "Mobile Devices" OR DE "Mobile Health" OR DE "Mobile Applications" OR DE "Mobile Technology" OR DE "Computer Software" OR DE "Internet" OR DE "Digital Interventions" OR DE "Videoconferencing" OR DE "Mobile Phones" OR DE "Tablet Computers" OR DE "Social Media" OR DE "Online Social Networks" OR DE "Text Messaging" OR DE "Websites" OR DE "Wireless Technologies"

S11	TI (tele* OR technolog* OR ict* OR electronic* OR "e health" OR ehealth OR "m health" OR mhealth OR virtual* OR digital* OR remote OR computer* OR software OR video* OR audiovisual* OR "audio visual*" OR internet* OR online OR "on line" OR website* OR "web site*" OR "web based" OR "world wide web" OR app OR apps OR facebook OR "social media" OR "social network*" OR smartphone* OR phone* OR iphone* OR android OR ipad* OR tablet* OR mobile OR "text messag*" OR "text based" OR sms) OR AB (tele* OR technolog* OR ict* OR electronic* OR "e health" OR ehealth OR "m health" OR mhealth OR virtual* OR digital* OR remote OR computer* OR software OR video* OR audiovisual* OR "audio visual*" OR internet* OR online OR "on line" OR website* OR "web site*" OR "web based" OR "world wide web" OR app OR apps OR facebook OR "social media" OR "social network*" OR smartphone* OR phone* OR iphone* OR android OR ipad* OR tablet* OR mobile OR "text messag*" OR "text based" OR sms) OR KW (tele* OR technolog* OR ict* OR electronic* OR "e health" OR ehealth OR "m health" OR mhealth OR virtual* OR digital* OR remote OR computer* OR software OR video* OR audiovisual* OR "audio visual*" OR internet* OR online OR "on line" OR website* OR "web site*" OR "web based" OR "world wide web" OR app OR apps OR facebook OR "social media" OR "social network*" OR smartphone* OR phone* OR iphone* OR android OR ipad* OR tablet* OR mobile OR "text messag*" OR "text based" OR sms)
S12	S10 OR S11
S13	S3 AND S9 AND S12
S14	S4 OR S6 OR S13
S15	DE "Randomized Controlled Trials" OR DE "Randomized Clinical Trials" OR DE "Placebo" OR DE "Treatment Effectiveness Evaluation"
S16	TI (random* OR factorial* OR crossover* OR "cross over*" OR placebo* OR control OR ((singl* OR doubl* OR tripl* OR trebl*) N3 (blind* OR mask*)) OR assign* OR allocat* OR volunteer* OR trial OR rct) OR AB (random* OR factorial* OR crossover* OR "cross over*" OR placebo* OR control OR ((singl* OR doubl* OR tripl* OR trebl*) N3 (blind* OR mask*)) OR assign* OR allocat* OR volunteer* OR trial OR rct) OR KW (random* OR factorial* OR crossover* OR "cross over*" OR placebo* OR control OR ((singl* OR doubl* OR tripl* OR trebl*) N3 (blind* OR mask*)) OR assign* OR allocat* OR volunteer* OR trial OR rct)
S17	S15 OR S16
S18	S14 AND S17

ClinicalTrials.gov
Date Searched: June 25, 2021

Search 1:

- Condition or Disease: breastfeed OR breastfeeding OR breast feeding OR breast fed OR breastfed OR lactation OR chestfeeding OR chest feeding
- Other terms: tele OR telemedicine OR telehealth OR technology OR ict OR electronic OR e health OR ehealth OR m health OR mhealth OR virtual OR digital OR remote OR computer OR software OR video OR audiovisual OR audio visual OR internet
- Applied Filters: Interventional Studies

Search 2:

- Condition or Disease: breastfeed OR breastfeeding OR breast feeding OR breast fed OR breastfed OR lactation OR chestfeeding OR chest feeding
- Other terms: online OR on line OR website OR web site OR web based OR app OR apps OR facebook OR social media OR social network OR smartphone OR telephone OR phone OR iphone OR android OR ipad OR tablet OR mobile OR text messaging OR text based OR sms
- Applied Filters: Interventional Studies

WHO ICTRP
Date Searched: June 25, 2021

Search 1 (Run on the basic search screen):
- breastfeeding AND support OR breast feeding AND support OR lactation AND support

Search 2 (Advanced Search):
- Title: breastfeed OR breastfeeding OR breast feeding OR breast fed OR breastfed OR chestfeeding OR chest feeding OR lactation OR telelacation
- Intervention: tele* OR technolog* OR ict OR electronic* OR e health OR ehealth OR m health OR mhealth OR virtual* OR digital* OR remote* OR computer* OR software OR video* OR audio* OR internet OR online OR web* OR app* OR facebook OR phone OR mobile OR text OR sms

Search 3 (Advanced Search):
- Title: breastfeed OR breastfeeding OR breast feeding OR breast fed OR breastfed OR chestfeeding OR chest feeding OR lactation OR telelacation
- Intervention: support OR educate OR education OR train OR training OR teach OR promote OR promotion OR counseling OR counselling OR consultation

Appendix 4.3. Formulas used to calculate and impute Relative Risk (RR) and Confidence Intervals (CIs)

The relative risk formula was used to calculate the risk ratio between the control group and intervention group. Those "exposed" would be those exposed to an information communication technology to encourage exclusive breastfeeding.

Relative Risk (RR) Calculation

$$RR = [a / (a + b)] / [c / (c + d)]$$

a is the number of members of the exposed group who exclusively breastfed;

b is the number of members of the exposed group who did not exclusively breastfeed;

c is the number of members of the control group who exclusively breastfed;

d is the number of members of the control group who did not exclusively breastfeed;

Results can be interpreted according to the guidelines below:

> If the relative risk is equal to 1, it means that there is no difference in the risk between the two groups.
>
> If relative risk is lower than 1, it means that the risk is lower in the exposed group. (i.e., the likelihood of EBF for longer durations is lower in exposed)
>
> If relative risk is higher than 1, it means that the risk is higher in the exposed group. (i.e., the likelihood of EBF for longer durations is higher in exposed)

Confidence Interval (CI) Calculation

CI lower bound = $\exp[\ln(RR) - Zc * \sqrt{(1/a + 1/c - 1/(a + b) - 1/(c + d))}]$

CI upper bound = $\exp[\ln(RR) + Zc * \sqrt{(1/a + 1/c - 1/(a + b) - 1/(c + d))}]$

a through d are defined above;

Zc stands for the Z-score corresponding to the chosen confidence level. Z score used: 1.959 (Confidence level: 95%)

Results can be interpreted according to the following:

> With a 95% CI we can be 95% sure that the real relative ratio lies somewhere in between the upper and lower bound.

Appendix 4.4. Quality rating of included studies based on the Revised Cochrane risk-of-bias tool for randomized trials (RoB 2)

	Author (Year)																		
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19
Domain 1: Risk of bias arising from the randomization process																			
1.1 Was the allocation sequence random?	Y	N	Y	Y	Y	Y	Y	Y	Y	Y	NI	Y	Y	Y	Y	Y	Y	Y	Y
1.2 Was the allocation sequence concealed until participants were enrolled and assigned to interventions?	Y	N	Y	Y	N	NI	NI	NI	Y	Y	NI	Y	Y	Y	Y	Y	Y	Y	Y
1.3 Did baseline differences between intervention groups suggest a problem with the randomization process?	N	N	N	N	N	N	N	N	N	N	PN	N	N	N	N	N	N	N	N
Risk-of-bias judgement	L	H	L	L	L	L	S	L	L	L	S	L	L	L	L	L	L	L	L
Domain 2: Risk of bias due to deviations from the intended interventions (effect of assignment to intervention)																			
2.1. Were participants aware of their assigned intervention during the trial?	NI	NI	Y	NI	Y	Y	NI	NI	NI	Y	Y	N	Y	Y	Y	N	N	NI	Y
2.2. Were carers and people delivering the interventions aware of participants' assigned intervention during the trial?	N	NI	Y	NI	Y	Y	NI	NI	NI	N	Y	Y	N	N	N	N	N	N	Y
2.3. If Y/PY/NI to 2.1 or 2.2: Were there deviations from the intended intervention that arose because of the trial context?	NA	N	N	N	PN	N	N	N	N	N	N	N	N	N	N	NA	N	N	N
2.4 If Y/PY to 2.3: Were these deviations likely to have affected the outcome?	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA

	Author (Year)																		
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19
2.5. If Y/PY/NI to 2.4: Were these deviations from intended intervention balanced between groups?	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
2.6 Was an appropriate analysis used to estimate the effect of assignment to intervention?	PY	Y	Y	Y	Y	Y	Y	Y	Y	Y	N	Y	Y	Y	Y	Y	Y	N	N
2.7 If N/PN/NI to 2.6: Was there potential for a substantial impact (on the result) of the failure to analyse participants in the group to which they were randomized?	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	Y	NA	NA	NA	NA	NA	NA	Y	Y
Risk-of-bias judgement	L	L	S	L	L	L	L	L	L	L	H	L	L	L	L	L	L	L	L
Domain 2: Risk of bias due to deviations from the intended interventions (effect of adhering to intervention)																			
2.1. Were participants aware of their assigned intervention during the trial?	NI	NI	Y	N	Y	Y	NI	NI	NI	Y	Y	N	Y	Y	Y	N	N	NI	Y
2.2. Were carers and people delivering the interventions aware of participants' assigned intervention during the trial?	N	NI	Y	N	Y	Y	N	NI	NI	N	Y	Y	N	N	Y	N	N	N	Y
2.3. [If applicable:] If Y/PY/NI to 2.1 or 2.2: Were important non-protocol interventions balanced across groups?	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
2.4. [If applicable:] Were there failures in implementing the intervention that could have affected the outcome?	N	N	N	N	N	N	N	N	N	N	N	N	N	N	NA	N	N	N	N
2.5. [If applicable:] Was there non-adherence to the assigned intervention regimen that could have the outcomes?	N	N	N	NA	NA	N	N	N	N	N	N	N	N	Y	NA	N	NA	N	N

	Author (Year)																		
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19
2.6. If N/PN/NI to 2.3, or Y/PY/NI to 2.4 or 2.5: Was an appropriate analysis used to estimate the effect of adhering to the intervention?	NA	NA	NA	NA	Y	NA	Y	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Risk-of-bias judgement	L	L	L	L	L	L	L	L	L	L	S	L	L	L	L	L	L	L	L
Domain 3: Missing outcome data																			
3.1 Were data for this outcome available for all, or nearly all, participants randomized?	Y	Y	N	Y	PN	Y	Y	PY	N	Y	Y	Y	N	PY	Y	Y	Y	N	N
3.2 If N/PN/NI to 3.1: Is there evidence that the result was not biased by missing outcome data?	NA	NA	NI	NA	Y	NA	NA	NA	NI	NA	NA	NA	N	Y	NA	NA	NA	NI	NI
3.3 If N/PN to 3.2: Could missingness in the outcome depend on its true value?	NA	NA	NA	NA	NA	NA	NA	NA	NI	NA	NA	NA	Y	NA	NA	NA	NA	NI	N
3.4 If Y/PY/NI to 3.3: Is it likely that missingness in the outcome depended on its true value?	NA	NA	NA	NA	NA	NA	NA	NA	NI	NA	NA	NA	N	NA	NA	NA	NA	NI	NA
Risk-of-bias judgement	L	L	L	L	L	L	L	L	S	L	L	L	S	L	L	L	L	S	S
Domain 4: Risk of bias in measurement of the outcome																			
4.1 Was the method of measuring the outcome inappropriate?	N	N	N	N	N	N	N	N	N	N	N	N	Y	N	N	N	N	N	N
4.2 Could measurement or ascertainment of the outcome have differed between intervention groups?	PN	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
4.3 If N/PN/NI to 4.1 and 4.2: Were outcome assessors aware of the intervention received by participants?	N	NI	N	N	N	Y	N	Y	NI	N	NI	N	Y	Y	N	N	N	N	N

	Author (Year)																		
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19
4.4 If Y/PY/NI to 4.3: Could assessment of the outcome have been influenced by knowledge of intervention received?	NA	PY	NA	NA	NA	N	NA	NA	N	NA	N	NA	NA	NI	NA	NA	NA	NA	NA
4.5 If Y/PY/NI to 4.4: Is it likely that assessment of the outcome was influenced by knowledge of intervention received?	NA	N	NA	NA	NA	NA	NA	NA	N	NA	NA	NA	NA	NI	NA	NA	NA	NA	NA
Risk-of-bias judgement	L	S	L	L	L	L	L	L	L	L	L	L	L	S	L	L	L	L	L
Domain 5: Risk of bias in selection of the reported result																			
5.1 Were the data that produced this result analysed in accordance with a pre-specified analysis plan that was finalized before unblinded outcome data were available for analysis?	Y	NI	Y	Y	Y	Y	NI	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
5.2 Is the numerical result being assessed likely to have been selected, based on the results, from multiple eligible outcome measurements?	N	Y	N	N	N	N	Y	N	N	N	N	N	N	Y	N	N	N	N	N
5.3 Is the numerical result being assessed likely to have been selected, based on the results from multiple eligible analyses of the data?	N	Y	N	N	N	N	PY	N	NI	N	N	N	N	N	N	N	N	N	N
Risk of bias judgement	L	S	L	L	L	L	S	L	S	L	L	L	L	L	L	L	L	L	L
Overall Risk of Bias																			
Risk of bias judgement	L	H	S	L	L	L	H	L	H	L	H	L	S	S	L	L	L	S	S

*Risk of bias judgment: L (Low Risk), S (Some Concerns), H (High Risk)

1. Dennis (2002)
2. Wong (2007)
3. Hoddinott (2012)
4. Simonetti (2012)
5. Tahir (2013)
6. Fu (2014)
7. Giglia (2015)
8. Ahmed (2016)
9. Maslowsky (2016)
10. Ericson (2018)
11. Patel (2018)
12. Cavalcanti (2019)
13. Chaves (2019)
14. Forster (2019)
15. Uscher Pines (2019)
16. Lewkowitz (2020)
17. Puharic (2020)
18. Wu (2020)
19. Ogaji (2021)

Appendix 4.5 Excluded Studies

Wrong Study Design (N = 24)		
Title	Authors	Published Year
Effectiveness of educational and supportive intervention for primiparous women on breastfeeding related outcomes and breastfeeding self-efficacy: A systematic review and meta-analysis	Wong, M. S.; Mou, H.; Chien, W. T.	2021
Improving Exclusive Breastfeeding Via Mobile Phone Text Messages	University, Mutah	2018
Online Education for WIC Professionals: Teaching Child Development to Extend Breastfeeding Duration	Tedder, Jan; Quintana, Elsa M.	2018
Development of an m-health intervention for the infant and young child feeding counselling in the plantation sector of Sri Lanka	Senarath, U.; Godakandage, S.; Jayawickrama, H.; Wickramasinghe, A.; Siriwardena, I.; Partheepan, K.; Gamagedera, N.; Weerasinghe, M.; Alam, A.; Dibley, M.	2017
Breastfeeding During a Pandemic: The Influence of COVID-19 on Lactation Services in the Northeastern United States	Schindler-Ruwisch, J.; Phillips, K. E.	2021
Facebook support for breastfeeding mothers: A comparison to offline support and associations with breastfeeding outcomes	Robinson, A.; Lauckner, C.; Davis, M.; Hall, J.; Anderson, A. K.	2019
The Effectiveness of Lactation Consultants and Lactation Counselors on Breastfeeding Outcomes	Patel, S.	2016
Multi-site trial using short mobile messages (SMS) to improve infant feeding practices among participants in the WIC program	Palacios, C.; Campos, M.; Gibby, C.; Banna, J.	2017

Effectiveness of educational interventions conducted by telephone to promote breastfeeding: a systematic review of the literature	Oria, M. O. B.; Dodou, H. D.; Chaves, A. F. L.; Santos, L.; Ximenes, L. B.; Vasconcelos, C. T. M.	2018
Improving Preterm Infant Outcomes With Family Integrated Care and Mobile Technology	Nct (Clinical Trials Link)	2018
Novel Approach To Improving Lactation Support With Mobile Health Technology	Nct (Clinical Trials Link)	2017
An integrative review on mothers' experiences of online breastfeeding peer support: Motivations, attributes and effects	Moon, H.; Woo, K.	2021
Telephone support for women during pregnancy and the first six weeks postpartum	Lavender, T.; Richens, Y.; Milan, S. J.; Smyth, R. M.; Dowswell, T.	2013
TOWARD EVIDENCE-BASED PRACTICE. Online Participatory Intervention to Promote and Support Exclusive Breastfeeding: Randomized Clinical Trial	Krowchuk, Heidi V.	2019
Does telephone peer support and/or a midwife home visit in the early postnatal period increase breastfeeding duration?	Isrctn (Clinical Trials)	2004
Can a text message a week improve breastfeeding?	Gallegos, D.; Russell-Bennett, R.; Previte, J.; Parkinson, J.	2014
Effectiveness of interventions on breastfeeding self-efficacy and perceived insufficient milk supply: A systematic review and meta-analysis	Galipeau, R.; Baillot, A.; Trottier, A.; Lemire, L.	2018
An evaluation of a telephone-based postnatal support intervention for infant feeding in a regional Australian city	Fallon, A. B.; Hegney, D.; O'Brien, M.; Brodribb, W.; Crepinsek, M.; Doolan, J.	2005

Postpartum education and support on breastfeeding duration	Eichmann, Kelly; Baghurst, Timothy; Jayne, Chris	2016
Lactation education and breastfeeding duration	Eichmann, Kelly; Baghurst, Timothy; Jayne, Chris	2015
A systematic review of telephone support for women during pregnancy and the early postpartum period	Dennis, C. L.; Kingston, D.	2008
Interventions in primary care to promote breastfeeding: an evidence review for the U.S. Preventive Services Task Force	Chung, M.; Raman, G.; Trikalinos, T.; Lau, J.; Ip, S.	2008
Wrong Population (N = 2)		
Title	Authors	Published Year
Effectiveness of "home-but not alone" mobile-health application on parental outcomes	Isrctn (Clinical Trials)	2016
The comparison of access to an eHealth resource to current practice on mother and co-parent teamwork and breastfeeding rates: A randomized controlled trial	Abbass-Dick, J.; Sun, W.; Newport, A.; Xie, F.; Godfrey, D.; Goodman, W. M.	2020
Wrong Outcome (N = 17)		
Title	Authors	Published Year
Efficacy of a videoconferencing intervention compared with standard postnatal care at primary care health centres in Catalonia	Seguranyes, G.; Costa, D.; Fuentelsaz-Gallego, C.; Beneit, J. V.; Carabantes, D.; Gomez-Moreno, C.; Palacio-Tauste, A.; Pauli, A.; Abella, M.; Postpartum Telematics Research, G.	2014
Effect of telephone follow-up to improve self-efficacy, duration and exclusivity of breastfeeding	s7j, R. B. R.	2017
Providing an optimal start for vulnerable mother and child dyads during the early postpartum period	Nl (Clinical Trials)	2019

Breastfeeding preterm infants - a randomized controlled trial of the effectiveness of an Internet-based peer-support group	Niela-Vilen, H.; Axelin, A.; Melender, H. L.; Loyttyniemi, E.; Salantera, S.	2016
Essai contr√¥l√© d'un soutien t√©l√©phonique r√©gulier donn√© par une b√©n√©vole sur le d√©roulement et l'issue de l'allaitement	Mongeon, M.; Allard, R.	1995
Effect of telephone counseling on exclusive breastfeeding and postpartum depression	Irct201105093706N	2011
Pragmatic Trial to Evaluate the Effect of a Promotora Telephone Intervention on the Duration of Breastfeeding	Harris-Luna, M. L.; Badr, L. K.	2018
'Supporting a first-time mother': Assessment of success of a breastfeeding promotion programme	Gonzalez-Darias, A.; Diaz-Gomez, N. M.; Rodriguez-Martin, S.; Hernandez-Perez, C.; Aguirre-Jaime, A.	2020
Evaluation of an e-Learning Breastfeeding Program for Postpartum Mothers of Moderately High-Risk Newborn Infants Admitted to the Special Care Nursery	Fu, M. L.; Lee, T. Y.; Kuo, S. C.	2021
Assessing the Feasibility and Effectiveness of Two Prenatal Breastfeeding Intervention Apps in Promoting Postpartum In-Hospital Exclusive Breastfeeding	Farr, Rebecca S.; Rahman, Farah; O'Riordan, Mary Ann; Furman, Lydia	2019
Use of an interactive computer agent to support breastfeeding	Edwards, R. A.; Bickmore, T.; Jenkins, L.; Foley, M.; Manjourides, J.	2013
Telephone-based support prolongs breastfeeding duration in obese women: a randomized trial	Carlsen, E. M.; Kyhnaeb, A.; Renault, K. M.; Cortes, D.; Michaelsen, K. F.; Pryds, O.	2013
Telephone support for breastfeeding by primary care: a randomised multicentre trial	Balaguer Martinez, J. V.; Valcarce Perez, I.; Esquivel Ojeda, J. N.; Hernandez Gil, A.; Martin Jimenez, M. D. P.; Bernad Albareda, M.	2018

Breastfeeding Monitoring Improves Maternal Self-Efficacy and Satisfaction	Ahmed, A. H.; Roumani, A. M.	2020
Wrong Intervention (N = 13)		
Title	Authors	Published Year
Short message service communication improves exclusive breastfeeding and early postpartum contraception in a low- to middle-income country Setting: a randomised trial	Unger, J. A.; Ronen, K.; Perrier, T.; DeRenzi, B.; Slyker, J.; Drake, A. L.; Mogaka, D.; Kinuthia, J.; John-Stewart, G.	2018
Exclusive breastfeeding promotion by peer counsellors in sub-Saharan Africa (PROMISE-EBF): a cluster-randomised trial	Tylleskar, T.; Jackson, D.; Meda, N.; Engebretsen, I. M.; Chopra, M.; Diallo, A. H.; Doherty, T.; Ekstrom, E. C.; Fadnes, L. T.; Goga, A.; Kankasa, C.; Klungsoyr, J. I.; Lombard, C.; Nankabirwa, V.; Nankunda, J. K.; Van de Perre, P.; Sanders, D.; Shanmugam, R.; Sommerfelt, H.; Wamani, H.; Tumwine, J. K.; Group, P. E. S.	2011
Effect of a breastfeeding educational intervention: a randomized controlled trial	Souza, E.; Pina-Oliveira, A. A.; Shimo, A. K. K.	2020
Project to Promotion of Breastfeeding	Nct (Clinical Trials Link)	2017
A randomized controlled trial of telephone peer support's influence on breastfeeding duration in adolescent mothers	Meglio, G. D.; McDermott, M. P.; Klein, J. D.	2010
Effects of an educational technology on self-efficacy for breastfeeding and practice of exclusive breastfeeding	Javorski, M.; Rodrigues, A. J.; Dodt, R. C. M.; Almeida, P. C.; Leal, L. P.; Ximenes, L. B.	2018
Effects of an Infant Care Education Program for Mothers of Late-preterm Infants on Parenting Confidence, Breastfeeding Rates, and Infants' Growth and Readmission Rates	Eun Hye, Jang; Hyeon Ok, Ju	2020
The effect of lactation educators implementing a telephone-based intervention among low-income Hispanics: A randomised trial	Efrat, M. W.; Esparza, S.; Mendelson, S. G.; Lane, C. J.	2015

An assets-based intervention before and after birth to improve breastfeeding initiation and continuation: the ABA feasibility RCT	Clarke, J. L.; Ingram, J.; Johnson, D.; Thomson, G.; Trickey, H.; Dombrowski, S. U.; Sitch, A.; Dykes, F.; Feltham, M. G.; MacArthur, C.; et al.	2020
Effectiveness of breastfeeding peer counseling in a low-income, predominantly Latina population: a randomized controlled trial	Chapman, D. J.; Damio, G.; Young, S.; Perez-Escamilla, R.	2004
The effect of peer counseling on breastfeeding behavior of primiparous mothers: A randomized controlled field trial	Azimi, Nasimeh; Nasiri, Ahmad	2020
Effect of telephone follow-up on postdelivery breastfeeding and maternal attachment	Adib-Hajbaghery, Mohsen; Hashemi-Demneh, Tayebeh	2017
Postnatal counseling on exclusive breastfeeding using video - experience from a tertiary care teaching hospital, south India	Adhisivam, B.; Vishnu Bhat, B.; Poorna, R.; Thulasingam, M.; Pournami, F.; Joy, R.	2017
Wrong Comparator (N = 1)		
Title	Authors	Published Year
Impact of the Lactation Advice Through Texting Can Help (LATCH) Trial on Time to First Contact and Exclusive Breastfeeding among WIC Participants	Martinez-Brockman, J. L.; Harari, N.; Segura-Perez, S.; Goeschel, L.; Bozzi, V.; Perez-Escamilla, R.	2018
Study Protocol (N = 7)		
Title	Authors	Published Year
The effectiveness of using a WeChat account to improve exclusive breastfeeding in Huzhu County Qinghai Province, China: protocol for a randomized control trial	Wu, Q.; Huang, Y.; van Velthoven, M. H.; Wang, W.; Chang, S.; Zhang, Y.	2019
A 3-Arm randomised controlled trial of Communicating Healthy Beginnings Advice by Telephone (CHAT) to mothers with infants to prevent childhood obesity	Wen, L. M.; Rissel, C.; Baur, L. A.; Hayes, A. J.; Xu, H.; Whelan, A.; Hua, M.; Shaw, M.; Phongsavan, P.	2017

WeChat-based intervention to support breastfeeding for Chinese mothers: protocol of a randomised controlled trial	Tang, L.; Lee, A. H.; Binns, C. W.; Duan, L.; Liu, Y.; Li, C.	2020
Ringing Up about Breastfeeding: a randomised controlled trial exploring early telephone peer support for breastfeeding (RUBY) - trial protocol	Forster, D. A.; McLachlan, H. L.; Davey, M. A.; Amir, L. H.; Gold, L.; Small, R.; Mortensen, K.; Moorhead, A. M.; Grimes, H. A.; McLardie-Hore, F. E.	2014
The effectiveness of proactive telephone support provided to breastfeeding mothers of preterm infants: study protocol for a randomized controlled trial	Ericson, J.; Eriksson, M.; Hellstrom-Westas, L.; Hagberg, L.; Hoddinott, P.; Flacking, R.	2013
Evaluation of the impact of breastfeeding support groups in primary health CENTRES in Andalusia, Spain: a study protocol for a cluster randomized controlled trial (GALMA project)	Rodriguez-Gallego, I.; Leon-Larios, F.; Ruiz-Ferron, C.; Lomas-Campos, M. D.	2020
Latch On: A protocol for a multi-centre, randomised controlled trial of perinatal support to improve breastfeeding outcomes in women with a raised BMI	O'Reilly, S. L.; O'Brien, E. C.; McGuinness, D.; Mehegan, J.; Coughlan, B.; O'Brien, D.; Szafranska, M.; Callanan, S.; Hughes, S.; Conway, M. C.; Brosnan, M.; Sheehy, L.; Murtagh, R.; O'Hagan, L.; Murray, S.; Scallon, C.; Dunn, E.; Power, P.; Woodcock, M.; Carroll, A.; Corbett, M.; Walsh, M.; Keogh, R.; McAuliffe, F. M.	2021
Improving Breastfeeding by Empowering Mothers in Vietnam: A Randomised Controlled Trial of a Mobile App	Doan, T. T. D.; Binns, C.; Pham, N. M.; Zhao, Y.; Dinh, T. P. H.; Bui, T. T. H.; Tran, T. C.; Nguyen, X. H.; Giglia, R.; Xu, F.; Lee, A.	2020
Multiple Reasons (N = 6)		
Title	Authors	Published Year
Effectiveness of supportive parenting educational programme	Isrctn (Clinical Trials)	2017
Evaluating effects of a prenatal web-based breastfeeding education programme in Taiwan	Huang, M. Z.; Kuo, S. C.; Avery, M. D.; Chen, W.; Lin, K. C.; Gau, M. L.	2007

The effect of postpartum lactation counseling on the duration of breast-feeding in low-income women	Grossman, L. K.; Harter, C.; Sachs, L.; Kay, A.	1990
Volunteers' experiences of providing telephone-based breast-feeding peer support in the RUBY randomised controlled trial	Grimes, H. A.; Shafiei, T.; McLachlan, H. L.; Forster, D. A.	2020
Impacts of the 10 Steps for Healthy Feeding in Infants: a Randomized Field Trial	Alegre, Federal University of Health Science of Porto; Tecnol√≥gico, Conselho Nacional de Desenvolvimento Cient√≠fico e	2001
Study Duplicate (N = 51)		
Title	Authors	Published Year
Telephone peer counselling of breastfeeding among WIC participants: a randomized controlled trial	Shalofsky, Teresa	2015
The Use of and Experiences With Telelactation Among Rural Breastfeeding Mothers: Secondary Analysis of a Randomized Controlled Trial	Kapinos, K.; Kotzias, V.; Bogen, D.; Ray, K.; Demirci, J.; Rigas, M. A.; Uscher-Pines, L.	2019
Use of virtual breastfeeding support among underserved, rural mothers	Uscher-Pines, L.; Kapinos, K.; Demirci, J.; Ghosh-Dastidar, B.; Ray, K.; Kotzias, V.; Bogen, D.	2019
Telephone Support Intervention to Improve Breastfeeding	University of Colorado, Denver; Control, Centers for Disease; Prevention	2005
Cell phone based peer counselling can support exclusive breastfeeding: A randomized controlled trial in Kenya	Sellen, D.; Mbugua, S.; Webb-Girard, A.; Lou, W.; Duan, W.; Kamau-Mbuthia, E.	2014
The Effect of Varied Intensities of Breastfeeding Peer Support on Duration of Breastfeeding Among Oregon WIC Participants	Program, Oregon WIC; Food, USDA; Service, Nutrition	2005
A Mobile, Semi-automated Text Message-based Intervention to Prevent Perceived Low or Insufficient Milk Supply	Pittsburgh, University of; Research, National Institute of Nursing	2017

Effectiveness of Mobile Phone-Based Support on Exclusive Breastfeeding and Infant Growth in Nigeria: a Randomized Controlled Trial	Ogaji, D. S.; Arthur, A. O.; George, I.	2020
Effects of an online social network on promoting and supporting breastfeeding	nwbg, R. B. R.	2016
Mother's Milk Messaging: Evaluation of a Bilingual Application (APP) to Support Initiation and Exclusive Breastfeeding in New Mothers	NCT02958475 (Clinical Trials)	2016
Evaluation of Effectiveness of Cell Phone Technology as Community Based Intervention to Improve Exclusive Breast Feeding	NCT01383070 (Clinical Trials)	2011
The LATCHING Pilot Project	Nct (Clinical Trials Link)	2018
The Effectiveness of Proactive Telephone Support Provided to Breastfeeding Mothers of Preterm Infants	Nct (Clinical Trials Link)	2013
The Effect of Varied Intensities of Breastfeeding Peer Support on Duration of Breastfeeding Among Oregon WIC Participants	Nct (Clinical Trials Link)	2014
Telephone Support Intervention to Improve Breastfeeding	Nct (Clinical Trials Link)	2008
Providing Peer Mother Support Through Cell Phone and Group Meetings to Increase Exclusive Breastfeeding in Kenya	Nct (Clinical Trials Link)	2011
Professional Breastfeeding Support Intervention	Nct (Clinical Trials Link)	2013
Impact of a Smartphone Application on Postpartum Weight Loss and Breastfeeding Rates Among Low-income, Urban Women	Nct (Clinical Trials Link)	2017

Expanding Rural Access to Breastfeeding Support Via Telehealth: the Tele-MILC Trial	Nct (Clinical Trials Link)	2016
Lactation Achievement With Texts at Home	Nct (Clinical Trials Link)	2019
Improving Exclusive Breastfeeding Via Mobile Phone Text Messages	Nct (Clinical Trials Link)	2019
A Mobile-health Pilot Experiment Targeting Mothers With Newborns in Rural Areas of San Juan Sacatepequez, Guatemala	Nct (Clinical Trials Link)	2014
Controlled study of a regular telephone support program given by volunteers on the establishment of breastfeeding	Mongeon, M.; Allard, R.	1995
Process indicators for a randomized trial of cell phone based peer counseling to support exclusive breastfeeding in Kenya	Mbugua, S.; Kamau-Mbuthia, E.; Webb, A.; Kalungu, S.; Sarange, C.; Lou, W.; Duan, W.; Dennis, C.; Aidams, B.; Nommsen-Rivers, L.; Sellen, D.	2013
Impact of the lactation advice through texting can help (LATCH) randomized controlled trial	Martinez-Brockman, J. L.; Harari, N.; Segura-Perez, S.; Goeschel, L.; Perez-Escamilla, R.	2017
Effect of a Novel Smartphone Application on Breastfeeding Rates Among Low-Income, First-Time Mothers Intending to Exclusively Breastfeed: Secondary Analysis of a Randomized Controlled Trial	Lewkowitz, A. K.; Lopez, J. D.; Werner, E. F.; Ranney, M. L.; Macones, G. A.; Rouse, D. J.; Savitz, D. A.; Cahill, A. G.	2021
Effect of a Novel Smartphone Application on Breastfeeding Rates Among Low-Income, First-Time Mothers Intending to Exclusively Breastfeed: secondary Analysis of a Randomized Controlled Trial	Lewkowitz, A. K.; Lopez, J. D.; Werner, E. F.; Ranney, M. L.; Macones, G. A.; Rouse, D. J.; Savitz, D. A.; Cahill, A. G.	2020
45: Impact of a novel smartphone application on low-income women's breastfeeding rates: a randomized controlled trial	Lewkowitz, A. K.; Lopez, J. D.; Carter, E. B.; Duckham, H.; Strickland, T.; Macones, G. A.; Cahill, A. G.	2020

Cell phone based peer counseling to support exclusive breastfeeding is associated with more frequent help and decreased breastfeeding problems	Kamau-Mbuthia, E.; Mbugua, S.; Webb Girard, A.; Kalungu, S.; Sarange, C.; Lou, W.; Duan, W.; Dennis, C. L.; Nommsen-Rivers, L.; Aidam, B.; Sellen, D.	2013
The effects of breastfeeding peer support on breastfeeding satisfaction among Japanese mothers: a randomized controlled trial	JPRN-UMIN000019626	2015
The effects of breastfeeding peer support on breastfeeding satisfaction among Japanese mothers: a randomized control trial	Jprn, U.	2015
Proactive telephone support for breastfeeding women in disadvantaged areas provided by a postnatal ward feeding support team	Isrctn (Clinical Trials)	2010
The effect of peer support on the pattern of breastfeeding among mothers with a history of unsuccessful breastfeeding
.	IRCT2013010111964N1 (Clinical Trials)	2013
Process evaluation for the FEeding Support Team (FEST) randomised controlled feasibility trial of proactive and reactive telephone support for breastfeeding women living in disadvantaged areas	Hoddinott, P.; Craig, L.; Maclennan, G.; Boyers, D.; Vale, L.; Grampian, N. H. S.; the University of Aberdeen, F. p t	2012
Impact of SMS text messages to improve exclusive breastfeeding and reduce other adverse infant feeding practices in yangon, Myanmar: A randomized controlled trial	Hmone, M. P.; Li, M.; Agho, K.; Dibley, M.	2017
Does increased use of breastfeeding smartphone applications improve breastfeeding rates among low-income women?	Griffin, L.; Lopez, J.; Macones, G.; Cahill, A.; Lewkowitz, A.	2020
Effect of Novel Breastfeeding Smartphone Applications on Breastfeeding Rates	Griffin, L. B.; Lopez, J. D.; Ranney, M. L.; Macones, G. A.; Cahill, A. G.; Lewkowitz, A. K.	2021

Effectiveness of Midwife Phone Support With the to Reduce the Early Abandonment of Breastfeeding	Foundation, Jordi Gol i Gurina	2012
Ringing up about breastfeeding: a random controlled trial exploring early telephone peer support for breastfeeding (RUBY) ‚Äì primary outcomes	Forster, D.; McLardie-Hore, F.; McLachlan, H.; Davey, M. A.; Amir, L. H.; Gold, L.; Mortensen, K.; Moorhead, A. M.; Grimes, H.; Shaifei, T.	2018
Role of phones in improving breast feeding rates	CTRI/2016/12/007538	2016
Effectiveness of Wechat health education on improve breastfeeding	ChiCtr (Clinical Trials)	2018
Randomized controlled trial to evaluate a telephone support intervention for breastfeeding in low-income Latina mothers	Bunik, M.; Shobe, P.; O'Connor, M. E.; Beaty, B.; Langendoerfer, S.; Crane, L.	2007
Telephone Support Intervention for Breastfeeding in Low-Income Latina Mothers	Bunik	2007
Ringing Up about Breastfeeding: a randomised control trial exploring earlY telephone peer support for breastfeeding.	ACTRN12612001024831 (Clinical Trials)	2012
Telephone lactation counseling and breast feeding practices: a randomized controlled trial	ACTRN12611001014943 (Clinical Trials)	2011
Using the Internet to support breastfeeding duration	ACTRN12610000062022 (Clinical Trials)	2010
Improving infant and young child feeding practices: assessing the effectiveness of breastfeeding promotion program (randomized controlled trial) using mobile phone as a communications tools in Yangon and nearby regions, Myanmar	Actrn (Clinical Trials)	2015
Feasibility and Effectiveness of Telelactation among Rural Breastfeeding Women		2019

Lactation advice through texting can help (LATCH): An analysis of intensity of engagement via two-way text messaging	Martinez-Brockman, J. L.; Harari, N.; Perez-Escamilla, R.	2017
Impact of SMS text messages to improve exclusive breastfeeding: A randomized controlled trial in Myanmar	Hmone, M. P.; Li, M.; Agho, K.; Dibley, M. J.	2017
Telephone-based support prolongs breastfeeding duration in obese women: a randomized trial	Carlsen, E. M.; Kyhnaeb, A.; Renault, K. M.; Cortes, D.; Michaelsen, K. F.; Pryds, O.	2014
Abstract/Conference Abstract (N =8)		
Title	Authors	Published Year
A randomized controlled trial indicates benefits of cell phone based peer counseling to support exclusive breastfeeding in Kenya	Sellen, D.; Mbugua, S.; Webb Girard, A.; Kalungu, S.; Sarange, C.; Lou, W.; Duan, W.; Dennis, C. L.; Nommsen-Rivers, L.; Aidam, B.; Kamau-Mbuthia, E.	2013
An innovative, mobile-health enhanced, peer-counseling program to improve breastfeeding among low-income, minority populations in washington, DC	Robert, R.; Roess, A.; Cleaves, E.; Kuehn, D.; Thompson, P.	2017
Effect of Telephone Counseling on Continuity and Duration of Breastfeeding among Primiparus Women	Raisi Dehkordi, Ziba; Raei, Mehdi; Ghassab Shirazi, Morvarid; Ahmad Reza Raisi Dehkordi, Seyed; Mirmohammadali, Mandana	2012
Midwives' mobile phone support for breastfeeding	Pauli Cabezas, M. A.; Gol Gomez, R.; Amoros Ferrer, P.	2014
Application of mobile-phone consultation for follow-up of breast feeding continuation in primiparous women	Parsa, P.; Boojar, A.; Bakht, R.; Roshanaie, G.	2018
98 Smartphone-based counseling and support platform and the effect on postpartum lactation-a randomized controlled trial	Miremberg, H.; Yirmiya, K.; Rona, S.; Gonen, N.; Marom, O.; Pohol, A.; Kovo, M.; Bar, J.; Weiner, E.	2021
Telemedicine breastfeeding support following late preterm delivery: A randomized trial	Kair, L. R.; Schwarz, E. B.; Marcin, J. P.; Tancredi, D. J.; Chantry, C. J.	2019

Low-income Latina mothers' perspectives on breastfeeding issues and participation in a telephone based support intervention	Bunik, M.; Shobe, P.; Crane, L.; Kempe, A.	2007
Report Not Retrieved (N = 38)		
Title	Authors	Published Year
The Development and Evaluation of a Text Message Program to Prevent Perceived Insufficient Milk Among First-Time Mothers: Retrospective Analysis of a Randomized Controlled Trial	Demirci, J. R.; Suffoletto, B.; Doman, J.; Glasser, M.; Chang, J. C.; Sereika, S. M.; Bogen, D. L.	2020
Phone Breastfeeding Support for Premature Babies	Nct (Clinical Trials Link)	2021
Effect of telephone-based postnatal care on the health of mothers and their newborns	Isrctn (Clinical Trials)	2021
Effectiveness of SMS text messaging to fathers and mothers to improve exclusive breastfeeding in Tigray region, Northern Ethiopia	ACTRN12618001481268 (Clinical Trials)	2018
Telephone peer counseling of breastfeeding among WIC participants: a randomized controlled trial	Reeder, J. A.; Joyce, T.; Sibley, K.; Arnold, D.; Altindag, O.	2014
Effectiveness of Web-based programs in improving breastfeeding self-efficacy	Pate, B. L.	2009
Walezi Pamoja: evaluating the impact of breastfeeding support and information on rates of exclusive breastfeeding among mothers in Kiambu County, Kenya	Pactr	2019
Telephone Support From Primary Care for Breastfeeding Mothers	Nct (Clinical Trials Link)	2014
Telemonitoring to improve maternal confidence in breastfeeding	m7vc, R. B. R.	2018

The effect of support through telephone counseling on breastfeeding problems and exclusive breastfeeding	Irct20190718044259N (Clinical Trials)	2019
An educational intervention based on a mobile phone application for improving maternal breastfeeding of infants in their first six month of life in Urmia, Iran	Irct20190705044103N (Clinical Trials)	2020
Effectiveness of the Distance Education Program on the Mothers' Empowerment in Breast-Feeding	Irct20180520039728N (Clinical Trials)	2018
breast feeding and support	Irct2017080735540N (Clinical Trials)	2017
Effect of tele counseling on the continuity and duration of breastfeeding in women In Minudasht health center on summer 2014	Irct20170707034931N (Clinical Trials)	2019
The Effect of Telephone Supportive Counseling in The Breastfeeding Self-efficacy of Mothers with Preterm Infant 34-36 Weeks	Irct20150731023423N (Clinical Trials)	2020
Mobile Phone Short Messages to Improve Exclusive Breastfeeding and Reduce Adverse Infant Feeding Practices: Protocol for a Randomized Controlled Trial in Yangon, Myanmar	Hmone, M. P.; Li, M.; Alam, A.; Dibley, M. J.	2017
video assisted counseling for mothers on breastfeeding	Ctri (Clinical Trials)	2013
Efectividad de una consulta online de Enfermer√≠a en el seguimiento e instauraci√≥n de la lactancia materna	Araque Garc√≠a, Jenifer; Garc√≠a Perea, Eva; Pedraz Marcos, Azucena; Alba Diego, Rosa Mar√≠a	2018
Does post-natal breastfeeding support improve rates of breastfeeding?	Actrn (Clinical Trials)	2018
The Effect of Breastfeeding Support Provided Via Video-conferencing	University, Kahramanmaras Sutcu Imam	2020

Using Mobile Phone Text Messaging System to Improve Exclusive Breastfeeding Rate in a Resource-poor Caribbean Island	University of California, Davis; Public Hospital Roatan, Honduras; University of California, San Francisco	2017
LIFT: Telemedicine Breastfeeding Support	University of California, Davis; Health, National Institutes of	2019
Lactation Achievement With Texts at Home	Pennsylvania, University of	2020
Happy, Healthy, Loved: A Mobile-delivered Breastfeeding Self-efficacy Intervention for First Time Parents	OhioHealth; University, Denison; College, Claremont McKenna	2020
Web-based Educational Intervention on Breastfeeding Self-efficacy and Breastfeeding Outcome	Nct (Clinical Trials Link)	2021
The Impact of a Daily Smartphone-based Communication Among Postpartum Women on Breastfeeding Rates	Nct (Clinical Trials Link)	2019
Feasibility and Effectiveness of WhatsApp Online Group on Breastfeeding by Peer Counsellors	Nct (Clinical Trials Link)	2021
A WeChat-based Intervention to Support Breastfeeding	Nct (Clinical Trials Link)	2020
The Effect of Telephone Support for Breastfeeding Follow-up on Infantile Colic and Maternal Breastfeeding Self-efficacy	Nct (Clinical Trials Link)	2020
The Impact of Telelactation Services on Breastfeeding Outcomes	Nct (Clinical Trials Link)	2021
A Smartphone-Based Approach to Improved Breast-Feeding Rates And Self-Efficacy	Nct (Clinical Trials Link)	2021
Telemedicine Breastfeeding Support	Nct (Clinical Trials Link)	2019
Breastfeeding Support Provided to Mothers Through WhatsApp Messaging Application	Nct (Clinical Trials Link)	2020
Effectiveness of Midwife Phone Support With the to Reduce the Early Abandonment of Breastfeeding	Nct (Clinical Trials Link)	2019

MAMA NO STRESS Project. The Effects of the "HAPPY MAMA" Intervention	Nct (Clinical Trials Link)	2019
Comparison of Breast Feeding Counseling and Video Demonstration on Exclusive Breast Feeding Rates at 6 Weeks	Nct (Clinical Trials Link)	2009
A Mobile-health Pilot Experiment Targeting Mothers With Newborns in Rural Areas of San Juan Sacatepequez, Guatemala	Marroqu√≠n, Universidad Francisco; Ecole Polytechnique, France; The SHM Foundation, UK	2013
A smartphone application to support breastfeeding for new mothers in Vietnam	Actrn (Clinical Trials)	2019