Health Effects for Infants and Young Children Associated with Breastfeeding

A Rapid Review

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Region of Peel
working with you

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Key Messages

Breastfeeding offers protection against otitis media, gastrointestinal and lower respiratory infections in infancy; more breastfeeding increases the protective effect.

Ever having been breastfed offers a modest protective effect against becoming overweight or obese in childhood.

Night-time breastfeeding beyond 12 months of age may increase the risk of dental caries.

There is no evidence of an association between the amount of breastfeeding and development of food allergies.

Evidence is inconclusive for an association between breastfeeding and the development of Types 1 and 2 diabetes, asthma, eczema and allergic rhinitis.

Executive Summary

Research Questions

What are the health effects of being breastfed or fed expressed mother's milk for healthy term infants? Is there evidence of a dose-response relationship?

Context

Key messages about the health benefits of breastfeeding for infants, based on evidence from one systematic review (1) informed a Region of Peel – Public Health media campaign in 2009. These key messages have not been updated. In 2017, Family Health staff identified a need to update messaging about breastfeeding for new and expectant parents and health care professionals.

Nine health outcomes of interest in infancy and early childhood were identified by the review team, including: ear, gastrointestinal, and respiratory infections; asthma, eczema and allergies; oral health; overweight/obesity and diabetes. Local data indicate that respiratory and gastrointestinal infections are among the top five leading causes of emergency department visits for children from birth to age nine years (See Appendix A).

Methods and Results

Librarian-conducted searches of published literature identified 300 unique titles. One additional title was suggested by a key informant. Seven relevant systematic reviews were assessed for quality; all were included. A search of grey literature was not conducted.

Synthesis of Findings

Reported health effects of being breastfed include a protective effect against development of:

- **Otitis media**, in the first two years of life, with increased protection when infants are exclusively breastfed compared to partially breastfed.
- **Gastrointestinal infections**, in the first six months of life, with increased protection when infants are exclusively breastfed compared to partially breastfed and when breastfed for a longer rather than shorter number of months.
- **Lower respiratory infections,** in the first year of life, when exclusively breastfed for four months and then partially breastfed. No effect was detected for infants partially breastfed for up to six months.
- **Overweight/obesity** in childhood, with reduced odds in children who were ever breastfed compared to never breastfed. The effect was not modified by breastfeeding exclusivity or duration.

Breastfeeding for longer than 12 months, particularly nocturnal breastfeeding, may increase the risk of **dental caries**.

No association between breastfeeding and development of **food allergies** was detected.

Evidence is inconclusive for an association between breastfeeding and the development of **Types 1 and 2 diabetes**, **asthma, eczema,** and **allergic rhinitis.**

Practice Recommendations

1. Develop key messages about the importance of breastfeeding in reducing the odds of adverse health outcomes in infancy and childhood.

    - Breastfeeding offers protection against otitis media, gastrointestinal, and lower respiratory infections; more breastfeeding increases the protection.

    - Ever having been breastfed offers a modest protective effect against becoming overweight or obese in childhood.

    - Night-time breastfeeding beyond 12 months of age may increase the risk of dental caries.

2. Consider three audiences residents of Peel region who are pregnant, or parents of young infants, and health care practitioners – when developing key messages about the health effects of breastfeeding.

3. Incorporate key messages into the Family Health Division's nursing practice standards.

4. Monitor the literature for emerging evidence examining relationships between infant feeding and development of the gut microbiome and overweight/obesity.

1 Issue

The Region of Peel - Public Health encourages parents to make informed decisions about infant feeding during pregnancy and right from birth. Key messages about the health benefits of breastfeeding for infants, based on evidence from one systematic review (1) informed a Region of Peel – Public Health media campaign developed in 2009; these key messages have not been updated.

The practice question is:

What are the health effects of being breastfed or fed expressed mother's milk for healthy term infants? Is there evidence of a dose-response relationship?

This evidence will be used when updating key messages for expectant and new parents, and health care professionals. In addition, updated messaging could be used when marketing Region of Peel – Public Health services.

Anecdote:

In 2017, there was much discussion locally, provincially and nationally about the pressure women feel to breastfeed which contributed to a movement to change the slogan "Breast is Best" to "Fed is Best". During this time, mothers in Peel expressed concern about the pressures of breastfeeding through the Parenting in Peel Facebook page with comments such as "the benefits (of breastfeeding) were not worth the price we were both paying". One mother enrolled in the Breastfeeding Companions peer support program expressed feelings of guilt around her inability to provide breastmilk – "I can't provide him with a thousand other things that are richly available in breastmilk but not in formula".

2 Context

Local data show that almost all Peel mothers surveyed in 2016 began breastfeeding in hospital or during the first few days at home.(2) When asked to recall their intentions (during pregnancy) about feeding their baby in the first four weeks of life, the majority of mothers in Peel (78%) planned to feed breast milk only.(2) The amount of breastfeeding declined over the next six months until 67% were providing any breast milk and 14% of mothers were exclusively breastfeeding.(2) These figures are slightly higher than in 2015.(2)

The Region of Peel - Public Health achieved Baby-Friendly Initiative (BFI) designation in 2009. We are committed to providing parents with evidence to use in deciding how and what to feed their infants and young children. Currently, within the Family Health Division, all staff provide information to clients based on breastfeeding key messages which were developed nearly a decade ago. It is time to update these messages.

In addition to providing evidence to update key messages for parents, this research review will inform the planning of infant feeding programs and services in the community and our local hospitals. Hospital Liaison public health nurses supported Trillium Health Partners through the process to achieve BFI designation in 2017. A second Peel hospital, William Osler Health Services, is in the preliminary phases of planning for BFI designation at their two sites.

Local data indicate that respiratory and gastrointestinal infections are among the top five leading causes of emergency department visits for children from birth to age nine years. (See Appendix A).

The review team identified nine health outcomes of interest including: ear, gastrointestinal, and respiratory infections; asthma, eczema and allergies; oral health; overweight/obesity and diabetes when formulating the questions - What are the health effects of being breastfed or fed expressed mothers' milk for healthy term infants? Is there evidence of a dose-response relationship?

3 Conceptual Framework

The Family Health Division adopted *Healthy Eating Right from the Start*, a conceptual model developed in 2016, to inform the Nurturing the Next Generation strategic priority. See Appendix B. The centre of the model depicts healthy eating from a life stage perspective; this review is focused on breastfeeding right from birth. The outcomes of interest linked to healthy eating, fall within the spheres of disease prevention and healthy weights.

4 Literature Review Question

Family Health staff are interested in answering the questions:

> **What are the health effects of being breastfed or fed expressed mother's milk for healthy term infants? Is there evidence of a dose-response relationship?**

Formulating the question using the Population, Exposure, Outcome framework identified the following search terms:

Population – healthy infants born at term

Exposure – breastfeeding or expressed breast milk

Outcomes – health outcomes in infancy and early childhood including ear, gastrointestinal, and respiratory infections; overweight/obesity; diabetes; asthma, eczema, allergies; and dental caries.

5 Literature Search

A librarian specialist conducted searches of published literature in April 2017. The following databases were searched: Medline, EBM Reviews, Cochrane Database of Systematic Reviews, Global Health, Ovid Healthstar and CINAHL (Cumulative Index for Nursing and Allied Health Literature). Searches were restricted to synthesized evidence (guidelines, reviews, and meta-analyses) published from 2007 onwards. (See Appendix C). In addition to these searches, the reference list of an updated Cochrane Review was checked for additional citations, and one new textbook was identified by the rapid review team. A grey literature search was not conducted.

One reviewer sent emails asking four experts[1] to identify individuals conducting research where exposure to breast milk or breastfeeding is more accurately quantified than exclusive, partial or mixed feeding. No responses were received after two requests.

In January, 2018, Dr. John Frank[2] was asked to identify research evidence which illustrated the correlation between exclusive breastfeeding and the prevention of

[1] Dr. Michael Kramer, Dr. Katie Hinde (seen on TED talks) and Dr. Leon Mitoulas (identified by Dr. Cindy-Lee Dennis), and Dr. Stephen Lye.

[2] Dr. John Frank, Director of Scottish Collaboration for Public Health Research and Policy, University of Edinburgh, gave a lecture on chronic disease prevention at the University of Waterloo (2017.10.03) attended by Judy Buchan who contacted him via email (2018.01.16).

obesity. He suggested one systematic review on the long-term consequences of breastfeeding completed for the World Health Organization in 2015.(3)

6 Relevance Assessment

Two reviewers independently screened all titles and abstracts and together selected articles for full text review using the following criteria:

- Inclusion criteria: English language; systematic reviews including studies in settings comparable to Canada; explicit reference to breastfeeding or feeding breast milk; report infant or child health outcomes including: ear, gastrointestinal, and respiratory infections; overweight/obesity; diabetes; asthma, eczema and allergies; oral health.

- Exclusion criteria: Duplicates; focus on health outcomes in adults; report infant or child health outcomes related to: cognitive development, childhood leukemia, or development of the gut microbiome.

7 Results of the Search

Librarian searches identified 396 titles of which 96 were duplicates. After screening titles and abstracts, 12 articles were identified for full text review. Six articles were excluded for the following reasons: two were included in other reviews; two were set in developing countries; one article was not retrievable; one article had an outcome that was not relevant, leaving six systematic reviews for critical appraisal. The textbook was excluded due to data duplication. One additional systematic review, identified by an expert, was added to those to be appraised. (See Appendix D).

8 Critical Appraisal

Two independent reviewers critically appraised the seven relevant articles, using the Health Evidence Quality Assessment Tool – review articles.(4) Consensus on scoring was reached through discussion. Six systematic reviews were rated strong and one was rated moderate quality; all seven were included.

9 Description of Included Studies

Studies of the effect of exposure to breastfeeding/being fed breast milk are mainly observational, since it would be unethical to randomly assign type of feeding at birth. The results of case-control studies, a type of observational study, are reported either as odds ratios (OR) or adjusted odds ratios (AOR). Adjustment indicates that selected confounders have been controlled for in data analysis and reporting. All included reviews indicate whether or not potential confounders were controlled for in the primary studies and the meta-analyses.

The seven included reviews are described below in order of quality.

Long-term consequences of breastfeeding on cholesterol, obesity, systolic blood pressure and type 2 diabetes: a systematic review and meta-analysis. Horta BL, et al. (2015) (3,3)

This strong quality systematic review (rated 9/10) summarizes long-term health effects of breastfeeding using evidence from 105 primary studies of which 71 were set in high-income countries and 34 in middle- or low-income countries. Both observational and randomized study designs were included. Studies without an internal comparison group

were excluded. Evidence of an association between breastfeeding and the following health outcomes - overweight/obesity, blood pressure, cholesterol and type 2 diabetes – was reported as pooled odds ratios (OR). This review updates two systematic reviews completed for the World Health Organization in 2006 and 2011.

Breastfeeding, introduction of other foods and effects on health: a systematic literature review for the 5th Nordic Nutrition Recommendations. Hornell A, et al. (2013) (5,5)

This strong quality systematic review (rated 9/10) summarizes the short- and long-term health effects of breastfeeding using evidence from 60 publications: 13 systematic reviews/meta-analyses, 41 prospective cohort studies and 6 publications arising from the Promotion of Breastfeeding Interventions Trial (PROBIT)[3]. Studies were included if they reported on duration of any and exclusive breastfeeding and introduction of foods other than breast milk in study populations that were relevant to Nordic countries. Health outcomes included: acute otitis media, gastrointestinal infection, lower respiratory infection, overweight and obesity, diabetes mellitus (type 1 and 2), atopic disease, asthma, blood pressure, serum cholesterol, cancer, IQ and neurological development, celiac disease, inflammatory bowel disease and outcomes related to the introduction of complementary foods. Results are reported as relative risk (RR) and odds ratios (OR).

Breastfeeding and childhood acute otitis media: a systematic review and meta-analysis. Bowatte G, et al. (2015) (6)

[3] The PROBIT study was conducted in the Republic of Belarus by Dr. Michael Kramer and colleagues. Hospitals were randomized to follow the 10 steps of the BFI or to usual care. Health outcomes of children born in 1996/1997 were analyzed by hospital group.

In this strong quality meta-analysis (rated 9/10), the authors examined the association between duration and exclusivity of breastfeeding for infants born at term and the risk of acute otitis media (AOM) in infancy and childhood. The 24 observational studies were cohort (18/24) and cross-sectional (6/24) designs conducted in Europe and North America. The reviewers accepted the study authors' definitions of breastfeeding which included: exclusively breastfed compared to not exclusive/not breastfed; ever compared to never breastfed; shorter (≤3-4 months) compared to longer (≥3-4 months) duration of exclusive or partial breastfeeding; more or less breastfeeding. The sole health outcome of interest was acute otitis media diagnosed by a physician, reported by a parent or recorded in a health database.

Breastfeeding and asthma and allergies: a systematic review and meta-analysis. Lodge CK, et al. (2015) (7)

The objective of this strong quality systematic review (rated 9/10) was to examine the association between breastfeeding and childhood allergic disease in children who were born at term (≥37 weeks gestation). Eighty-nine observational studies of cohort, cross-sectional and case-control designs were included. Results were stratified by gross national income per capita into high-income and middle-/low-income countries. The exposure to breastfeeding was categorized as ever compared to never; more breastfeeding for up to 3-4 months; more or less breast milk. The authors reported on the following outcomes: asthma (onset between 5-18 years); eczema; allergic rhinitis/hay fever; and food allergies. Ascertainment of each outcome was by physician diagnosis, parent- or self-reported, or recorded in a health database. In addition,

diagnosis of food allergies was ascertained from serum IgE, skin prick testing, or oral food challenge.

Systematic review and meta-analyses of risk factors for childhood overweight identifiable during infancy. Weng SF, et al. (2012) (8)

The authors of this strong quality meta-analysis (rated 9/10) sought to identify risk factors for childhood overweight and obesity that can be identified in the first year of life. Overweight/obesity was diagnosed at two years of age or beyond and quantified using Body Mass Index (BMI). Cut off scores for BMI percentiles for overweight and obesity were set by reference groups and varied somewhat between countries. Overweight was defined as a sex-specific BMI ≥85th to 95th percentile and obesity defined as BMI ≥95th to 98th percentile. Thirty prospective studies were identified of which ten, conducted in countries comparable to Canada, examined breastfeeding.

Breastfeeding and the risk of dental caries: a systematic review and meta-analysis. Tham R, et al. (2015). (9)

Current evidence for an association between breastfeeding and dental caries was summarized in this strong quality systematic review (rated 9/10). The 63 studies included in the synthesis were of cross-sectional (n=46), cohort (n=14) and case-control (n=3) designs. Seventeen of the 63 studies were included in a meta-analysis. These 17 studies were conducted in low-, middle- and high-income countries which are not all comparable to Canada. The exposure to breastfeeding was categorized as never compared to any, and shorter compared to longer duration. The outcome of interest, development of dental caries in permanent teeth, was determined by reports by

qualified practitioners or researchers, by parents or through health records databases. The authors note that lack of control for confounders such as other foods/drinks in the diet, oral hygiene and maternal oral health, limits reliability of the results.

Current evidence on the associations of breastfeeding, infant formula and cow's milk introduction with type 1 diabetes mellitus: a systematic review. Patelarou, E. et al. (2012) (10)

This systematic review of moderate quality (rated 6/10) evaluated the potential impact of type of infant feeding, duration of breastfeeding, and timing of introduction of formula or cow's milk on development of type 1 diabetes. The 28 included studies were conducted in a variety of developed countries primarily European. All studies were case-control designs except for a single prospective cohort study. Studies of healthy children with a family history of type 1 diabetes were excluded. The reviewers described the effect of amount and duration of breastfeeding on the risk of developing type 1 diabetes, reporting a range of ORs without performing a meta-analysis.

10 Synthesis of Findings

Researchers use varying definitions of breastfeeding with respect to both the amount and duration which limits reviewers' ability to be specific about dose of breast milk and how this could impact health outcomes for infants.

Acute Otitis Media:

Breastfeeding is protective against acute otitis media in the first two years of life; there is some evidence of a dose-response relationship.

Children who were ever breastfed as infants compared to those who were never breastfed had reduced odds of developing acute otitis media in the first two years of life. The reduction in odds was between 33% and 23% (OR 0.67, 95% CI 0.56 to 0.80; AOR 0.77, 95% CI 0.64 to 0.91). (5,6) Extending partial breastfeeding for longer than 3-4 months did not offer increased protection. (6) No effect was detected in children older than two years of age. (6)

Being exclusively breastfed compared to never or partially breastfed increased the protective effect. The odds of otitis media in children who were exclusively breastfed for 6 months were decreased by 50% in comparison to those who were never breastfed and 43% compared to those partially or never breastfed (OR 0.50, 95% CI 0.36 to 0.70; OR 0.57, 95% CI 0.44 to 0.75). (5,6)

Gastrointestinal Infections:

Breastfeeding is protective against gastrointestinal infections (GI) with some evidence of a dose-response relationship.

No reduction in the risk of developing GI infections was detected for infants who were partially breastfed for up to six months in comparison to those never breastfed. (5)

However, exclusive breastfeeding has been shown to reduce the odds of developing GI infections. Among infants who were exclusively breastfed for four months and then partially breastfed, the odds of developing GI infections were reduced by nearly 60% compared to those infants who were never breastfed (AOR 0.41, 95% CI 0.26, 0.64). (5)

A longer period of exclusive breastfeeding, for up to six months, resulted in a 33% reduced risk of GI infections compared to infants exclusively breastfed for three to four months or those partially breastfed (RR 0.67, 95% CI 0.46 to 0.97). (5) Extending exclusive breastfeeding beyond six months reduced the odds of GI infections by 40% (AOR 0.60, 95% CI 0.44 to 0.82). (5)

Lower Respiratory Infections:

Breastfeeding is protective against lower respiratory infections; there is some evidence of a dose-response relationship.

No protective effect was detected in infants who were partially breastfed for up to six months. (5)

Infants who were exclusively breastfed for the first four months of life and then partially breastfed had half the odds of developing lower respiratory infections in the first year of life compared to those who were never breastfed (AOR 0.50, 95% CI 0.32 to 0.79 from birth to six months of age; AOR 0.46, 95% CI 0.31 to 0.69 from seven to twelve months). (5) The risk reduction, when comparing exclusive breastfeeding for six months to those partially breastfed or not breastfed was 35% (RR 0.65, 95% CI 0.43 to 0.96). (5)

Exclusive breastfeeding for a longer compared to a shorter period of time i.e. for six months rather than from three to four months made no significant difference in the risk of lower respiratory infections. (5)

When comparing infants exclusively breastfed for four months or longer to infants who were formula fed, the risk of being hospitalized for a lower respiratory infection in the first year of life was reduced by more than 70% (RR 0.28, 95% CI 0.14 to 0.54). (5)

Overweight/Obesity:

There is some evidence of an inverse relationship between ever being breastfed and overweight and obesity in childhood.

Children who were ever breastfed compared to those never breastfed had reduced odds of becoming overweight or obese in childhood. The reduction in odds lies between 26% and 4% (OR 0.74 to 0.96, 95% CI 0.67 to 0.99). (3, 5, 8) The effect is not modified by breastfeeding duration or exclusivity. (3)

Children aged 1-9 years had a 26% reduction in odds and children aged 10-19 years had a 37% reduction in odds of overweight/obesity (OR 0.74, 95% CI 0.68 to 0.79; OR 0.63 95% CI 0.54 to 0.73). (3) (3, 5, 8)

Dental caries:

More breastfeeding compared to less breastfeeding showed no effect on the risk of dental caries in the first year of life. (9)

The effect of ever compared to never being breastfed in the first year of life on the development of dental caries in young children is inconclusive.

Breastfeeding longer than 12 months, particularly nocturnal breastfeeding, may increase the risk of dental caries.

Children who were breastfed for longer than 12 months and more frequently compared to less or not at all, had twice the odds of developing dental caries (OR 1.99, 95% CI 1.35 to 2.95). (9) Children who were breastfed for longer than 12 months with more nocturnal breastfeeding compared to less nocturnal breastfeeding had a seven-fold increase in the odds of developing dental caries (OR 7.14, 95% CI 3.14 to 16.23). (9)

Four of the five primary studies included in the analysis of nocturnal breastfeeding were conducted in low- or middle-income countries and one in a high-income country which may limit the applicability of this finding to the Canadian population.

Food allergy:

There is no evidence of an association between the amount of breastfeeding and development of food allergies.

Diabetes, Asthma, Eczema and Allergic Rhinitis:

Evidence of an association between breastfeeding and the development of Type 1 and Type 2 diabetes (3,10) **asthma** (5,7) **eczema** (5,7) **or allergic rhinitis** (7) **in children is inconclusive.**

11 Applicability and Transferability

The rapid review team met with public health nurses, supervisors, managers, and a dietitian, plus clinical nursing leaders from three Peel hospitals, for a facilitated discussion of the findings and draft recommendations outlined in this report. The purpose of the meeting was to discuss the applicability (feasibility) and transferability (generalizability) of the recommendations to our local context. Questions from the Applicability and Transferability Worksheet (11) were used to guide our discussion. A summary of key points is outlined below.

Applicability

Political Acceptability:

The current political climate in Peel is supportive of parents making informed decisions about how to feed their infants and young children. A foundation of health within the public health Nurturing the Next Generation strategic priority is infant and child nutrition which identified that infants need to be breastfed as much as possible for as long as possible.

The Region of Peel - Public Health achieved Baby-Friendly Initiative (BFI) designation in 2009 as did Trillium Health Partners in 2017. Brampton Civic Hospital is working towards designation. Public health staff and community partners are committed to providing parents with evidence to facilitate decision making about how and what to feed their infants and young children. This evidence review aids in this messaging.

The public may welcome updated key messages about reducing risk of adverse health outcomes (or increasing the chance positive health outcomes) for their infants and young children.

Sensitivity will be required in developing messages which the public views as supportive rather than coercive.

Social Acceptability:

Mothers form intentions about how to feed their infants before and during pregnancy. The new Ontario Perinatal Record[4] prompts physicians and midwives to discuss breastfeeding during prenatal visits in the first and third trimesters of pregnancy and to discuss support for breastfeeding in the third trimester. Providing mothers with

[4] Available from: http://www.pcmch.on.ca/wp-content/uploads/2017/06/OPR-2017.pdf Accessed: July 19, 2018.

information about availability and accessibility of supports for infant feeding in hospital and the community will help new mothers and their babies learn to breastfeed.

The impact of information about health effects of breastfeeding for infants and young children on parents' decision making is unknown. It is anticipated that clear messaging, especially where there is a dose-response relationship, could have a positive impact.

Messaging should be in plain language to ensure it is understood by parents. The tone should be considerate of the stress new mothers experience, the pressure to do 'what is best' for their babies and the possible guilt they may experience if they choose to offer infant formula partially or exclusively.

Health care providers are encouraged to be realistic when discussing with parents the time and effort required when learning to breastfeed.

Recent changes in legislation afford some women the opportunity to extend maternity leave up to 18 months which could impact their intended duration of breastfeeding..

Parents may be interested in learning about the security breastfeeding provides in times of travel, periods of lower household income and during emergencies or evacuations.

Available Essential Resources:

Developing and sharing updated messaging about the health effects of breastfeeding for infants and young children is feasible with current Family Health resources, particularly through our many programs and services.

Communication channels to reach parents are used in the Family Health Division and beyond. Partnerships exist with local hospitals and some physicians caring for pregnant women, which would support the distribution of messages to parents beyond those who are accessing public health services.

The range of public health services offered to support all aspects of infant feeding will need to be considered. Connecting with the Oral Health program of the Chronic Disease and Injury Prevention Division will assist in developing messaging about promoting oral health for infants and young children.

Organizational Expertise and Capacity

The Region of Peel – Public Health is developing a new strategic plan which will foster integration across divisions to promote health for Peel's population including women in the preconception and prenatal periods.

Transferability

Magnitude of health issue

Overweight and obesity is an important health issue in Peel. The finding that ever having been breastfed is associated with a reduced risk of becoming overweight or obese in childhood is important, at the population level, in reducing the risk of related health conditions later in life such as hypertension and diabetes.

Parents and physicians will be interested in the contribution breastfeeding can make to reducing the risk of otitis media, gastrointestinal illness and lower respiratory infections, especially since the latter two outcomes can result in visits to hospital emergency departments . (See Appendix A)

Magnitude of the reach:

The Region of Peel - Public Health offers a range of infant feeding services which could be restructured to optimize coverage for priority populations. The length of maternity leave taken by mothers in Peel will provide an opportunity to optimize infant nutrition within the family context. Staff within the Family Health Division are developing a communication strategy to more effectively reach parents of infants and young children.

Target population characteristics:

To better serve families with young infants, the Family Health Division has adjusted its infant feeding service delivery model to offer more home visits, service on a walk-in basis as well as by appointment, and access to clinic services on some statutory holidays. Public health wants to reach as many families as possible to support infant feeding.

12 Recommendations

1. Develop key messages about the importance of breastfeeding in reducing the odds of adverse health outcomes in infancy and childhood.

- Breastfeeding offers protection against otitis media, gastrointestinal, and lower respiratory infections; more breastfeeding increases the protection.

- Breastfeeding offers modest protection against becoming overweight or obese in childhood.

- Night-time breastfeeding beyond 12 months of age may increase the risk of dental caries. Oral health care is important regardless of how children are fed.

2. Tailor messaging for three audiences – residents of Peel who are: a) pregnant b) parents of young infants c) health care practitioners – when developing key messages about the health effects of breastfeeding. Use language appropriate to the target audience.

3. Incorporate key messages into the Family Health Division's nursing practice standards.

4. Consider opportunities to incorporate key messages about the health effects of breastfeeding in the preconception period (e.g., into curricula for secondary school students, that of medical residents and college students).

5. Monitor the literature for emerging evidence examining relationships between infant feeding, development of the gut microbiome and overweight/obesity.

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Appendices

Appendix A: Table 1

Appendix B: Concept Model

Appendix C: Search Strategy

Appendix D: Literature Search Flowchart

Appendix E: Data Extraction Tables

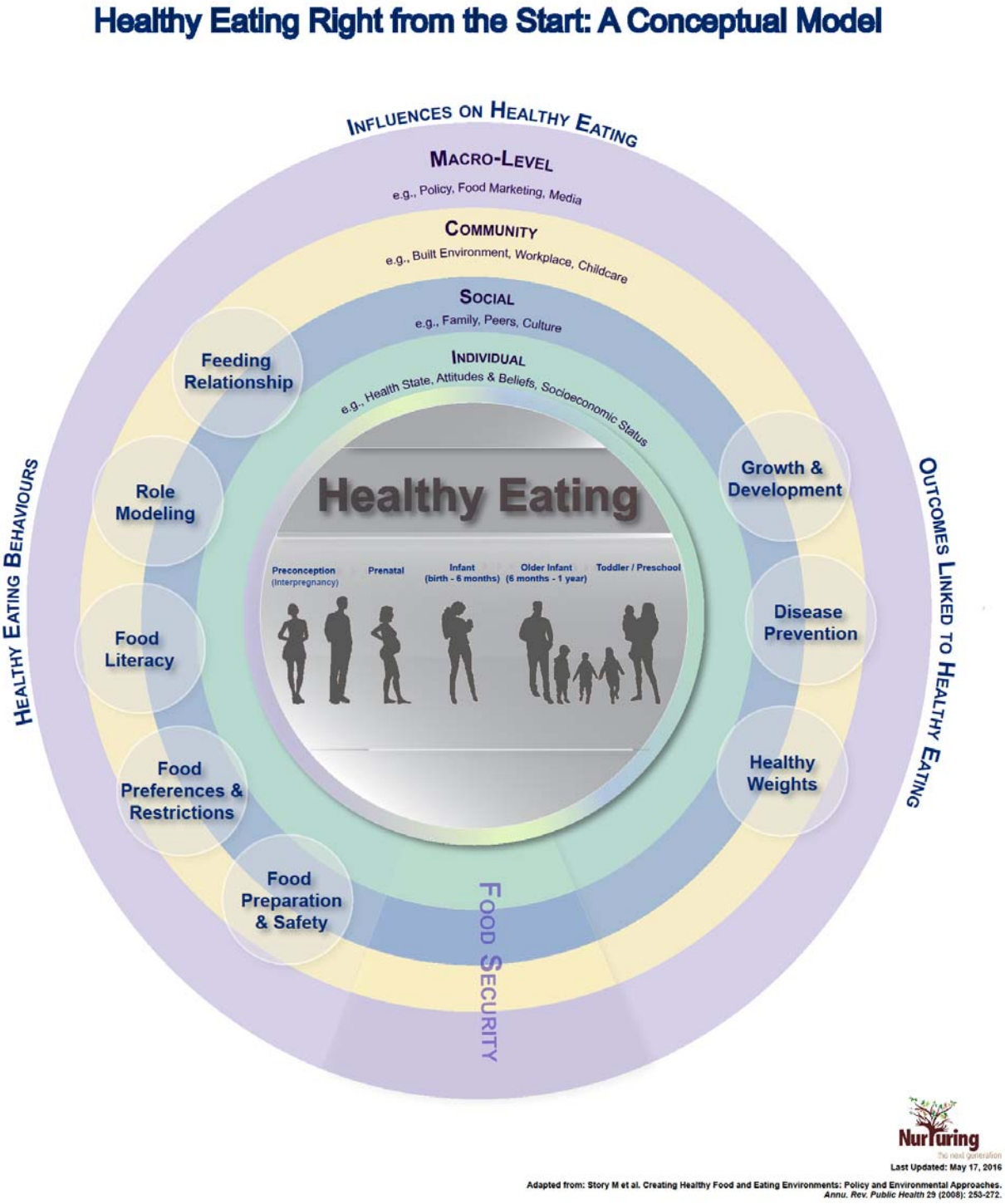
Appendix A: Table 1

Top Five Leading Causes of Emergency Department Visits by Age Group for Children from Birth to Nine Years of Age
Peel, 2016

Age Group (years)	Causes of Emergency Department visits	Number of Peel Emergency Department Visits
Less than 1	**Acute respiratory infections other than flu or pneumonia**	**2,129**
	Injury, poisoning and certain other consequences of external causation	947
	Intestinal infectious diseases	**492**
	Haemorrhagic and haematological disorders of fetus and newborn	469
	Disease of the skin and subcutaneous tissue	298
	All causes for less than 1 year old	9,541
1-9	Injury, poisoning and certain other consequences of external causation	13,080
	Acute respiratory infections other than flu or pneumonia	**7,268**
	Intestinal infectious diseases	**2,538**
	Diseases of the ear and mastoid process	2,229
	Influenza and pneumonia	**2,119**
	All causes for 1-9 year old	48,942

Data Sources: National Ambulatory Care Reporting System 2016, IntelliHEALTH Ontario, Ministry of health and Long-Term Care, extracted December 2017.

Appendix B: Concept Model



Appendix C: Search Strategy

Database: EBM Reviews - Cochrane Database of Systematic Reviews <2005 to April 19, 2017>, Global Health <1973 to 2017 Week 15>, Ovid Healthstar <1966 to March 2017>, Ovid MEDLINE(R) <1946 to April Week 3 2017>, Ovid MEDLINE(R) In-Process & Other Non-Indexed 95% CItations <April 26, 2017>
Search Strategy:
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1 exp Breast Feeding/ (76102)
2 exp Infant/ (1732681)
3 ("breastfeed*" or "breast feed*" or "breast fed*" or "breastfed").ti,ab. (83168)
4 ("infant feed*" or "breast milk" or "mothers milk" or "human milk").ti,ab. (55644)
5 1 or 3 or 4 (135683)
6 ("infant*" or "neonate*" or "newborn*").ti,ab. (854299)
7 2 or 6 (2041281)
8 ("dose*" or exposure or duration).ti,ab. (3473779)
9 ("review*" or "meta-analys*" or "synthes*" or "guideline*").ti. (1212428)
10 5 and 7 and 8 and 9 (776)
11 limit 10 to yr="2007 -Current" (545)
12 remove duplicates from 11 (264)

****

MY

EBSCOhost

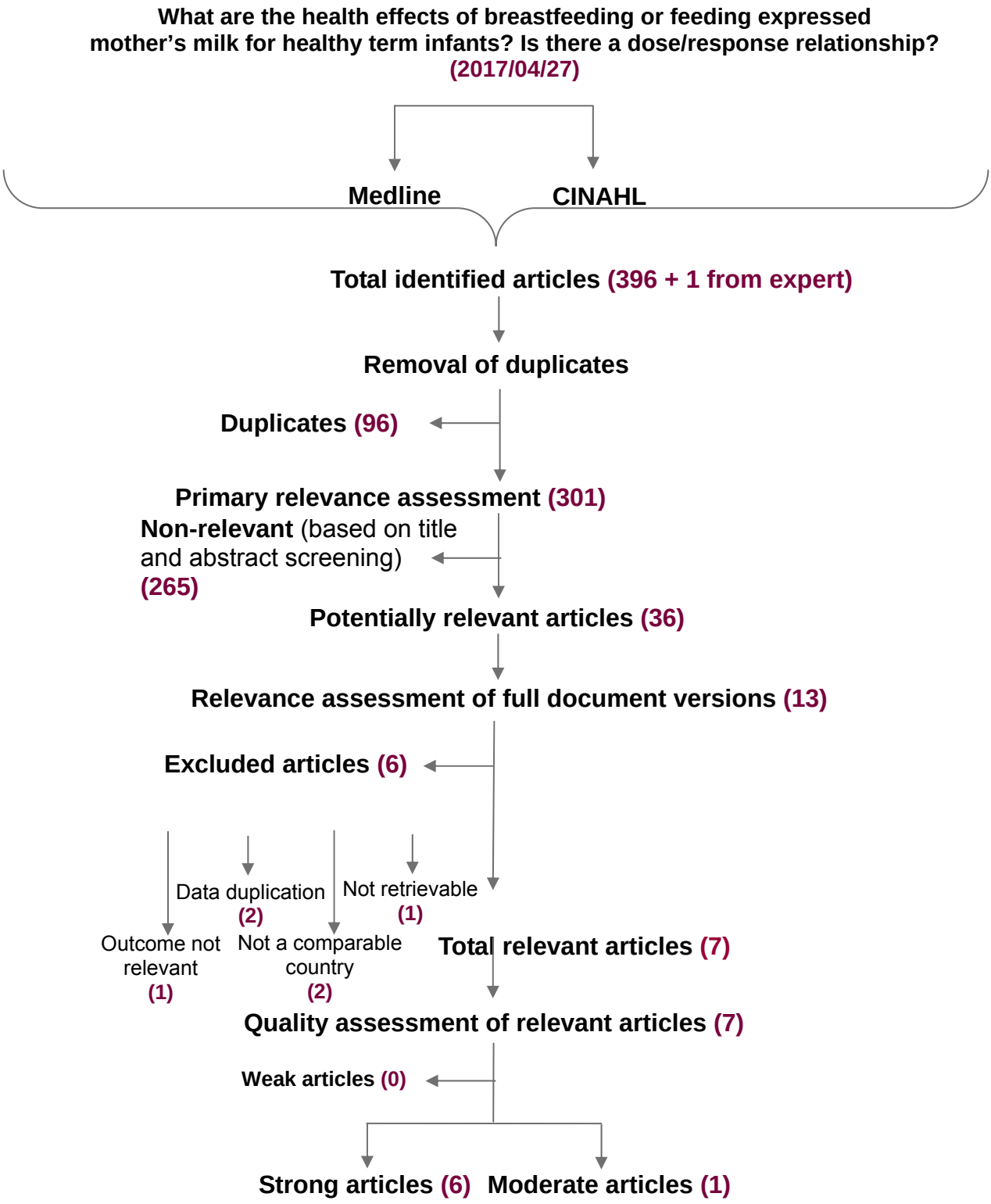
Thursday, April 27, 2017 10:35:44 AM

#	Query	Limiters/Expanders	Last Run Via	Results
S14	S8 AND S9 AND S10 AND S11	Limiters - Exclude MEDLINE records Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - Nursing & Allied Health Collection: Comprehensive;CINAHL Plus with Full Text	69
S13	S8 AND S9 AND S10 AND S11	Limiters - Published Date: 20070101-20171231 Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - Nursing & Allied Health Collection: Comprehensive;CINAHL Plus with Full Text	206
S12	S8 AND S9 AND S10 AND S11	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - Nursing & Allied Health Collection: Comprehensive;CINAHL Plus with Full Text	331
S11	TI ("review*" OR "meta-analys*" OR "synthes*" OR "guideline*") OR AB ("review*" OR "meta-analys*" OR "synthes*" OR "guideline*")	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - Nursing & Allied Health Collection: Comprehensive;CINAHL Plus with Full Text	798,163
S10	S5 OR S7	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases	262,760

			Search Screen - Advanced Search Database - Nursing & Allied Health Collection: Comprehensive;CINAHL Plus with Full Text	
S9	S4 OR S6	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - Nursing & Allied Health Collection: Comprehensive;CINAHL Plus with Full Text	238,507
S8	S1 OR S2 OR S3	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - Nursing & Allied Health Collection: Comprehensive;CINAHL Plus with Full Text	21,531
S7	(MH "Dose-Response Relationship")	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - Nursing & Allied Health Collection: Comprehensive;CINAHL Plus with Full Text	4,067
S6	TI ("infant*" OR "neonate*" OR "newborn*") OR AB ("infant*" OR "neonate*" OR "newborn*")	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - Nursing & Allied Health Collection: Comprehensive;CINAHL Plus with Full Text	108,068
S5	TI (dose OR exposure OR duration) OR AB (	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases	260,753

	dose OR exposure OR duration)		Search Screen - Advanced Search Database - Nursing & Allied Health Collection: Comprehensive;CINAHL Plus with Full Text	
S4	(MH "Infant+")	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - Nursing & Allied Health Collection: Comprehensive;CINAHL Plus with Full Text	194,445
S3	TI ("infant feed" OR "breast milk" OR "mothers milk" OR "human milk") OR AB ("infant feed" OR "breast milk" OR "mothers milk" OR "human milk")	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - Nursing & Allied Health Collection: Comprehensive;CINAHL Plus with Full Text	4,332
S2	TI ("breast feed*" OR "breast fed*") OR AB ("breast feed*" OR "breast fed*")	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - Nursing & Allied Health Collection: Comprehensive;CINAHL Plus with Full Text	4,368
S1	(MH "Breast Feeding+")	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - Nursing & Allied Health Collection: Comprehensive;CINAHL Plus with Full Text	17,064

Appendix D: Literature Search Flowchart



Appendix E: Data Extraction Tables

Systematic Review #1		
General information and quality rating for review		
Author(s) and title	Horta BL, de Mola CL, Victora CG. **Long-term consequences of breastfeeding on cholesterol, obesity, systolic blood pressure and type 2 diabetes: a systematic review and meta-analysis.** ACTA Paediatrica; 2015. 104, 30-37.	
Country of publication	Authors are located in Brazil.	
Quality rating	Rated 9/10 (strong) using Health Evidence Quality Assessment tool by two independent appraisers (EW and MC January 16, 2018)	
Generalisability to local population	Setting for primary studies: Overweight/obesity: 71 studies from high income countries; 34 from middle-/low income countries. Total cholesterol: 39 studies from high income countries; 7 from middle-/low income countries. Blood pressure: 34 studies from high income countries; 9 from middle-low income countries Type 2 diabetes: setting for primary studies not provided.	
Details of the review		
Objective	To systematically review the evidence of the associations between breastfeeding and overweight/obesity, blood pressure, total cholesterol and type 2 diabetes.	
Number of primary studies included	Overweight and obesity: 105 Total cholesterol: 46 Blood pressure: 43 Type 2 diabetes: 11	
Types of studies included	Observational and randomized studies	
Search period	September 2011 to August 2014, since this review updates a review completed in 2011, which was an update of a 2006 review.	
Number of databases searched	Four – MEDLINE, LILACS, SCIELO, Web of Science.	
Inclusion and exclusion criteria	Inclusion: - Observational and randomized studies - Comparison group of any type	Exclusion: - Studies restricted to infants - Studies without an internal comparison group
Details of population, exposures and outcomes included in review		
Population		
Description of relevant exposure	Breastfed (BF) ever compared to never; BF for more compared to less than a given number of months.	
Outcome measures	Blood pressure: mean difference in systolic and diastolic blood pressure Cholesterol: mean difference in total cholesterol Overweight and obesity: OR comparing breastfed and non-breastfed subjects Type 2 diabetes : OR comparing breastfed and non-breastfed subjects	
Results of review		
Results relevant to health outcomes of interest *Results for blood pressure and cholesterol not extracted*	**Overweight and obesity:** Breastfed subjects were less likely to be obese/overweight pooled OR 0.74 (95% CI 0.70 to 0.78). (113 studies) No effect modification by categorization of breastfeeding: - Ever BF OR 0.77 (95%CI 0.69 to 0.86) (26 studies) - BF for a given number of months OR 0.74 (95% CI 0.68 to 0.80)(54	

	studies) - Exclusively BF for a given number of months 0.69 (95% CI 0.61 to 0.79) (24 studies) Associations larger among studies evaluating overweight/obesity in children compared to studies of adults. - Children 1-9 years OR 0.74 (95% CI 0.68 to 0.79) (74 studies) - Children 10-19 years OR 0.63 (95% CI 0.54 to 0.73) (25 studies) - Adults ≥20 years OR 0.88 (95% CI 0.82 to 0.94) (14 studies) Limiting to high-quality studies OR 0.87 (95%CI 0.76 to 0.99) (11 studies) Sub group analysis based on study size, year of birth of subjects, study design, control for confounding and study setting (high-income compared to. middle/low income countries) reported but not extracted. **Type 2 diabetes:** Breastfed subjects were less likely to develop Type 2 diabetes pooled OR 0.65 (95% CI 0.49 to 0.86) Association larger among studies evaluating diabetes in children compared to studies of adults. - Children 10-19 years OR 0.46 (95% CI 0.33 to 0.66) - Adults ≥20 years OR 0.76 (95% CI 0.55 to 1.04) Combining the 3 studies which controlled for confounders including birthweight, BMI and SES produced OR 0.79 (95% CI 0.43 to 1.44)
Comments by author:	The evidence suggests that breastfeeding may reduce the odds of Type 2 diabetes Given the small number of studies, further studies that adjusted the estimates for confounding by socio-economic variables and birthweight, are needed.

Systematic Review #2	
General information and quality rating for review	
Author(s) and title	Hornell A, Lagstrom H, Lande B, Thorsdottir I. **Breastfeeding, introduction of other foods and effects on health: a systematic literature review for the 5th Nordic Nutrition Recommendations** Food and Nutrition Research; 2013. 57:1, 20823
Country of publication	Sweden, Finland, Norway, Iceland.
Quality rating	Rated 9/10 (strong) using Health Evidence Quality Assessment tool by two independent appraisers (EW and LG May 18, 2017)
Generalisability to local population	Inclusion criterion: study population similar to Nordic countries
Details of the review	
Objective	To review recent scientific data valid in a Nordic setting on the short- and long-term effects of breastfeeding (BF) (duration of both any and exclusive BF) and introduction of foods other than breast milk
Number of primary studies included	60 papers included: systematic reviews/meta-analyses 13; 41prospective cohort studies; 6 papers reporting on the PROBIT study (cluster-randomized intervention trial)
Types of studies included	Systematic literature reviews with meta-analysis, prospective cohort
Search period	Jan 2000 - Jan 2012
Number of databases searched	One – PubMed

Inclusion and exclusion criteria	Inclusion: - Human subjects - English or Nordic language - Study population relevant to Nordic countries - Systematic literature reviews and meta-analyses with recall periods longer than 3 years or where BF was only defined as never or ever	Exclusion: - If exposure was pro- and/or prebiotics, special formulas, supplements to mother or infant - contamination of breastmilk (eg. lead or mercury) - if mother or child were sick at start or at increased risk for disease - if the outcome was other than those stated in the research questions - Cross-sectional studies only describing breastfeeding status without relevant outcomes of interest for this review - Studies with recall periods longer than 3 years - Studies where breastfeeding was only defined as never or ever BF, where the definition ever is wide ranging - Papers that were incorporated into an included SLR/MA or published before the search years of an included SLR/MA with the same outcome - Premature births - Non-European/"Western" countries
Details of population, exposures and outcomes included in review		
Population	Infants	
Description of relevant exposure	Breastfeeding (duration of both any and exclusive BF) and the introduction of complementary foods.	
Outcome measures	Overweight/obesity, Diabetes mellitus (T1DM and T2DM), Acute otitis media, gastrointestinal infection, lower respiratory infection, atopic disease, asthma, blood pressure, serum cholesterol, cancer, IQ and neurological development, celiac disease, and inflammatory bowel disease.	
Results of review		
Results relevant to health outcomes of interest *Results not extracted for:* *introduction of complementary foods, blood pressure, serum cholesterol, cancer,*	**Acute otitis media (AOM)** BF was associated with a significant reduction in odds of developing AOM (one systematic review; two cohort studies) One systematic review of 5 cohort studies (Ip 2007). - Ever BF compared to never BF infants had reduced odds of developing AOM AOR 0.77 (95% CI; 0.64, 0.91). - Exclusive BF for 3 or 6 months compared never BF infants had reduced odds of developing AOM AOR 0.50 (95% CI; 0.36, 0.70)	

IQ and neurological development, celiac disease inflammatory bowel disease.	One cohort study found a non-significant association between breastfeeding duration and ear infection at 0-6 months and at 6-12 months. (data not provided) A second cohort study concluded that - Exclusive BF for 6 months vs partially BF or non BF infants had fewer infectious episodes of AOM AOR 0.37 (95% CI 0.13 to 1.05) NSD **Gastrointestinal infection (GI)** BF was associated with significant reduction in GI infections (one systematic review of 22 studies; 11 from developed countries) - Infants exclusively BF for 6 months compared to infants exclusively BF for 3-4 months had a significantly reduced risk of one or more episodes of GI infections RR 0.67 (95% CI; 0.46, 0.97) In a prospective cohort study, exclusive BF ≥6 months compared to BF < 4 months/or never BF significantly reduced the risk for GI episodes during months 1-9 AOR 0.60 (95% CI: 0.44, 0.82) In a second prospective cohort study, infants exclusively BF for 4 months and partially BF thereafter compared to infants never BF had a lower risk of GI infections until 6 months of age AOR 0.41 (95% CI 0.26, 0.64). - Partial BF, up to 6 months, did not significantly lower risks **Lower Respiratory Tract Infection (LRTI)** One systematic review concluded that 13/16 studies demonstrated a protective effect of BF. No data provided. A meta-analysis (Ip, 2007) combined 7 cohort studies Infants exclusively BF ≥4 mos compared to formula fed infants had a reduced risk of hospitalization due to LRTI in the first year of life RR 0.28 (95% CI 0.14 to 0.54) One systematic review reported that infants exclusively BF for 6 mos compared to exclusive BF for 3-4 mos with mixed feeding thereafter did not result in a reduced risk of LRTI in the first year of life (pooled RR 0.91; 95% CI 0.82 to 1.02) One cohort study found - Infants exclusively BF for 4 months and partially BF thereafter had a lower risk of LRTI compared to infants never BF, until 6 months of age AOR 0.50 (95% CI 0.32, 0.79) and from 7 - 12 months or age, AOR 0.46 (95% CI 0.31, 0.69). - Partial BF, even for 6 months, did not result in significantly lower risks A second cohort study found infants BF ≥6 mos compared to never BF had reduced risk of LRTI RR 0.65 (95%CI 0.43 to 0.96) **Overweight/obesity** (four systematic reviews and 19 prospective cohort studies) Only results for systematic reviews are included here:

	One systematic review included (but did not meta-analyse) three systematic reviews which reported that infants who were ever breastfed compared to those who were never breastfed had reduced odds of obesity in childhood and/or adult life (but cautioned that the observed association could reflect selective reporting and/or publication bias): - OR 0.76 (95% CI: 0.67, 0.86) - OR 0.93 (95% CI: 0.88, 0.99) - OR 0.96 (95% CI: 0.94, 0.98) **Type 1 Diabetes Mellitus (T1DM)** One systematic review (Ip, 2007) included two meta-analyses (total of 17 case-control studies) and six later studies. - The two meta-analyses found that among those BF the odds of developing T1DM were 1.23 (95% CI, 1.12 to 1.35) and among those BF <3 mos vs ≥3 mos the odds were 1.43 (95% CI 1.15 to 1.77) Five of six later studies showed similar results (data not provided). **Type 2 Diabetes Mellitus (T1DM)** One systematic review (Ip, 2007) reported pooled analysis of 7 studies (3 historical cohort, 2 cross-sectional, 1 prospective cohort, 1 case-control). - Among those who were BF compared to those who were formula fed the risk of developing T2DM was AOR 0.61 (95% CI; 0.44, 0.85). **Asthma** (3 systematic reviews/meta-analyses and 12 prospective cohort studies) One systematic review (15 prospective cohort studies) - BF for ≥ 3 mos vs not breastfed reduced the risk of asthma in children without a family history of asthma OR 0.73 (95% CI 0.59 to 0.92) A second systematic review found no significant reduction in the risk of developing asthma when comparing exclusive BF for 6 mos to exclusive BF for 3-4 mos. Of 10 prospective studies, three found no effect; one found the lowest prevalence of asthma among those breastfed for 4-6 months; six found diminished wheeze or asthma risk with breastfeeding. **Eczema (Atopic dermatitis)** One systematic review (21 studies) - EBF for ≥3 months vs EBF of partial BF < 3 mos made no significant difference in atopic dermatitis by age 1-7 years OR 0.89 (95% CI 0.74, 1.04) in children without family history and OR 0.78 (95% CI 0.58, 1.05) in children with family history. Results for single studies not extracted.
Comments/limitations by author	The evidence is convincing (grade 1) that longer duration of exclusive BF or any BF is associated with a protective effect against overweight and obesity in childhood and adolescence. Three studies show a dose-response

	relationship with longer duration giving more protection. Probable evidence (grade 2) that any BF has a protective effect against T1DM. The evidence for a stronger protective effect for longer duration of BF is limited but suggestive (grade 3). Supplementary Table 4 “Comparisons of ORs between studies with long-term recall of BF data and those more recent showed significant differences in T1DM risk only with long-term retrospective data.” Probable evidence (grade 2) that any BF has a protective effect against T2DM. The evidence for a stronger protective effect for longer duration of BF is limited but suggestive (grade 3). Limited and inconsistent evidence (grade 4) and no conclusions can be drawn for any preventive effects of BF on the risk for asthma in children. Methodological problems associated with BF studies: long recall, poor definition of exclusive BF, comparisons only between ever-never BF.

Systematic Review #3		
General information and quality rating for review		
Author(s) and title	Bowatte, G. Tham, R. Allen, K J. Tan, D J. Lau, MXZ. Dai, X. et al. **Breastfeeding and childhood acute otitis media: a systematic review and meta-analysis** Acta Paediatrica 2015 Dec; 104(467):85-95	
Country of publication	Australia.	
Quality rating	Rated 9/10 (strong) using Health Evidence Quality Assessment tool by two independent appraisers (EW and KK May 17, 2017)	
Generalisability to local population	Studies conducted in comparable countries (North America and Europe), however studies include high-risk groups (e.g. low socio-economic communities, children at high risk of allergies).	
Details of the review		
Objective	To synthesise the evidence on the association between duration and exclusivity of breastfeeding and the risk of acute otitis media (AOM)	
Number of primary studies included	24 individual studies based in Europe and North America - 18 cohort studies - 6 cross-sectional studies	
Types of studies included	Observational studies (cohort and cross-sectional)	
Search period	Database inception - 2014	
Number of databases searched	Three – PubMed, CINAHL and EMBASE	
Inclusion and exclusion criteria	Inclusion: - Observational studies - High risk groups (e.g. low socioeconomic communities and children at high risk of allergies) - English language - Association between BF and AOM - Only studies that reported effect estimates	Exclusion: - Infants born prematurely or infants with co-morbidities (eg. cleft palate) - Studies where the only outcome was otitis media with effusion
Populations, exposures and outcomes included in review		
Study Population	Children 0-24 months	
Description of relevant exposure	Breastfeeding categorized by the authors as: Exclusively BF compared to not exclusively or not BF during the first 6 months Ever compared to never BF Any BF ≥3-4 months (exclusive or partial) compared to ≤3-4 months (exclusive or partial) More or less breastfeeding - infants who were breastfed more compared to infants who were BF less within each study regardless of the duration or type of BF	
Outcomes	Development of AOM in childhood defined as physician diagnosed AOM, parent or self-reported AOM, or AOM recorded on health-related database	
Results of review		
Relevant results	*Exclusive BF for 6 months compared to nonexclusive BF for 6 months and AOM up to 2 years of age (5 cohort studies, 4 adjusted for confounders).* - Infants exclusively BF for the first 6 months of life had reduced risk of AOM to 24 months of age compared to infants not exclusively BF OR 0.57 95%CI 0.44 to 0.75)	

	Any BF > 3-4 months compared to any BF <3-4 months and AOM up to 2 years of age (5 studies – 2 cross sectional studies, one study adjusted for confounders and 3 cohort, 1 adjusted for confounders.) - Infants BF >3-4 months vs <3 mos NS reduction in AOM within the first 24 months - compared to infants who were BF for <3-4 months OR 0.85 95%CI 0.70, OR 0.85 (95% CI 0.70 to 1.02) (3 cohort studies) - Risk of AOM at 18 mos - 3 years for those BF > 3-4 months compared to BF <3-4 months OR 0.71 95%CI 0.42, 1.20) (2 cross sectional studies) *Ever compared to never BF and AOM up to 2 years of age (5 cohort, 1 cross sectional study)* - Infants who were ever BF were protected against AOM during the first 24 months of life compared to infants never BF OR 0.67 95%CI 0.56 to 0.80) (5 cohort studies) - No significant association between BF and AOM during the first year of life OR 1.57; 95% CI 0.91 to 2.71) (1 cross sectional study) *More compared to less BF and AOM up to 2 years of age (12 cohort studies, 5 cross sectional studies)* - Infants BF longer had greater protection from AOM in the first 2 years of life when compared with infants who were BF for shorter time periods - OR 0.67 (95%CI 0.59 to 0.76) (12 cohort studies) - No protective effect OR 1.21 (95%CI 0.60, 2.45) (5 cross sectional studies) *More compared to less BF and risk of AOM after 2 years of age (up to 8 years of age) (3 cohort, 4 cross sectional studies)* - No beneficial effect against AOM of longer BF duration compared to shorter BF duration during infancy when outcome measures beyond 2 years of age OR 1.03 95% CI 0.59, 1.79)
Comments/limitations identified by authors	Some estimates included were not adjusted for any confounders, some adjusted for only a few
Comments by reviewers	*Reviewer finds that results are not significant as CI crosses the point of no effect (KK).

Systematic Review #4		
General information and quality rating for review		
Author(s) and title	Lodge CL, Tan DJ, Lau MXZ, Dai X, Tham R, Lowe AJ, et al. **Breastfeeding and asthma and allergies: a systematic review and meta-analysis**. Acta Paediatrica. 2015 Dec; 104(467):38-53.	
Country of publication	Australia	
Quality rating	Rated 9/10 (strong) using Health Evidence Quality Assessment tool by two independent appraisers (EW and KK May 16, 2017)	
Generalisability to local population	Results stratified by high-income countries, and middle/low income countries	
Details of review		
Objective	To systematically review the association between breastfeeding and childhood allergic disease	
Number of primary studies included	89 individual studies	
Types of studies included	Observational (cohort, cross sectional, case-control)	
Search period	Database inception – 2014	
Number of databases searched	Three – PubMed, CINAHL and EMBASE	
Inclusion and exclusion criteria	Inclusion: -English only -full text available -breastfeeding and allergic disease -observational and experimental studies -any age for allergy outcomes -≥5 years for asthma outcomes	Exclusion: -premature births (<37 weeks gestation) -asthma outcomes <5 years of age to avoid misclassification with viral associated early transient wheeze
Populations, exposures and outcomes included in review		
Study population	Full term infants	
Description of relevant exposure	Ever compared to never – children receiving breastmilk at any time compared to those never breastfed More or <3-4 months – children fed breastmilk up to 3-4 months compared to other feeding methods More or less – compared groups with relatively more and relatively less breastmilk exposure	
Outcome measures	Asthma at 5-18 years defined as: physician diagnosed, parent or self-reported, spirometrically diagnosed or asthma recorded on health-related databases Eczema defined as: physician diagnosed, parent or self-reported, by validated eczema diagnostic criteria or reported on health-related databases Allergic Rhinitis defined as: allergic rhinitis/hay fever diagnosed by physician, parent or self-reported, or recorded on health-related databases (16 studies) Food allergy defined as: physician diagnosed, parent or self-reported, by objective measures (serum IgE, skin prick testing, oral food challenge) or recorded on health-related databases	

Results of review	
Relevant primary results **atopy defined as the genetic tendency to develop allergic diseases such as allergic rhinitis, asthma and atopic dermatitis (eczema) (as per the American Academy of Asthma, Allergy and Immunology)*	**Asthma at 5-18 years (29 studies)** *Ever compared to never BF and asthma at 5-18 years (13 studies; 3 cohort, 10 cross sectional studies)* - Children in high-income countries that were breastfed had a reduced risk of asthma; OR 0.90 (95% CI; 0.83, 0.97) *Exclusive BF ≥3-4mths compared to <3mths and asthma at 5-18 years (5 cohort, 8 cross sectional/case control)* - No significant association found between exclusive breastfeeding for longer than 3-4mths and asthma at 5-18yrs OR 0.89; (95% CI; 0.71, 1.11) *More compared to less BF and asthma at 5-18 years (29 studies; 13 cohort, 14 cross sectional, 2 case control)* - Risk of asthma not statistically significant OR 0.93; (95% CI; 0.83, 1.04) *More compared to less breastfeeding and asthma at 5-18 years, with parental or family history of asthma/atopy* (5 studies)* - No association between breastfeeding and asthma either in children with or without a family history (ORs: 1.08 (95% CI; 0.74, 1.58) and 1.2 (95% CI; 0.91, 1.59) respectively **Eczema (42 studies; 26 studies in high income countries)** *Exclusive BF>3-4 months compared to other feeding types (6 cohort)* - Reduced risk of eczema up to age 2 years OR 0.74; (95% CI 0.57, 0.97) *More compared to less BF (15 cohort,1 cross sectional)* - No association with risk of eczema up to age 2 years OR 0.95; (95% CI; 0.85, 1.07) *Ever compared to never BF (9 cross sectional, 1 cohort)* - No association with risk of eczema beyond age 2 years OR 1.07 (95 % CI: 0.98 to 1.16) *More compared to less BF (14 cross sectional, 6 cohort)* - No association with risk of eczema beyond age 2 years OR 1.09 (95% CI; 0.99 to 1.20) **Allergic Rhinitis (16 studies)** *More compared to less BF (12 studies; design not specified)* - in children of all age groups, no protective effect for allergic rhinitis OR 0.92; (95% CI; 0.84 to1.01) - in children < 5 years of age (4 cross sectional, 2 cohort) reduced risk of allergic rhinitis OR 0.79 (95% CI 0.63 to 0.98) - in children > 5 years of age (5 cross sectional, 4 cohort) no association with the risk of allergic rhinitis OR 1.05 (95% CI 0.99 01.12) **Food allergy (12 studies)** *More compared to less BF (12 studies)(6 cohort, 6 cross sectional)* - No association with food allergy OR 1.02 (95% CI 0.88 to 1.18) - In children < 5 years of age (6 cohort, 6 cross sectional) OR 1.07(95% CI 0.92 to 1.24) - In children >5 years of age (3 cohort and 1 cross-sectional) OR 1.08 (0.73 to 1.58)
Comments/limitations identified by authors	Possible bias due to length of breastfeeding recall. Evidence level very low to low. Studies that found a more protective effect were of weaker methodology

<table>
<tr><td colspan="3">Systematic Review #5</td></tr>
<tr><td colspan="3">General information and quality rating for review</td></tr>
<tr><td>Author(s) and title</td><td colspan="2">Weng SF, Redsell SA, Swift JA, Yang M, Glazebrook CP.
Systematic review and meta-analyses of risk factors for childhood overweight identifiable during infancy.
Arch Dis Child 2012; 97(12):1019-1026</td></tr>
<tr><td>Country of publication</td><td colspan="2">United Kingdom</td></tr>
<tr><td>Quality rating</td><td colspan="2">Rated 9/10 (strong) using Health Evidence Quality Assessment tool by two independent appraisers (EW and KK May 16, 2017)</td></tr>
<tr><td>Generalisability to local population</td><td colspan="2">Majority of studies from comparable populations. Ten studies relevant to breastfeeding (BF) findings: Germany (2), Australia (2), United Kingdom (3), Hong Kong (1), United States (2)</td></tr>
<tr><td colspan="3">Details of the review</td></tr>
<tr><td>Objective</td><td colspan="2">To determine risk factors for childhood overweight that can be identified during the first year of life to facilitate early identification and targeted intervention</td></tr>
<tr><td>Number of primary studies included</td><td colspan="2">30 individual studies conducted in North America (10), Europe (12), Australia (3) South/Central America (2) and Asia (3)</td></tr>
<tr><td>Types of studies included</td><td colspan="2">Prospective studies</td></tr>
<tr><td>Search period</td><td colspan="2">1990-2011</td></tr>
<tr><td>Number of databases searched</td><td colspan="2">Three – MEDLINE, EMBASE and CAB Abstracts</td></tr>
<tr><td>Inclusion and exclusion criteria</td><td>Inclusion:
- Prospective studies
- Minimum follow-up of 2 years from birth to allow for diagnosis of childhood overweight
- Potential risk factors that occurred prenatally, in the first year of life or when the child was 1 year of age
- BMI</td><td>Exclusion:
- Studies only including children with specific medical conditions or children from rare groups (may have a different set of risk factors)
- Follow up after 16 years of age</td></tr>
<tr><td colspan="3">Populations, exposures and outcomes included in review</td></tr>
<tr><td>Study population</td><td colspan="2">Children 0-12 months</td></tr>
<tr><td>Description of relevant exposure</td><td colspan="2">Children who were ever breastfed - exclusively BF, ever BF or fed a mixture of breastmilk and formula during first year of life</td></tr>
<tr><td>Outcome measures</td><td colspan="2">Overweight in childhood defined as:
<table>
<tr><td rowspan="2">Organization</td><td colspan="2">BMI</td></tr>
<tr><td>Overweight</td><td>Obesity</td></tr>
<tr><td>International Obesity Task Force (IOTF)</td><td>Corresponding to an adult BMI of ≥25kg/m²</td><td>Corresponding to an adult BMI of ≥30kg/m²</td></tr>
<tr><td>Centres for Disease Control and Prevention</td><td>≥85th percentile</td><td>≥95th percentile</td></tr>
<tr><td>UK 1990 reference</td><td>≥95th percentile</td><td>≥98th percentile</td></tr>
<tr><td>French reference and German reference</td><td>≥90th percentile</td><td>≥97th percentile</td></tr>
</table>
Studies that defined children as obese were considered to also include overweight children for the purpose of this review</td></tr>
</table>

Results of the Review	
Results relevant to BF. *Results for maternal pre-pregnancy overweight, infant birth weight, infant rapid weight gain, maternal smoking during pregnancy, and introduction of solid foods not extracted.*	*Breastfeeding in the first year of life (10 studies):* - Ever BF compared to never BF during the first year of life AOR 0.85 (95% CI 0.74 to 0.99) for obesity during childhood (age at outcome not stated) *Impact of BF duration on childhood overweight (5 studies):* - No significant differences (4 studies) - Infants who were breastfed for > 6 months compared with infants who were breastfed for < 3 months had reduced odds of overweight at 2 years of age AOR 0.4 (95% CI 0.2 to 0.8) (1 study)
Comments/limitations identified by authors	- late cut off age of 16 years (some children close to their final height included) - children sampled from a range of different socio-economic and cultural backgrounds - great deal of heterogeneity between overweight outcomes in childhood depending on the particular growth reference data used

Systematic Review #6		
General information and quality rating for review		
Author(s) and title	Tham, R. Bowatte, G. Sharmage, SC. Tan, DJ, Lau, MXZ. Dai, X et al. **Breastfeeding and the risk of dental caries: a systematic review and meta-analysis** Acta Paediatricia. 2015 Dec; 104(467):62-84	
Country of publication	Australia	
Quality rating	Rated 9/10 (strong) by two independent appraisers (SK & KK July 12, 2017)	
Generalisability to local population	Studies included children and adolescents from general and high risk populations (e.g. low socioeconomic communities) in Japan, China, Australia, USA, Mexico, Italy, Lithuania, Syria, Jordan, Tanzania, Sri Lanka, Burma.	
Details of review		
Objective	To summarize the current evidence for the association between breastfeeding and dental caries with specific reference to exposure windows and breastfeeding practices.	
Number of primary studies included	Included in synthesis = 63 Included in meta-analysis = 17	
Types of studies included	Cohort (14 – 6 of which were nested in RCTs of BF promotion interventions) Case-control (3) Cross-sectional (46)	
Search period	Database inception – October 2014	
Number of databases searched	Three: PubMed, CINAHL and EMBASE	
Inclusion and exclusion criteria	Inclusion: - Observational and experimental studies - Full text - Children and adolescents from general and high-risk populations - Dental caries as reported by qualified	Exclusion: - Participants born prematurely (<36 weeks)

	practitioner/researchers, a parent or through health records databases	
Populations, exposures and outcomes included in review		
Study population	Children and adolescents	
Description of relevant exposure	Exposure to BF: i) Up to 12 months of age and ii) Beyond 12 months of age BF categorized as: i) Never BF compared to ever BF ii) More compared to less BF - includes studies which compared groups with relatively more (longer duration of BF) and relatively less breast milk exposure (shorter duration).	
Outcome measures	- The development of dental caries, as reported by qualified practitioner/researchers, a parent or through health records databases, in deciduous or permanent teeth	
Results of review		
Relevant results	More BF compared to less BF or never breastfed up to 12 months *(5 studies: 1 cohort, 4 cross-sectional):* - Risk of developing dental caries OR 0.50 (95% CI 0.25 to 0.99) Ever BF compared to never BF (2 studies) showed a protective effect against dental caries (data not provided) More compared to less BF excluding never BF (3 studies) showed no protective effect OR 0.92 (95% CI 0.69 to 1.23) BF beyond 12 months of age *(7 studies: 2 cohort, 1 case control, 4 cross sectional):* More compared to less BF - OR 1.99 (95% CI 1.35 to 2.95) of development of dental caries Nocturnal BF in those BF longer than 12 months *(5 studies: 1 cohort, 1 case control, 3 cross-sectional)* Studies set in: Burma, Tanzania, Sri Lanka, Mexico, and Japan. More compared to less nocturnal BF: - OR 7.14 (95% CI 3.14 to 16.23) of developing dental caries One study embedded in an RCT of BF promotion via home visits in Brazil: - Frequency of BF at 12 months - 3-6 times/day (RR 2.04 (95 % CI 1.22 to 3.39) compared to 0-2 times/day - ≥ 7 times/day RR 1.97 (95% CI 1.45, 2.68) compared to 0-2 times/day - BF > 6 months, prevalence ratio (PR) of caries in BF children increased compared to BF < 6 months was only significant when still BF≥ 24 months • 6-11 months PR = 1.45; 95% CI 0.83, 2.53 • 12-23 months PR = 1.39; 95% CI 0.73, 2.64 • ≥ 24 months PR = 1.85; 95% CI 1.11, 3.08 - NSD in caries incidence or prevalence when children were aged 6.5 years	

	Ever BF compared to never BF*(12 studies: 2 cohort, 10 cross sectional)* - Six cross-sectional studies found NSD in prevalence of caries - Lower adjusted caries risk in BF compared to bottle fed children (1 cross-sectional study) OR 0.61 (95% CI 0.39 to 0.97) - Two studies (1 cohort, 1 cross-sectional)found significantly lower rate of caries (data not reported) BF duration *(17 studies: 4 cohort, 13 cross sectional)* - BF > 12 months compared shorter durations was associated with increased caries prevalence compared with shorter durations of BF (3 of 4 cohort studies) - In children BF ≥ 24 months compared to children BF < 6 months AOR 2.1 (95% CI 1.5 to 3.25) (1 study) - In children BF longer compared to those BF for shorter times 11 cross sectional studies found increased caries prevalence. Two found no difference. The few studies that controlled for confounding factors found decreased caries risk with shorter BF duration (6-12 months) compared to longer duration (>13 months) and increased risk of caries if BF <6 months
Comments/limitations identified by authors	- High heterogeneity between the studies included in the meta-analysis (possibly due to differing comparison groups) - Lack of controlling for key confounders (e.g. other foods/drinks in the diet, oral hygiene, maternal oral health status) limits the reliability of the results.

Systematic Review #7	
General information and quality rating for review	
Author(s) and Title	Patelarou E, Girvalaki C, Brokalaki H, Patelarou A, Androulaki Z, Vardavas C **Current evidence on the associations of breastfeeding, infant formula and cow's milk introduction with type 1 diabetes mellitus: a systematic review** Nutrition Reviews 2012; 70(9):509-519.
Country of publication	Greece.
Quality rating	Rated 6/10 (moderate) using Health Evidence Quality Assessment tool by two appraisers (EW and KK May 12, 2017).
Generalisability to local population	Studies conducted predominantly in developed countries
Details of the review	
Objective	To evaluate the type of feeding, duration of breastfeeding (BF), time of introduction of formula or cow's milk, and the potential impact on developing type 1 diabetes (T1D)
Number of primary studies included	28 individual studies conducted in Finland (2), Australia (2), United States (3), Sweden (2), Germany (2), Great Britain (3), Italy (3), Lithuania and Sweden (1), Norway and Denmark (1), Canada (1), Denmark (1), British Isles (1), Ireland and Scotland (1), United Kingdom and Ireland (1), Chile (1), Serbia (1), Austria, Lithuania, Latvia, Luxembourg and the United Kingdom (1), Czech Republic (1)
Types of studies included	Case-control 27/28 (96%) Prospective cohort 1/28 (4%)
Search period	January 1974 to May 2011 Majority of studies (21/28) were published after 1990

Number of databases searched	One database – MEDLINE Manual searching from reference articles	
Inclusion and exclusion criteria	Inclusion - Studies with an epidemiological design that evaluated the type of nutritional intake during the first months of life, the duration of total exclusive BF, the time of introduction to formula or cow's milk during infancy, and the effect on type 1 diabetes (T1D) presence during childhood	Exclusion - Studies not in English - Studies referring to animals or adults - Studies conducted among healthy children with a positive family history of T1D
Population, exposures and outcomes included in review		
Population	Young infants (within the first few months of life)	
Description of exposure	Breastfeeding (total or exclusive) Early exposure to cow's milk Combinations of nutritional habits (BF and infant formula or cow's milk)	
Primary outcomes	Development of Type 1 Diabetes	
Results of the Review		
Results relevant to BF *Results for early introduction of cow's milk or formula not extracted*	**Authors report eight studies found that total or exclusive breastfeeding plays a protective role against the development of type 1 diabetes:** Exclusive BF had a protective effect against T1D (4 studies) AOR 0.54 (95% CI 0.36 to 0.81) to OR 0.66 (95% CI 0.45 to 0.97). BF was protective against the development of T1D (4 studies) OR 0.64 (95% CI 0.42 to 0.98) to OR 0.76 (95% CI 0.54 to 1.07) BF >12 months was protective against the development of T1D (1 study) OR 0.54 (95% CI 0.27 to 1.08) Note: NSD **Authors report seven studies found that a short period or an absence of BF could be a major risk factor for T1D development.** Two studies found that infants BF for < 3 months had an increased risk of T1D OR 1.7; 95% CI, 1.02, 2.89 to OR 1.74, 95% CI, 1.40, 2.45) One study found children who were BF for less than 4 months were at a greater risk of developing T1D OR, 2.09, 95% CI, 1.30, 3.36) Two studies found infants BF for < 5 months were at an increased risk of T1D (AOR, 1.31; 95% CI, 1.01, 1.69 to AOR, 1.40; 95% CI, 1.13, 1.73 Two studies found the absence of BF increased the risk of developing T1D (RR, 1.33; 95% CI, 0.76, 2.34 to OR, 1.93; 95% CI, 1.33, 2.80) **Authors report five studies indicated that, in comparison with healthy children, diabetic children were either BF for a shorter period of time or were not BF at all.** Two studies found that diabetic children were less likely to have been BF	

	Three studies found that duration of BF was shorter for children with diabetes (1 study OR 0.70; 95% CI, 0.50, 0.97) **Authors report five studies found no or weak association between the risk of T1D and either a short period of BF or early introduction of cow's milk**
Comments/limitations from authors	- Possible recall bias or evaluator bias - Inadequate methodological quality (sample size, sub-optimal adjustments for potential confounder in the primary studies)
Comments by reviewers	Although authors report eight studies found that total or exclusive breastfeeding plays a protective role against the development of type 1 diabetes, two of these studies report confidence intervals which include a value of 1.0.