

Breastfeeding and Oral Health: Evidence and Methodological Challenges

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Title page**Breastfeeding and oral health: evidence and methodological challenges****Authors and institutions****Karen G Peres***

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Abstract

Breastfeeding is a powerful health promoting behaviour. A 2016 Lancet global collaboration to review the health implications of breastfeeding was among the first to consider oral health outcomes. While a role was suggested for breastfeeding in preventing malocclusion, caries was the only included disease condition unfavourably associated with breastfeeding. The present critical review examines the evidence connecting breastfeeding practices to these outcomes and discusses the methodological challenges inherent in reaching causal conclusions. Published systematic reviews show some evidence of a protective effect of breastfeeding against primary dentition malocclusion but no supportive evidence for mixed dentition and permanent dentition malocclusions. Regarding caries, well-conducted studies report a benefit with breastfeeding up to 12 months but a positive association between caries and breastfeeding of longer duration, at times which vary between 12 and 24 months, as well as nocturnal feeding. Future studies would be methodologically stronger if focused on specific malocclusion traits that are plausibly associated with sucking movements rather than using general malocclusion indices. Studies should use detailed and consistent terminology for breastfeeding definition, including frequency, intensity, and timing. Analytical studies should be carried out to distinguish between confounders (e.g. prematurity) and mediators (e.g. use of pacifier). Regarding a link to caries, standard terminology for exposures (e.g. nocturnal feeding) is recommended. Statistical analyses must account for known confounding factors (e.g. socioeconomic conditions) but avoid inappropriate adjustment for variables on a causal path between exposure and outcome or for variables not associated with breastfeeding (e.g. tooth brushing), as can be guided using tools such as direct acyclic graphs. For dental practice, the potential caries risk of long-duration breastfeeding should be part of individual patient counselling that incorporates patient values and circumstances. Given the unquestioned overall health benefits of breastfeeding, the dental community should support World Health Organization guidelines that encourage and promote breastfeeding.

Key words: human milk, dental caries, malocclusion, infant, oral health, epidemiology

Introduction

Breastfeeding is a critical and natural behaviour, which may shape an individual's life course (Victora et al. 2016). In the Global Strategy for Infant and Young Child Feeding, the World Health Organization (WHO) recommends immediate initiation of breastfeeding within an hour of birth, exclusive breastfeeding for up to 6 months of age and continued complementary breastfeeding thereafter, up to 2 years and beyond. WHO recommends that breastfeeding should be 'on demand' as often as the child wants day and night (WHO 2008).

Despite recommendations, many countries fall short of these breastfeeding targets, with wide variation across countries. Figure 1 shows the global prevalence of children receiving any breast milk at 12 months of age. Breastfeeding is one of the few positive health behaviours that is more prevalent in low and middle-income countries than in high-income countries.

In low and middle-income countries, any breastfeeding between ages of 6-12 months was associated with 50% reduced mortality, largely through prevention of diarrhoea and pneumonia (WHO 2000). A meta-analysis of breastfeeding studies in high-income countries showed that ever breastfeeding was associated with a 36% reduction in sudden infant deaths (Ip et al. 2007). Long-term breastfeeding was associated with a 13% reduced risk of childhood overweight or obesity (Victora et al. 2016) and an increase in child IQ of 2.6 points (Horta et al. 2015). Additionally, breastfeeding has health benefits for the mother: it improves birth spacing and significantly reduces type 2 diabetes risk (Aune et al. 2014). Longer duration of breastfeeding reduces risk of breast and ovarian cancers (Chowdhury et al. 2015).

The health-promoting role of breastfeeding for child and mother is so profound that it has the potential to help achieve some of the proposed Sustainable Development Goals (SDGs), the new development framework for all countries (Doyle and Stiglitz 2014). For example, breastfeeding may help to break the cycles of poverty (1st SDG), contribute to economic growth (8th SDG), and reduce economic inequalities (10th SDG). A comprehensive summary of the best evidence on the impact of breastfeeding on health (Victora et al. 2016) highlighted the importance of breastfeeding in reducing neonatal mortality (2nd SDG), promoting good health and wellbeing in both mother and child (3rd SDG), and increasing learning performance and intelligence (4th SDG).

As part of an international collaboration, the Lancet launched a special issue on breastfeeding (Victora et al. 2016). Among the many general health outcomes considered, two oral health conditions - dental caries and malocclusion - were included as long-term health outcomes potentially associated with exposure to breast milk. It was reported that breastfeeding may prevent malocclusion, potentially via the mechanical feeding action. Notably, however, dental caries was the only health outcome for which breastfeeding beyond the age of 1 year was associated with worse health (greater child tooth decay). This critical review evaluated the strengths and weaknesses regarding the existing evidence linking breastfeeding to malocclusion and dental caries. Rather than detail methodological aspects of each included study, the plausible mechanisms by which breastfeeding may affect oral health are described and analytical approaches and general methodological challenges in investigating the benefits of breastfeeding on oral health are critically discussed.

Breastfeeding and malocclusion

Importance

Malocclusion can impair quality of life in children (Kragt et al. 2016) and adults (Massod et al. 2017). Orthodontic treatment has been shown to produce immediate and longer-term improvements on patient's quality of life, including social and emotional wellbeing (Healey et al. 2016). Based on these findings early prevention of any developing malocclusion could have a major impact on any individual's life course and help to avoid lengthy and expensive orthodontic treatment.

Plausibility

The hypothesis that breastfeeding can influence craniofacial development is based on the potential morphological consequences of breastfeeding compared with bottle-feeding and on the malleability of oral structures during craniofacial growth and development. Suckling movements that occur during breastfeeding, in contrast to the sucking movements during bottle-feeding, involve tongue peristaltic motions around the breast nipples that can help guide palate morphology by rounding and flattening it (Woolridge 1986). These movements also assist development and harmonization of the peripheral oral musculature required for efficient swallowing (Palmer 1988). Additionally, development of oral functions facilitates a proper deciduous dentition eruption process with functional tooth interdigitation. There is some evidence that lip and tongue movements during breastfeeding encourage the infant to

draw breast milk through peristaltic action (Weber et al. 1986), allowing for proper function and maturation of the oral musculature needed for swallowing and adequate growth and development of the maxillo-mandibular complex (Palmer 1988). In contrast, when bottle-feeding infants place their tongues in relatively inferior positions, lips do not come together as tightly (depending on the material, configuration and size of the artificial nipple). In those cases, lips are likely to generate less oral motor stimulation, because fluid flow can be easily stimulated via light lingual pressure. These factors may lead to initial malocclusion developmental due to a combination of a deeper palate with a constricted maxillary dental arch and, sometimes, a more repositioned mandible linked to posterior displacement of the tongue base (Sanchez-Molins et al. 2010).

Epidemiologic studies of breastfeeding and malocclusion

Anthropological studies suggest that malocclusion traits have become more common in the last 150 years. This change could be attributed to environmental factors, such as a softer, more processed diet that requires less muscular force in mastication (Corruccini et al. 1990). More contemporary cross-sectional studies that address the role of environmental conditions on occlusion, including dietary habits and non-nutritive sucking, have not employed consistent definitions of outcomes and exposures. This could explain the large variation in the associations reported.

Breastfeeding duration beyond 12 months was associated with a lower proportion of children with malocclusions in the United States (Labbok and Hendershot 1987). When focussing exclusively on malocclusion in the primary dentition, the average duration of exclusive breastfeeding and the total duration of any type of breastfeeding were lower among children with posterior crossbite than in those without this condition (Karjalainen et al. 1999). This study is notable in that it considered a specific occlusal condition, as well as explicitly defined breastfeeding.

Two recent systematic reviews consider the topic of breastfeeding and malocclusion (Peres et al. 2015a; Abreu et al. 2016). The first (Peres et al. 2015a) included 48 studies and grouped studies by breastfeeding exposure: 1) any breastfeeding compared with absence of breastfeeding; 2) exclusive breastfeeding compared with absence of exclusive breastfeeding; 3) duration of any breastfeeding . All included studies were cross-sectional with the exemption of two nested in birth cohorts and one longitudinal study. Assessments of malocclusions occurred in any dentitional stage, but conclusions were based mostly on

studies on the primary dentition. This review concluded that breastfeeding was associated with a lower risk of malocclusions, but raised some methodological issues for careful consideration (see below). The authors suggested that breastfeeding compared with absence of breastfeeding decreased the odds of developing a non-specific malocclusion by 66%; that exclusive breastfeeding vs. non-exclusive breastfeeding decreased the odds of developing a non-specific malocclusion by 46%; and that a longer breastfeeding period decreased the odds of developing a non-specific malocclusion by 60%. In subgroup analyses for specific malocclusion traits, results were mostly consistent in a preventive direction.

The second review (Abreu et al. 2016) focused on the association between breastfeeding vs. bottle-feeding and its impact on mixed and permanent dentition malocclusion. Six studies were included, with most being cross-sectional studies with high risk of bias. Unlike the other systematic review, this review suggested that there was not enough evidence to support an association between breastfeeding, bottle-feeding and the occurrence of malocclusions in mixed and permanent dentitions. No meta-analysis was presented, as included studies were not considered sufficiently homogeneous.

Methodological challenges

Definition of malocclusion

Malocclusion can be manifested in multiple forms, making standardized diagnosis and classification difficult. Since first attempts of using the spatial relation of the first permanent molars as the earliest attempt to classify malocclusions, a myriad of dentoalveolar and craniofacial variables have been proposed during the century-long process of refining malocclusion classification. Underlying craniofacial skeletal imbalances, not just clinical findings, became a keystone piece of information to consider. However, while two- or three-dimensional cephalometry and cast or digital dental occlusal reproductions can reveal these imbalances, these tools are impractical in large epidemiological studies. In most epidemiological settings, malocclusions are classified by visually evident occlusal features, such as overjet, overbite, and crossbites, often under less than ideal lighting. Hence, the diagnostic process for individual patients in clinical practice differs from that used in population-based assessments, which may lead to considerable misclassification errors.

To study breastfeeding and malocclusion, it may be more revealing to focus on specific malocclusion measures that are plausibly associated with sucking movements. By analysing malocclusion as an overall diagnosis, confounding from other potentially unrelated

malocclusion traits may obscure the underlying relationship. When factors that can be influenced by suckling movements are considered, then focus on overbite, overjet and crossbites seems warranted, because these features can be reasonably classified in epidemiological settings. Thus, a recommendation would be not to use indexes or classifications that provide an overall malocclusion assessment but to rely on instruments that provide sound information on a handful of cornerstone variables plausibly influenced by suckling habits.

Analytical approaches

In any epidemiologic analysis, understanding the causal and non-causal relationship between variables, including confounding, selection bias, and mediation, is paramount. Directed acyclic graphs (Figures 2 & 3) are powerful visual tools to identify structural relationships between study variables, with growing use in dental research. Investigators draw on prior evidence and qualitative assumptions in crafting DAGs and thus identify which variables to include as confounders in statistical analyses and which variables may serve as mediators or selection factors. A detailed discussion of DAGs is beyond the scope of this review, but excellent resources are available (Akinkugbe et al. 2016).

In considering malocclusion, characteristics at birth such as prematurity might be associated with the exposure (breastfeeding) and the outcome (malocclusion) and, therefore, should be analysed as confounders. Alternatively, genetic aspects are highly unlikely to influence breastfeeding, so adjustment for genotypic malocclusion predictors is unnecessary in evaluating the breastfeeding-malocclusion association (Figure 2). Sophisticated statistical approaches can distinguish between confounders and mediators in estimating defined effects of breastfeeding on malocclusion (VanderWeele 2010). Few existing studies have considered a large number of factors in multivariable analysis of the association between specific breastfeeding behaviors and malocclusion. Sex, feeding practices, non-nutritive sucking habits, sleep disorder breathing, among others were considered whenever breastfeeding vs. never breastfeeding, exclusive breastfeeding vs. non-exclusive breastfeeding (Appendix Table 1), and longer vs. shorter breastfeeding (Appendix Table 2) were analysed. However, none of these listed studies made a distinction between confounders and mediators.

Malocclusion in the permanent dentition takes over a decade to develop. Hence, any residual impact of earlier suckling deficiencies will be diluted with time when other important environmental and genetic factors come into play. One of the few studies that

investigated primary-dentition malocclusion as a risk factor for permanent-dentition malocclusion, reinforces the association between crossbite and open bite in deciduous dentition with needed orthodontic treatment in permanent dentition (Peres et al. 2015b). Another study highlights the importance of early morphological changes and the incorrect orofacial functions developed in early stages due to feeding habits as cause of later malocclusion (Ovsenik et al. 2007). Future longitudinal studies may help to investigate any mediating effect of primary dentition malocclusion in the association between breastfeeding and permanent dentition malocclusion.

Another methodological challenge is the classification of breastfeeding and bottle-feeding. In the 48 studies identified in a recent review (Peres et al. 2015a), multiple definitions of breastfeeding timing, intensity and length complicated the synthesis of results across studies. Another area awaiting detailed exploration in methodologically sound studies is the impact of suckling movements during breastfeeding. These movements could help shape the palate by rounding and flattening it, synchronous with tooth eruption, and influence eruption direction and future interocclusal relationships. Thus, frequency, intensity, and timing of the suckling movements that take place during breastfeeding may be the most important factors driving any malocclusion benefits associated with exclusive breastfeeding.

Breastfeeding and dental caries

Importance

Early childhood caries (ECC) is the most prevalent chronic childhood disease and negatively impacts on oral health related quality of life of children and their families at all socioeconomic levels, but especially in low socioeconomic levels (Kassebaum et al. 2017). Poor dental health early in childhood is a risk factor for continued poor dental health throughout the lifecourse (Broadbent et al 2016).

Plausibility

Breast milk has superior nutritional composition and bioavailability; however, sugars provide approximately 40% of the energy in mature breast milk. Mature breastmilk contains more sugars than bovine milk, approximately 7% compared with 4.8%. Breast milk is also significantly lower in calcium and phosphate; factors that protect against dental caries; compared to bovine milk (Poskitt and Stewart 2017).

Laboratory studies report that human breast milk can reduce dental plaque pH and cause greater dissolution of the enamel compared with bovine milk (Rugg-Gunn et al. 1985), but this was not a consistent finding (Erickson et al 1999; Neves et al. 2016). However, this potential is likely to be less than infant formula (Peres et al. 2009). Frequent feeding will increase cariogenic potential as will nocturnal feeding due to decreased salivary flow during sleep (Nakayama and Mori 2015). On the other hand, a protective role of breastfeeding in the first year of life has been reported, possibly associated with less sugars consumption and delayed use of the bottle among children who are breastfed. Considering that permanent teeth erupt long after children are usually weaned, a breastfeeding effect on the occurrence of caries in the permanent dentition is not plausible, unless occurring through long-term changes in the microbiological environment of the oral cavity.

Epidemiologic studies of breastfeeding and dental caries

Generally, different epidemiologic study designs offer particular strengths and weaknesses and are intended to answer specific research questions. An example of weaker study design for causal questions, four decades ago, several case series reported caries in young children who had been breastfed (Kotlow 1977). The case series featured just nine participants combined, with no caries-free or non-breastfed comparison groups (Ribeiro and Ribeiro 2004). At a time when the terms "nursing caries" or "baby-bottle tooth decay" seemingly implied the bottle's necessity for maxillary anterior caries, these studies suggested the possibility of caries in the bottle's absence. However, while many publications later cited these articles with caution and scepticism (Tinanoff and O'Sullivan 1997), other authors ascribed an unwarranted etiologic role to "inappropriate" or "at will" breastfeeding based on these publications alone (Bruerd and Jones 1996).

Randomized controlled trials generally offer strong causal evidence but are ethically constrained in that infants cannot be allocated to experimental conditions that withhold breastfeeding. Two breastfeeding promotion trials included a dental caries secondary outcome: one a hospital-based postnatal breastfeeding promotion in Belarus (Kramer et al. 2007) and the other a peer counselling intervention to promote exclusive breastfeeding in Uganda (Birungi et al. 2015). Neither trial identified greater caries occurrence at age 5-7 years in children allocated to the intervention, suggesting that caries risk should not deter breastfeeding promotion and support in infancy. However, in both studies, total breastfeeding duration varied widely within trial arms, with no mean difference in the Uganda setting (Birungi et al. 2015). Thus, comparing trial arms does not directly assess, for example, caries

risk in all children breastfed to a later age versus those who ceased breastfeeding earlier. Notably, a nested secondary analysis of the Belarus trial showed no association with later caries experience between children exclusively breastfed for 3 versus 6 months (Kramer et al. 2009).

Well-conducted cohort studies are generally the next best design to provide causal evidence, because the design allows investigators to collect variables prospectively, and measurements do not necessarily rely on recall of past events. This is important for predictors, such as dietary habits, that can be difficult for participants to remember accurately (Hulley et al. 2013). In addition, the validity of studies investigating risk factors depends on whether measurement of the exposure and outcome accurately representing those variables for which some effect is plausible (Hulley et al. 2013). If correct measures and timing are not chosen, an association between risk factor and disease may not be evident (Fletcher et al. 2012). Specifically, detecting any deleterious effect of breastfeeding patterns on childhood caries can hinge on how exposures and outcomes are specified. For example, the primary teeth normally complete eruption at 30 months; thus, studies that define a binary cut-point for exposure to "long" duration breastfeeding at much younger ages, such as 6 months, are less likely to detect any effect on childhood caries (Hong et al. 2014; Bernabé et al. 2017). The reference category has a critical influence on the findings. Notably, comparing breastfeeding vs. bottle-feeding suggests a false dichotomy that does not capture the reality that many children engage in both breastfeeding and bottle-feeding at different points in time (Avila et al. 2015). Furthermore, exposure variables that combine practices, such as "breastfeeding or bottle feeding duration >1 year" or "high frequency of breast or bottle-feeding" make it difficult to isolate potentially independent effects of different types of feeding behaviors (Wagner et al. 2017). For the dental caries, all cohort participants should be at-risk of developing this outcome. In this sense, it is important to consider that the maxillary anterior teeth, which are the teeth most likely to be affected by infant feeding practices, are exfoliated between 6 and 7 years of age. Therefore, caries outcomes should be collected no later than age 6 years, which may partly explain the lack of an association with breastfeeding in some studies (Ollila et al. 2007).

Cohort studies meeting these assumptions have generally been consistent in reporting a positive association between breastfeeding and caries after adjustment for other feeding practices. These studies used different cut-points for breastfeeding duration, such as 12-months of age, ≥ 18 -months, and ≥ 24 -months (Appendix Table 3). In contrast, a protective

breastfeeding association was described in a meta-analysis of studies comparing breastfeeding duration up to 12-months (Tham et al. 2015). Two included studies were cross-sectional (Du et al. 2000; Qadri et al. 2012), and both studies compared children who had ever breastfed in the first 12-months with never breastfed. It is possible that early breastfeeding may protect against dental caries by delaying the introduction of free sugars-containing foods or substituting for nursing bottle use. This question is worthy of further investigation, particularly in studies that separate early (e.g. <6-months) and late duration (e.g. >18-months) breastfeeding behaviors.

Methodological challenges

Definition of breastfeeding

Heterogeneity in study design, measurement, and analytic protocol represents a vexing general challenge in synthesizing evidence. In their systematic review covering the breastfeeding and ECC literature from 1980 to 1996, Valaitis and colleagues (2000) graded most studies as weak and cited inconsistent and ambiguous breastfeeding definitions (e.g. "demand breastfeeding" or "breastfed only") as barriers to pooling study findings. Such non-standard and imprecise terminology not only cloud interpretation of the literature, but can generate participant confusion during data collection, as well. While the past 20 years have yielded enough studies featuring sufficiently defined breastfeeding variables to allow meta-analysis (Tham et al. 2015), poorly described variables (e.g. "breastfed only" or "nocturnal feeding") remain a lamentable source of uncertainty. While consistent, explicit exposure definitions would reduce ambiguity across the literature, not all study heterogeneity is preventable. However, variability may indirectly strengthen causal evidence, as Hill (1965) suggested when noting that "consistency" of an association across studies executed in different ways offers credence to an underlying causal effect.

The problem of confounding

Observational studies must account appropriately for confounding factors; yet, selecting appropriate confounding variables for statistical adjustment must rely on subject matter expertise that statistical software does not provide. Investigators should avoid including in models variables on a causal path between exposure and outcome, variables not associated with exposure, or excluding variables due to arbitrary cut-points for statistical significance. For instance, tooth brushing and dental utilization are questionable candidate confounders of the breastfeeding-caries relationship. These variables may predict caries

status but are unlikely to precede (and do not cause) breastfeeding behaviors and could only be associated with breastfeeding through other factors, such as socioeconomic status. Socioeconomic variables, in contrast, are critical to take into account, given stark global inequalities in dental health (Kassebaum et al 2017).

Breastfeeding is a multifaceted behaviour that evolves during a period of rapid infant development, closely intertwined with other feeding practices. For instance, if early weaning from the breast is accompanied invariably with nursing bottle use, researchers must reconsider whether independent effects of these collinear behaviors can be isolated. Additionally, breastfeeding early in infancy may influence food introduction, while those food experiences may in turn help determine the duration of later breastfeeding (Wright et al. 2004). This variable structure, known as time-dependent confounding, requires specific statistical analysis techniques, such as structural nested models (Daniel et al. 2013), or marginal structural models estimated with inverse probability weighting, as have recently been applied to breastfeeding and caries (Chaffee et al. 2014; Peres et al. 2017).

Whether breastfeeding leads to caries may depend on the population context. How breastfeeding might affect the cariogenicity of the oral microbiota is an area for further study. Notably, archeological data suggest that complementary feeding typically extended into the third year of life in ancient Rome, but caries affected less than 5% of the primary dentition (Prowse et al. 2008). In the modern context, sugars-rich diets and the type and virulence of biofilm bacteria could plausibly account for the cariogenicity of long-duration breastfeeding. Disrupting diet and bacteria to control and prevent caries are long-standing, if incompletely achieved, goals in dental practice and research (Scherp 1971), and are arguably more attractive anti-caries intervention targets than breastfeeding.

Recommendations for patients and policy

Breastfeeding is the unquestioned optimal source of infant nutrition. Complete implementation of the WHO guidelines for breastfeeding has potential to reduce significantly child mortality and morbidity worldwide. However, evidence is less complete and consistent for breastfeeding to age 2 years or beyond (Delgado and Matijasevich 2013). Considering oral health, some evidence supports a protective effect of breastfeeding on primary-dentition malocclusion. No consistent evidence is available for the mixed and permanent dentitions.

Prolonged breastfeeding, with studies suggesting either longer than 12 (Tham 2015); 18 (Chaffee et 2014) or 24 (Peres et 2017) months, increases caries risk, as does high frequency

(Tham 2015). Clearly, replacement of breastfeeding with infant formula should not be recommended. However, potential recommendations to reduce frequent or nocturnal breastfeeding (Nakayama and Mori 2015) from the second year of life must weigh caries prevention against any risk of eroding beneficial breastfeeding behaviours earlier in infancy.

For dental care providers, there is a professional obligation to deliver accurate information to patients, which may vary between countries depending on context, particularly available resources. In the case of breastfeeding, dentists should support the evidence-based WHO guidelines including emphasis on its benefits for general health. However, they should consider the potential caries risk of long-duration breastfeeding in individual patient counselling. During patient care, a two-way conversation about risks and benefits allows for personalized counselling that aligns with patient values, beliefs, and specific circumstances, using the best evidence to include those identified during caries risk assessment (Divaris 2016). Unlike counselling individual patients, guidelines for practice, policy, or public information require messages that are brief, simple, and actionable. Recommendations could emphasize the introduction of complementary foods and drinks after 6 months of age, avoiding free sugars, use of adequate fluoridated water and fluoride toothpaste twice daily after eruption of the first teeth.

Untreated dental caries of the primary teeth affects more children globally than any other chronic health condition (Kassebaum et al. 2017). A balanced consideration of all potential risk factors will make for informed guidelines and policy recommendations. There is substantial overlap in oral and systemic noncommunicable disease risk factors, including alcohol, tobacco, and nutrition, and it is therefore important the integration of oral and general health policies to meet the common risk factor approach. The dental profession will be well served to inform such approaches.

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Conflicts of interest.

The authors declare they have no conflicts of interest.

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Figures legends:

Figure 1: Map of breastfeeding. "Reprinted from The Lancet, Vol. 387, Cesar G Victora, Rajiv Bahl, Aluísio J D Barros, Giovanny V A França, Susan Horton, Julia Krusevec, Simon Murch, Mari Jeeva Sankar, Neff Walker, Nigel C Rollins, Breastfeeding in the 21st century: epidemiology, mechanisms, and lifelong effect, page 477, Copyright (2016), with permission from Elsevier (LN 4114510158651).

Figure 2: Example of DAG (Direct Acyclic Graph) for breastfeeding and malocclusion

Figure 3: Example of DAG (Direct Acyclic Graph) for breastfeeding and dental caries