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Prenatal Oral Health Care and Early Childhood Caries Prevention: A Systematic Review and Meta-Analysis

Jin Xiao[a] Naemah Alkhers[a] Dorota T. Kopycka-Kedzierawski[a]
Ronald J. Billings[a] Tong Tong Wu[b] Daniel A. Castillo[c] Linda Rasubala[a]
Hans Malmstrom[a] Yanfang Ren[a] Eli Eliav[a]

[a]Eastman Institute for Oral Health, University of Rochester Medical Center, Rochester, NY, USA; [b]Department of Biostatistics and Computational Biology, University of Rochester, Rochester, NY, USA; [c]Miner Library, University of Rochester Medical Center, Rochester, NY, USA

Keywords

Child dentistry · Early childhood caries · Prenatal oral health care

Abstract

Despite the advancement of early childhood caries (ECC) prediction and treatment, ECC remains a significant public health burden in need of more effective preventive strategies. Pregnancy is an ideal period to promote ECC prevention given the profound influence of maternal oral health and behaviors on children's oral health. However, studies have shown debatable results with respect to the effectiveness of ECC prevention by means of prenatal intervention. Therefore, this study systematically reviewed the scientific evidence relating to the association between prenatal oral health care, ECC incidence, and *Streptococcus mutans* carriage in children. Five studies (3 randomized control trials, 1 prospective cohort study, and 1 nested case-control study) were included for qualitative assessment. Tested prenatal oral health care included providing fluoride supplements, oral examinations/cleanings, oral health education, dental treatment referrals, and xylitol gum chewing. Four studies that assessed ECC incidence reduction were included in meta-analysis using an unconditional generalized linear mixed effects model with random study effects and age as a covariate. The estimated odds ratio and 95% confidence intervals suggested a protective effect of prenatal oral health care against ECC onset before 4 years of age: 0.12 (0.02, 0.77) at 1 year of age, 0.18 (0.05, 0.63) at 2 years of age, 0.25 (0.09, 0.64) at 3 years of age, and 0.35 (0.12, 1.00) at 4 years of age. Children's *S. mutans* carriage was also significantly reduced in the intervention group. Future studies should consider testing strategies that restore an expectant mother's oral health to a disease-free state during pregnancy.

Introduction

Although largely preventable, early childhood caries (ECC) remains the most common chronic childhood disease, with nearly 1.8 billion new cases per year globally [Dye et al., 2007, 2012; GBD 2016 Disease and Injury In-

KARGER

E-Mail karger@karger.com
www.karger.com/cre

Jin Xiao
625 Elmwood Avenue
Rochester, NY 14618 (USA)
E-Mail jin_xiao@urmc.rochester.edu

cidence and Prevalence Collaborators, 2017]. It afflicts approximately 37% of children aged 2–5 years in the USA [Dye et al., 2007, 2012] and up to 73% of socioeconomically disadvantaged preschool children in both developing and industrialized countries [Dye et al., 2015]. ECC is defined as the presence of ≥1 decayed, missing (due to caries), or filled tooth surface in primary teeth in a child 71 months of age or younger [Colak et al., 2013]. Severe ECC (S-ECC) occurs in children <3 years of age with ≥1 decayed, missing (due to caries), or filled tooth surfaces and in children 4–6 years of age with elevated caries scores [Colak et al., 2013]. The short-term consequences of untreated ECC include pain, hospitalization, and emergency room visits due to abscess and systemic infection, and even death [American Academy of Pediatric Dentistry Council on Clinical Affairs, 2005; Casamassimo et al., 2009]. Once decay has reached this stage, children often require total oral rehabilitation (TOR) under general anesthesia [Koo and Bowen, 2014] with multiple tooth extractions and restorations/crowns, at a cost of nearly USD 7,000 per child (2009–2011 US data) [Rashewsky et al., 2012]. In the long term, there is strong evidence that children who experienced ECC are much more likely to have a diminished oral health-related quality of life and higher risk of caries lesions in permanent teeth [Powell, 1998; Heller et al., 2000].

Despite the advancement of ECC prediction and treatment strategies, ECC remains a public health burden. In the USA, more than USD 1.5 billion per year is spent on treatment. However, children remain at high risk for recurrent caries even after extensive TOR treatment. Up to 40% of children treated for S-ECC experience recurrent disease by the 6-month checkup post-TOR [Graves et al., 2004; Berkowitz et al., 2011], despite pharmacologic interventions, such as topical fluoride/antimicrobial applications and dietary counseling to alter caries-promoting eating behaviors [O'Sullivan and Tinanoff, 1996; Li and Tanner, 2015]. Hence, more effective preventive strategies are critically needed.

Pregnancy is an ideal time to promote primary prevention of ECC in children given the profound influence of maternal health and behaviors on children's oral health outcomes [Iida, 2017]. ECC is a multifactorial bacterial disease with *Streptococcus mutans* as the prime cariogenic bacterium, and strongly influenced by diet [Caufield et al., 1993; Klein et al., 2004; Li et al., 2005; Kanasi et al., 2010; Slayton, 2011; Zhan et al., 2012; Klinke et al., 2014]. Studies have shown that maternal untreated caries and a greater level of salivary *S. mutans* increase the risk of ECC in children. Children's dietary and oral hygiene behaviors rely on their parents' or caregivers' oral health knowledge, beliefs, and behaviors [Finlayson et al., 2007; Wigen et al., 2011]. By revisiting the children's dental caries risk model described by Fisher-Owens et al. [2007] that included different levels of environmental elements, several factors that could potentially be influenced by mothers (marked with asterisks in Fig. 1) can be identified, including: (1) microflora, diet, and host in the oral health element positioning at the oral health circle; (2) health behaviors and practices, genetic endowment, demographic attributes, dental care utilization, oral health behaviors and practices, and dental insurance, that are included in the child-level influences element; (3) family position, socioeconomic status, physical safety, health status of parents, family function, family education, health behaviors, practices, and coping skills of the family, which lie in the family-level influences element. These factors in the aforementioned dental caries risk prediction model further emphasize the maternal role in ECC development. Thus, in theory, oral health care intervention during pregnancy presents an ideal entry point to preventing ECC.

Previously, studies have shown a positive ECC prevention outcome by providing prenatal oral health education or intervention [Günay et al., 1998; Nakai et al., 2010]; however, another study failed to show more effective ECC prevention when intervention during pregnancy was compared to the control group. Therefore, the aim of this study is to systematically review the scientific evidence relating to the association between prenatal oral health care, reduced carriage of *S. mutans*, and ECC prevention.

Methods

Search Strategy

Database searches were conducted in May 2018 to identify published studies on prenatal oral health care and ECC-related outcome (onset of ECC and/or oral *S. mutans* colonization). A medical reference librarian developed individual search strategies and retrieved citations from PubMed, Embase, Scopus, Web of Science, LILACS, Cochrane Library, and ClinicalTrials.gov. A combination of text words and controlled vocabulary terms were used (Prenatal Care, Oral Health, Child, Infant, Breast Feeding, Newborn, Dental Caries). A detailed search strategy is shown in the online supplementary Appendix 1 (for all online suppl. material, see www.karger.com/doi/10.1159/000495187).

Criteria

This systematic review included case-control studies, retrospective or prospective cohort studies, randomized or nonrandomized controlled trials that examined the effect of oral health

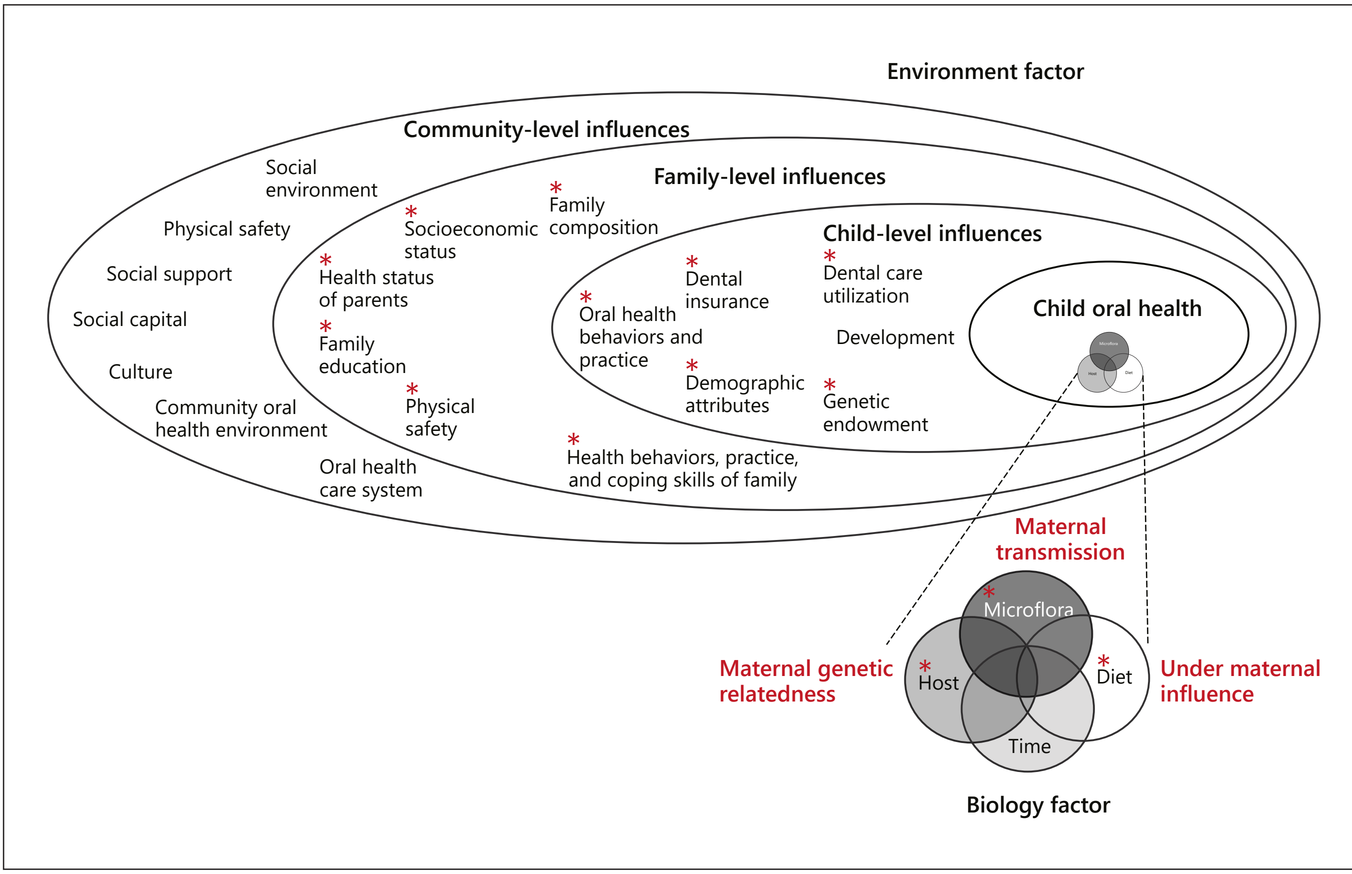

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Fig. 1. Modified Fisher-Owens conceptual model of child, family, and community influences on oral health outcomes of children. Factors marked with an asterisk (*) are those that could potentially be influenced by maternal attributes. This figure was modified from Keyes [1962] and the National Committee on Vital and Health Statistics [2002].

care during pregnancy on the incidence of ECC and/or oral carriage of *S. mutans* in children under the age of 6 years. Two trained independent reviewers completed the article selection in accordance with the inclusion/exclusion criteria. The agreement between reviewers was satisfactory (K = 0.81). Disagreements were resolved by consensus between the 2 reviewers.

The following inclusion and exclusion criteria were used for literature selection.

Inclusion Criteria

Types of participants: pregnant women and their children under the age of 6 years. Types of intervention(s)/phenomena of interest: prenatal oral health care utilization/intervention. Types of comparisons: pregnant women who received and did not receive prenatal oral health care. Types of outcomes: reduced dental caries in children; reduced oral carriage of *S. mutans*. Types of studies: case-control studies; retrospective or prospective cohort studies; randomized and nonrandomized controlled trials. Types of statistical data: odds ratios (OR); relative risk; confidence intervals (CI); *p* values, and frequency of an absolute number of events versus total number of individuals per group.

Exclusion Criteria

The exclusion criteria were: in vitro studies; animal studies; papers with abstract only; literature reviews; letters to the editor; editorials; patient handouts; case report or case series, and cross-sectional studies.

Data Extraction

Descriptive data, including clinical and methodological factors such as country of origin, study design, study site, dental examination, dental examiner calibration, age of subjects, type of prenatal oral health care intervention, outcome measures (ECC and/or oral *S. mutans*), as well as results from statistical analyses were obtained using an extraction form (online suppl. Appendix 2).

Qualitative Assessment and Quantitative Analysis

The quality of the selected articles was assessed using two methodological validities. (1) Cochrane Collaboration's tool for assessing risk of bias in randomized trials [Higgins et al., 2011]. Articles were scaled for the following bias categories: selection bias, performance bias, detection bias, attrition bias, reporting bias, and other bias. (2) Adapted Downs and Black scoring [Downs and Black,

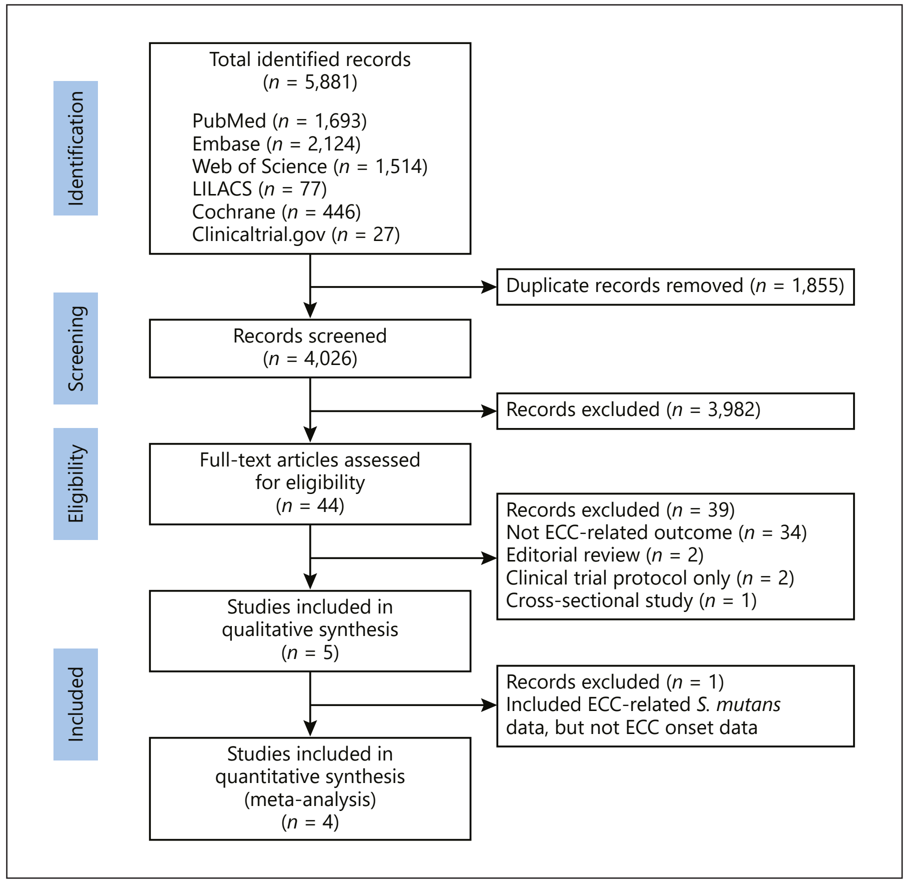

Fig. 2. Flow diagram of study identification. The 4-phase Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) flow diagram was used to determine the number of studies identified, screened, eligible, and included in the systematic review and meta-analysis (http://www.prisma-statement.org).

1998] that assesses the methodological quality of both randomized and nonrandomized studies of health care interventions. A total score of 26 represents the highest study quality.

For the articles selected for quantitative analysis, the R package Metafor was used for meta-analysis (https://cran.r-project.org/web/packages/metafor/). The OR and 95% CI and p values were estimated using an unconditional generalized linear mixed effects model with random study effects. Children's age at study endpoint was used as a covariate. Heterogeneity among the studies was evaluated using I^2 statistics and tested using the likelihood ratio test. A forest plot was created to summarize the meta-analysis study results.

Results

The literature analyses identified a total of 4,956 papers from the database search (Fig. 2). A total of 787 duplicate references were removed. The remaining 4,026 studies were imported into an Endnote Library for further review. From those, 3,854 studies were excluded after title screening and 128 studies were excluded after abstract screening. The remaining 44 articles were selected for a full text review. After the full text analysis, 40 studies were eliminated based on the exclusion criteria and 5 articles were chosen for qualitative assessment. For the quantitative assessment using meta-analysis to assess the effect of prenatal oral health care intervention on the onset of ECC, 4 out of 5 articles that received qualitative assessment were included. One article that was removed from the meta-analysis only included oral *S. mutans* carriage in children, but not ECC as the outcome [Nakai et al., 2010]. The full list of excluded articles after the full text review is shown in Appendix 3.

Study Characteristics

The characteristics of studies included in the qualitative review are summarized in Table 1. All 5 studies were published between 1997 and 2016. One was conducted in the USA [Leverett et al., 1997], 1 in Germany [Günay et al., 1998], and 1 in Australia [Plutzer and Spencer, 2008]. Two were conducted in Japan [Nakai et al., 2010, 2016]. Among the 5 studies, 3 were randomized control

Table 1. Characteristics of studies included in the qualitative assessment

Author, year	City, country, and study design	Study site	Child age at exam	Total subjects	Intervention	Control
Leverett [1997]	Maine, USA RCT	Private obstetric practice and hospital prenatal clinics	5 years	Subjects lived in an area without water fluoridation **Intervention:** 585 pregnant women at baseline 398 children at 5 years **Controls:** 590 pregnant women (baseline) 400 children at 5 years	**Mother:** daily intake of tablet containing 1 mg fluoride beginning with the 4th month of pregnancy until the end of pregnancy (approximately 6 months) **Infant:** daily drop of fluoride water from birth to 2 years of age; 0.5-mg tablet from 2 to 3 years of age	No fluoride intake
Günay [1998]	Germany Prospective cohort study	Medical University of Hannover (intervention group) Various kindergartens (control group)	3 and 4 years	**Intervention:** 86 pregnant women 54 mother-child dyads (3 years of age) 47 mother-child dyads (4 years of age) **Controls:** 65 children (3 years of age) 45 children (4 years of age)	**Primary–primary prevention** Pregnancy, 1st visit: – Dental examination findings – Individual preventive self-care OHI – Instruction on avoiding microbe transmission – Caries etiology education – Referral for dental treatment if needed Pregnancy, 2nd visit (>8 months gestational age) – Education about infection related to maternal-child caries transmission After birth visit (0–3 years): – Mother-child dyads: – Exam – OHI After birth visit (3–4 years): – OHI – Cleaning – Topical fluoride and chlorhexidine varnish	Children from various kindergartens who were not in the intervention group
Plutzer [2008]	Adelaide, Australia RCT	Adelaide Public Hospital	20 ± 2.5 months	**Intervention:** 327 pregnant women; 232 children **Controls:** 322 pregnant women; 209 children	Oral health promotion information was given to mothers in a total of 3 rounds, 1 during pregnancy and 2 between 6 and 12 months after birth Two subgroups were included with additional structured telephone consultation 6–12 months after birth in one subgroup	Oral health promotion information was NOT given
Nakai [2010]	Okayama, Japan RCT	Miyake Obstetrics and Gynecology Clinic and Hello Dental Clinic	15 months	**Intervention:** 56 pregnant women and 50 children examined at 6 months, 46 children examined at 15 months **Controls:** 51 pregnant women and 35 children examined at 6 months, 31 children examined at 15 months	At 6 months of pregnancy: basic prevention measures (oral examination, OHI, cleaning) From 6 months of pregnancy to 9 months after birth: xylitol gum (each gum pellet contains 1.32 g xylitol) chewing 4 times/day ≥5 min	At 6 months of pregnancy: basic prevention measures (oral examination, OHI, cleaning)
Nakai [2016]	Okayama, Japan Nested case control in a cohort study	Miyake Obstetrics and Gynecology Clinic and Hello Dental Clinic	2.1± 0.8 years	**Intervention:** 125 children **Controls:** 30 children	Antenatal health care (detail is not specified)	No antenatal health care

(Table continued on next page.)

trials [Leverett et al., 1997; Plutzer and Spencer, 2008; Nakai et al., 2010], 1 was a prospective cohort study [Günay et al., 1998], and 1 was a nested case-control in a cohort study [Nakai et al., 2016]. Oral health care intervention adopted in all qualitative studies extended the intervention period from the prenatal to infant stage. The interventions included: (a) fluoride-based intervention, where fluoride supplement intake was provided to pregnant women and their infant in a population that was not exposed to optimal water fluoridation [Leverett et al., 1997]; (b) primary-primary prevention originally proposed by Axelsson [1988], where all prophylactic measures were carried out in pregnant women in order to prevent the transmission of cariogenic bacteria and improve feeding behaviors after birth [Günay et al., 1998]; (c) oral health education promotion in pregnant women, which was used in the studies by Plutzer and Spencer [2008] and Nakai et al. [2016], who called it antenatal health care; (d) xylitol gum chewing in pregnant women [Nakai et al., 2010]. The intervention approaches are further detailed in Table 1.

Study outcomes were assessed when children reached 2–5 years of age. The onset of ECC and salivary *S. mutans* carriage are the two primary outcomes evaluated in these 5 studies. Quality and risk of bias for all 5 studies was assessed and are shown in Figure 3. Two studies with a randomized controlled trial design were of high quality based on the Cochrane risk of bias assessment tool [Higgins et al., 2011] and Downs and Black scoring system [Downs and Black, 1998]; the other 3 studies showed moderate quality.

Prenatal Oral Health Care and ECC Prevention

Three studies [Günay et al., 1998; Plutzer and Spencer, 2008; Nakai et al., 2016] revealed a lower ECC incidence in the group that received oral health care intervention

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Table 1 (continued)

Author, year	Dental examination calibration	Outcome measurement	Statistical analysis	Study findings	Limitations
Leverett [1997]	Not documented	DMFS/dmfs Fluorosis using Dean criteria	Relative risk and 95% CI	No statistical difference of caries incidence in children was seen between the intervention (8%) and control group (9%) There was no strong relationship between exposure to prenatal fluoride and fluorosis The tendency for deciduous maxillary second molars in females exposed to prenatal fluoride showed more fluorosis	There is no other prenatal oral health care intervention other than fluoride supplement
Günay [1998]	Not documented	DMFS/*dmfs* Proximal plaque index Salivary *S. mutans* (Dentocult SM)	*t* test	Caries and *S. mutans* reduction were significant between the intervention and control groups **Children at age 3 years:** Intervention: – 0% caries (+) – 100% *S. mutans* score 0 Controls: – 18.5% caries (+) with a *dmfs* mean value of 4.5 – 38.5% *S. mutans* score 0 – 29.2% *S. mutans* score 1 – 20% *S. mutans* score 2 – 12.3% *S. mutans* score 3 **Children at age 4 years:** Intervention: – 8.5% caries (+) with a *dmfs* mean value of 1.5 – 42.6% *S. mutans* score 0 – 36.2% *S. mutans* score 1 – 19.1% *S. mutans* score 2 – 2.1% *S. mutans* score 3 Controls: – 42.3% caries (+) with a *dmfs* mean value of 7.0 – 26.2% *S. mutans* score 0 – 13.3% *S. mutans* score 1 – 22.2% *S. mutans* score 2 – 37.7% *S. mutans* score 3 Mothers showed a significant improvement in plaque index and reduction in *S. mutans* score	Referral was given to mothers who needed dental treatment; however, whether mothers received dental treatment was not noted Whether pregnant women and their children in the control group received oral health care is unknown
Plutzer [2008]	Not documented	Incidence of S-ECC (AAPD definition)	Fisher's exact test	Caries reduction was significant between the intervention and control groups – Intervention: S-ECC 1.7% – Controls: S-ECC 9.6% No difference between intervention subgroups with/without additional structured telephone consultation	Dental examiners were blinded, but the subjects were randomized into the intervention or control group without blinding
Nakai [2010]	Intra-rate and interrate reliability tested Kappa >0.80	Salivary *S. mutans* (Dentocult SM)	*t* test, χ^2 and Fisher's exact tests	Significantly more children in the intervention group exhibited undetectable MS levels (score 0) on both the tongue and the gingival or tooth surfaces at 9, 12, and 24 months The children in the control group acquired *S. mutans* 8.8 months earlier than those in the intervention group (mean 12.0 *vs.* 20.8 months)	Caries was not evaluated in children Study did not use a control gum
Nakai [2016]	Not documented	*dmft*	OR and 95% CI	Receiving antenatal health care (AOR 3.27; 95% CI 1.30, 8.24) and the child having regular check-ups (AOR 3.42; 95% CI 1.35, 8.69) were significantly associated with a caries-free status among 3-year-old children	Many fewer subjects in the control group than the intervention group

S-ECC, severe early childhood caries; DMFS/dmfs, decayed, missing, filled surfaces (permanent/primary dentition); dmft, decayed, missing, filled teeth in primary dentition; OHI, oral hygiene instruction. *S. mutans* scoring in the study by Günay [1998]: 0, 0–10^3 cfu (colony forming unit)/mL; 1, 10^3–10^5 cfu/mL; 2, 10^5–10^6 cfu/mL; 3, >10^6 cfu/mL.

during pregnancy and early infancy when compared to the control group. The prenatal oral health care intervention approaches used in these 3 studies were primary-primary prevention, oral examination and cleaning, and oral health education. One study [Leverett et al., 1997] investigating fluoride supplement use during pregnancy showed no statistical difference ($p > 0.05$) in caries incidence in children between the intervention (8%) and control group (9%).

A meta-analysis was performed on 4 studies that assessed ECC incidence (results shown in Fig. 4). In particular, Günay et al. [1998] examined the same cohort of children at two time points, when they reached 3 and 4 years of age; their results were included as two data sets in the meta-analysis. Study heterogeneity (I^2 = 75.06%) and the related p value were calculated using the likelihood ratio test ($p < 0.0001$).

The empirical ORs and 95% CIs of the studies included in the meta-analysis are shown in Figure 4a. When compared to the control group, the empirical OR (95% CI) of ECC in children whose mothers received primary-primary prevention is 0.04 (0.00, 0.68) at 3 years of age

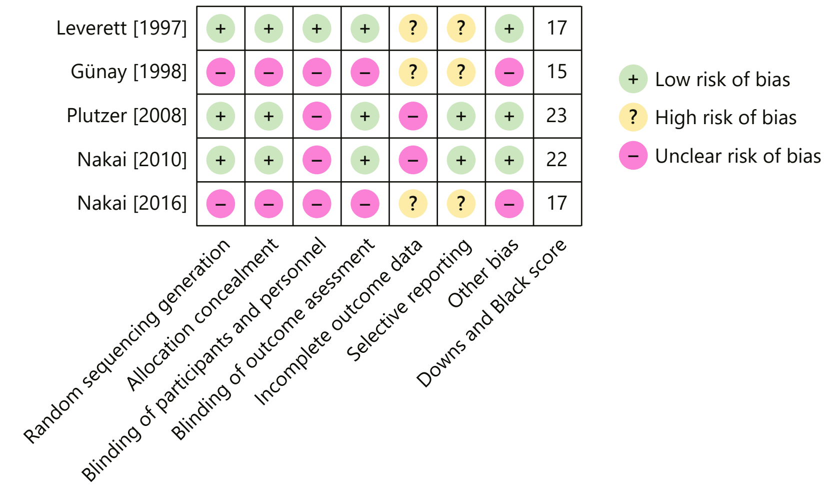

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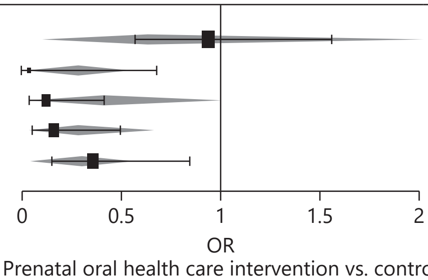
Fig. 3. Summary of quality and risk of bias assessment using the Cochrane Collaboration's tool for assessing risk of bias in randomized trials and the adapted Downs and Black scoring tool. The quality of the selected articles was assessed using two methodological validities: (1) Cochrane Collaboration's tool for assessing risk of bias in randomized trials [Higgins et al., 2011], and (2) Adapted Downs and Black scoring [Downs and Black, 1998] that assesses the methodological quality of both randomized and nonrandomized studies of health care interventions. A total score of 26 represents the highest study quality.

a

Study (child age at the exam)	Empirical OR (95% CI)	ECC/ intervention	ECC/ control
Leverett [1997] (5 years old)	0.94 (0.57, 1.56)	32/398	34/400
Günay [1998] (3 years old)	0.04 (0.00, 0.68)	0/54	12/65
Günay [1998] (3 years old)	0.13 (0.04, 0.42)	4/47	19/45
Plutzer [2008] (1.67 years old)	0.17 (0.06, 0.49)	4/232	20/209
Nakai [2016] (2.1 years old)	0.36 (0.15, 0.85)	57/125	21/30

I^2 (p < 0.01)



b

Estimated OR of experiencing ECC in children whose mothers received prenatal oral health care intervention vs. children in the control group

Child age, years	OR (95% CI)
1	0.12 (0.02, 0.77)
2	0.18 (0.05, 0.63)
3	0.25 (0.09, 0.64)
4	0.35 (0.12, 1.00)
5	0.49 (0.11, 2.24)

Fig. 4. OR of ECC events in the prenatal oral health care intervention group and control group. Meta-analysis was performed on 4 studies that assessed ECC incidence. In particular, Günay et al. [1998] examined the same cohort of children at two time points, when they reached 3 and 4 years of age; their results were included as two data sets in the meta-analysis. Study heterogeneity (I^2 = 75.06%) and the related p value were calculated using the likelihood ratio test (p < 0.0001). The empirical OR and 95% CI of each study included in the meta-analysis was shown in **a**. Based on the generalized linear mixed effects model with covariate age, the estimates of OR and 95% CI shown in **b** indicate that, regarding ECC incidence, there is a statistically significant difference between the intervention and control groups for children younger than 4 years of age. The solid line indicates when OR = 1.

and 0.13 (0.04, 0.42) at 4 years of age [Günay et al., 1998]. Compared to the control group, the empirical OR (95% CI) of ECC is 0.17 (0.06, 0.49) in children whose mothers received oral health education [Plutzer and Spencer, 2008], 0.36 (0.15, 0.85) in children whose mothers received antenatal health care [Nakai et al., 2016], and 0.94 (0.57, 1.56) in children whose mothers received a fluoride supplement [Leverett et al., 1997].

Based on the generalized linear mixed effects model with covariate age, the estimates of ORs and 95% CIs indicate that, regarding ECC incidence, there is a statistically significant difference between the intervention and control groups for children younger than 4 years old, regardless of intervention modalities (detailed in Fig. 4b). The odds of experiencing ECC among the children younger than 4 years whose mothers received prenatal oral health care is significantly less than those children in the control group, indicating a protective effect of prenatal oral health care against ECC development with 95% CIs whose upper bounds are smaller than 1. For instance, the estimated ORs (95% CI) are 0.12 (0.02, 0.77) for children at 1 year of age, 0.18 (0.05, 0.63) for children of 2 years of age, 0.25 (0.09, 0.64) at 3 years of age, and 0.35 (0.12, 1.00) at 4 years of age. For children 5 years of age or older, the estimated OR is still smaller than 1, but the 95% CI contains 1, indicating that the protective effect becomes insignificant.

Prenatal Oral Health Care and Reduction of S. mutans *Carriage in Children*

The effect of prenatal oral health care intervention on the reduction of children's *S. mutans* carriage was assessed in 2 studies [Günay et al., 1998; Nakai et al., 2010]. In the study by Günay et al. [1998], *S. mutans* reduction was significant between the intervention and control groups: 100% of children in the intervention group remained *S. mutans* free by the age of 3 years, whereas only 38.5% of children in the control group remained *S. mutans* free by the age of 3 years. Moreover, mothers in the intervention group also showed a significant improvement in plaque index and reduction in *S. mutans* score. The study by Nakai et al. [2010] showed that significantly more children in the xylitol chewing group remained *S. mutans* free at 9, 12, and 24 months. Furthermore, pre- and perinatal xylitol chewing by mothers delayed *S. mutans* carriage in children. The children's *S. mutans* acquisition age in the xylitol chewing group was 8.8 months later than that of the control group (mean age 20.8 vs. 12.0 months).

Discussion

The results of this review have shown a reduced ECC incidence in children whose mothers received prenatal oral health care. ECC is a multifactorial disease with complex socioeconomic, genetic, oral hygiene behaviors, and bacterial and diet factors that affect its risk [Ruby and Goldner, 2007; Wang et al., 2012]. *S. mutans* and, more recently, *Candida* species have been implicated as potential major etiological microorganisms that may be involved in the initiation and development of ECC [Tanzer et al., 2001; Gross et al., 2012; Xiao et al., 2018]. Studies have shown an association between maternal poor oral health and increased risk for ECC [Chaffee et al., 2014]. The association between mother's and child's oral health could possibly be explained by: (1) the mothers' oral health behavior, e.g., perception and knowledge influences the dental health of her children [Saied-Moallemi et al., 2008; Goettems et al., 2012; Olak et al., 2018]; (2) the mother might be a main source of her children's acquisition of oral *S. mutans* and *Candida* sp. [Waggoner-Fountain et al., 1996; Caufield et al., 2005; Bliss et al., 2008; Xiao et al., 2016; Childers et al., 2017].

The following points should be considered when interpreting the results of this review. (1) Various intervention modalities and frequencies were used across the 5 studies, which produced challenges for data analysis, e.g., the heterogeneity of studies included in the meta-analysis is significant ($p < 0.01$). (2) The timing of the main outcome measurement (ECC incidence) with respect to children's age lacks consistency throughout the 5 studies. The peak of ECC onset is 3 years of age, and there is a significant increase in incidence between the age of 2 and 3 years. Kopycka-Kedzierawski et al. [2008] reported a 26% ECC prevalence among 2-year-old children in Rochester, NY, USA; Quiñonez et al. [2001] reported a 20% ECC prevalence in children aged 18–36 months in North Carolina, USA; Rosenblatt and Zarzar [2002] reported a 46% S-ECC prevalence rate among Brazilian children aged 25–36 months. Two studies included in the quantitative analysis only monitored study children until the age of 2 years, which might have underestimated the preventive effect of prenatal oral health care on ECC. (3) As we were not able to collect study subjects' data on other caries determinants, e.g., demographic, socioeconomic, sugar consumption, etc., the meta-analysis performed in this review did not use multivariate analyses to consider the potential confounders mentioned above. Given the multifactorial nature of ECC, the ORs calculated might have under- or overestimated the effectiveness of prenatal oral health care. (4) For the strategies that used prenatal oral health education or primary-primary prevention, it was not clear to what degree the prenatal oral intervention had improved or restored pregnant women's oral health. Therefore, it is challenging to make recommendations on how much oral health care a pregnant woman needs to receive and how much oral health education is needed to demonstrate effective ECC prevention in children. Taking the aforementioned limitations into account, future randomized clinical trials are desired to test prenatal oral health care strategies that maintain or restore an expectant mother's oral health and that measure improvements in oral health knowledge.

Moreover, another dilemma that needs to be considered is that, although routine oral care during pregnancy has been demonstrated to be safe, and recommendations for prenatal oral care have been disseminated globally, utilization of prenatal oral health care is limited in both developed and developing countries [Rocha et al., 2018]. In contrast to the limited utilization of prenatal dental care, over 76% of US women admitted to suffering from oral health problems (pain, bleeding gums, and oral infection) during pregnancy, while more than 43% did not have a dental checkup during pregnancy [DentistryIQ Editors, 2015]. Furthermore, dental care utilization during pregnancy was lower among black women [Thompson et al., 2013], ethnic minorities [Marchi et al., 2010], and women with socioeconomic disadvantages [Singhal et al., 2014]. Thus, oral health represents an important often-neglected heath disparity during pregnancy among minority women and women who are socioeconomically disadvantaged [Guarnizo-Herreño and Wehby, 2012; Azofeifa et al., 2014]. In order to successfully use prenatal oral health care to prevent ECC, future efforts need to gain a better understanding of the factors that enable or inhibit the use of prenatal dental care at both the community and individual levels. Effective strategies might derive from collaborations among dental and medical providers involved in women's and children's dental and medical health, policy makers, and community social workers.

Conclusions

This review reports a reduced ECC incidence and *S. mutans* carriage in children whose mothers received prenatal oral health care. Maintaining oral health and improving oral health care knowledge during pregnancy is a critical and promising step towards ECC prevention. Future studies should consider testing strategies that maintain an expectant mother's oral health or restore an expectant mother's oral health to a disease-free state during pregnancy.

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Disclosure Statement

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Author Contributions

J.X. contributed to the study design; J.X., N.A., D.A.C., T.T.W. performed the data acquisition and analysis; J.X., D.A.C., D.T.K., R.J.B., L.R., H.M., E.E., and Y.R. contributed to the data interpretation, manuscript writing, and critical revision of the manuscript.

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