Risk Factors for Early Childhood Caries: An Umbrella Review

Article *in* Pediatric Dentistry · June 2021

CITATION
1

READS
118

4 authors, including:

Van Nhat Thang Le
Chonbuk National University
8 PUBLICATIONS **13** CITATIONS
SEE PROFILE

Jae-Gon Kim
Chonbuk National University
241 PUBLICATIONS **1,202** CITATIONS
SEE PROFILE

Dae Woo Lee
Chonbuk National University
25 PUBLICATIONS **107** CITATIONS
SEE PROFILE

SYSTEMATIC REVIEW

Risk Factors for Early Childhood Caries: An Umbrella Review

Van Nhat Thang Le, DDS[1] • Jae-Gon Kim, DDS, PhD[2] • Yeon-Mi Yang, DDS, PhD[3] • Dae-Woo Lee, DDS, PhD[4]

Abstract: ***Purpose:*** *The purpose of this umbrella review was to summarize and evaluate the available evidence concerning risk factors for early childhood caries (ECC).* ***Methods:*** *Literature searches were performed until July 2020 in Medline, Web of Science, and EMBASE databases. Systematic reviews were selected, and their methodological qualities were assessed using the AMSTAR 2 tool (16 items).* ***Results:*** *A total of 977 articles for possible inclusion were identified, and 15 studies were finally selected for qualitative analysis. In these 15 studies, the risk of bias varied from critically low to high. The included studies reported risk factors for ECC such as dietary factors, mutans streptococci, low maternal education, maternal age, low family income and parental education level, low social class, enamel defects, obesity, the presence of dentinal caries, presence of Candida albicans, moderate to late preterm birth, and prenatal maternal cigarette smoking.* ***Conclusions:*** *The potential risk factors for early childhood caries are enamel defects, high levels of mutans streptococci, the presence of dentinal caries, increased consumption of soda, daily intake of sugary snacks, and obesity. In the future, longitudinal studies are needed to explore the potential relationship between these risk factors and ECC.*
(Pediatr Dent 2021;43(3):176-84.E24-E33) Received September 7, 2020 | Last Revision February 9, 2021 | Accepted February 10, 2021

KEYWORDS: EARLY CHILDHOOD CARIES, UMBRELLA REVIEW, RISK FACTORS, PREVENTIVE DENTISTRY

Early childhood caries (**ECC**) is the 12th most common multifactorial disease in children younger than six years of age.[1] The development of a comprehensive preventive strategy for ECC is an urgent matter, given that ECC progresses very rapidly once established.[2] However, ECC is often untreated, leading not only to oral health problems such as oral pain, orthodontic issues, and an increased risk of dental caries in the permanent dentition but also to adverse effects on general health, including a reduction in food intake, malnutrition, and speaking issues.[2-7]

To provide a comprehensive preventive strategy, several previous systematic reviews have been performed to elucidate the risk factors for ECC. More than one decade ago, Harris et al. reported 106 risk factors for ECC[8]; more recently, Kirthiga et al.[9] not only identified 123 risk factors for ECC but also ranked them, with enamel defects, dentinal caries, and levels of mutans streptococcus being the strongest risk factors. However, the heterogeneity of risk factors can hinder accurate prevention efforts and lead to an ineffective intervention. Also, some systematic reviews only analyzed a single risk factor to ECC such as the presence of *Candida albicans*,[10] bottlefeeding,[11] moderate to late preterm birth,[12] and prenatal maternal cigarette smoking,[13] which individually do not provide enough evidence to support the development of a comprehensive strategy.

Until now, it has been difficult to determine the precise etiology of ECC because many conclusions remain inconsistent, creating uncertainty and confusion.[14] Therefore, the available evidence from individual reviews must be synthesized by an overview. Recently, an umbrella review has been introduced as the highest level of the evidence hierarchy.[15] Umbrella reviews can analyze existing relevant systematic reviews, collate results, identify consistencies or contradictions, and attempt to establish concrete conclusions.[16]

With an increase in the number of systematic reviews available, a logical and appropriate next step has been to carry out an overview of existing systematic reviews. A comparison of risk factors for ECC from separate reviews of this kind is needed. Furthermore, a newly raised yet pertinent question is: Are the quality of existing systematic reviews on the risk factors for ECC sufficient to provide accurate and reliable evidence?

Therefore, the purpose of this umbrella review was to provide dentists, parents, and policymakers with essential and high information about the initial prevention of early childhood caries.

Methods

Protocol and registration. This umbrella review was performed following the guidelines of the Joanna Briggs Institute Umbrella Reviews for design, implementation, and reporting. The protocol was registered in the PROSPERO database (CRD42018102136).

Eligibility criteria. Inclusion and exclusion criteria were specified before the study, while a PECO (Population, Exposure, Comparison, and Outcome) framework was used to evaluate the association between risk factors and ECC as follows: the population included children under six years of age, regardless of gender, race, socioeconomic status, health status, or geographical location; the exposure factors included sociodemographic status, dietary, breastfeeding and bottlefeeding, and others; the comparison group was children without ECC; and the outcome was the presence of ECC. Case reports, comments, laboratory studies, letters, and narrative reviews were excluded.

[1]*Dr. Le is a lecturer, Faculty of Odonto-Stomatology, Hue University of Medicine and Pharmacy, Hue University, Hue, Vietnam; and a PhD student,* [2]*Drs. Kim and* [3]*Yang are professors; and* [4]*Dr. Lee is an associate professor, all in the Department of Pediatric Dentistry, School of Dentistry, Jeonbuk National University and Research Institute of Clinical Medicine of Jeonbuk National University-Biomedical Research Institute of Jeonbuk National University Hospital, Jeonju, South Korea. Correspond with Dr. Lee at oklee@jbnu.ac.kr*

eXtra Supplemental material available in the online version.

HOW TO CITE:
Le VNT, Kim J-G, Yang Y-M, Lee D-W. Risk Factors for Early Childhood Caries: An Umbrella Review. Pediatr Dent 2021;43(3):176-84.E24-E33.

Data sources and search strategy. Medline, EMBASE, and Web of Science electronic databases were searched to locate relevant systematic reviews of risk factors for ECC up to July 9, 2020. No language restriction was enacted during this search. The literature searches were carried out using the following keywords and Boolean operators: ("risk factors" OR "BMI" OR "obesity" OR "diet" OR "dietary" OR "feeding" OR "breast feeding" OR "parents" OR "parental" OR "parenting" OR "parenting" OR "family" OR "mothers" OR "maternal" OR "socioeconomic" OR "tooth" OR "teeth") AND ("dental caries") AND ("childhood" OR "child" OR "children") AND ("systematic review" OR "meta-analysis") (see **Supplemental Electronic Data–Appendix 1**). Additional assessments of the references of identified systematic reviews were performed.

For study selection, the authors independently screened the titles and abstracts to remove duplicates and read the full texts of all papers to identify relevant systematic reviews. Discrepancies were resolved by one of this study's authors. Attempts to collect missing data or clarify unclear information were made by contacting the relevant authors.

Data extraction. Regarding characteristics of the included systematic reviews, two of this study's authors independently focused on collecting details on the risk factors, author names, publication year, journal name, research questions, search strategies, study design, outcomes, and assessment tools of each study marked for inclusion in this investigation. Disagreements were discussed with one of the authors. Regarding meta-analysis summary, for this part of the present investigation the author names, year of publication, number and study design of the primary study, specific relative risk estimates with confidence intervals, I^2 statistics, and quality appraisal were collected.

Overlapping analysis in the included systematic reviews. In this umbrella review, the "corrected covered area" (**CCA**) was calculated after generating the citation matrix (Figure 1). Based on the CCA, the degree of overlap was classified as either low (zero to five), moderate (six to 10), high (11 to 15), or very high overlap (greater than 15).[17]

Quality appraisal. The included systematic reviews were assessed using the AMSTAR 2 tool with 16 items.[18] For each item, a "yes" response was indicated if the necessary information was available in the included systematic reviews, a "no" response was indicated if the necessary information was unavailable to rate the item, and a "partial yes" was indicated if the information adhered partially to the item. Quality appraisal was conducted by two independent authors.

A Cohen's kappa analysis was conducted to determine the agreement level of two independent authors in terms of the study selection and quality appraisal of the included systematic reviews.

Citation matrix	Systematic review 1	Systematic review 2	Systematic review 3	Systematic review 4
Primary study 1	x		x	x
Primary study 2		x		
Primary study 3		x	x	
Primary study 4	x		x	

$$\text{CA (covered area)} = \frac{N}{rc}$$

$$\text{CCA (corrected CA)} = \frac{N - r}{rc - r}$$

N is the number of included primary studies (including double counting, this is the sum of ticked boxes in the citation matrix), where r is the number of rows (number of primary studies) and c is the number of columns (number of systematic reviews).

Figure 1. Citation matrix and calculation formulae.

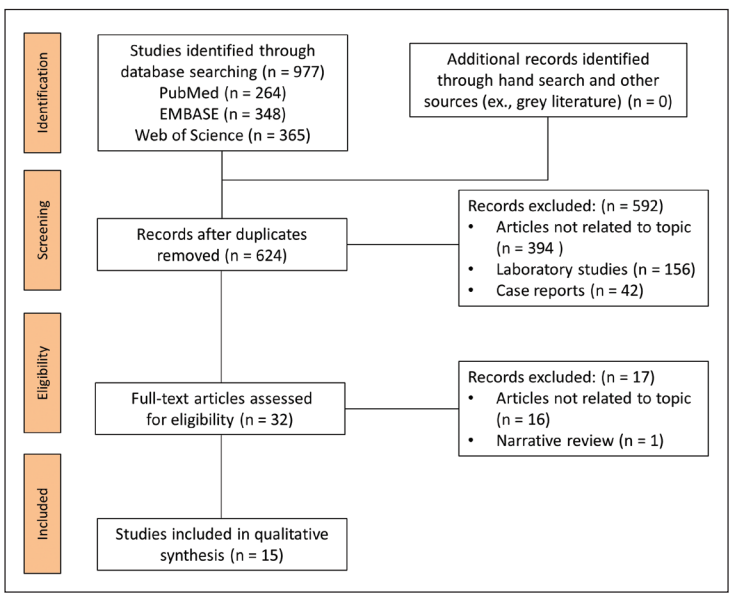

Figure 2. Flow diagram of the included systematic reviews.

Results

Search results. The initial literature search results consisted of a total of 977 articles (Figure 2). After removing 353 duplicates, 592 articles were excluded by screening titles and abstracts. The remaining 32 articles were read in full, and 17 were excluded (16 articles did not relate to the topic and one was a narrative review) (see **Supplemental Electronic Data–sTable**). Finally, a total of 15 articles were confirmed as eligible for inclusion in the analysis.

Description of the systematic reviews. As presented in Table 1, the earliest review was published in 2000 and the latest review was published in 2020. Four systematic reviews (28 percent) were conducted by authors in the United States,[10,13,19,20] three (22 percent) were conducted by authors in Australia,[21-23] two (14 percent) were conducted by authors in Brazil,[11,24] one (six percent) was conducted by authors in Ireland,[8] one (six percent) was conducted by authors in Switzerland,[25] one (six percent) was conducted by authors in England,[26] one (six percent) was conducted by authors in Sweden,[12] one (six percent) was conducted by authors in Canada,[27] and one (six percent) was conducted by authors in India.[9] The number of electronic databases surveyed by the included systematic reviews ranged between one and seven databases, and the search period within the systematic reviews was through 2020. Concerning general methodology, seven systematic reviews (47 percent) were descriptive[8,13,19,21,22,24,27] and eight (53 percent) were meta-analyses.[9-12,20,23,25-26]

Risk factors for ECC were reported in 15 systematic reviews and included dietary factors (N equals six),[9,11,21,22,26,27] mutans streptococci (N equals three),[9,24,25] sociodemographic factors such as low maternal education, maternal age (younger than 25 years), low family income and parental education level, and low social class (N equals three),[9,19,21] enamel defects (N equals two),[8,9] obesity (N equals two),[20,23] the presence of dentinal caries (N equals one),[9] the presence of *Candida albicans* (N equals one),[10] moderate to late preterm birth (N equals one),[12] and prenatal maternal cigarette smoking (N equals one).[13]

Table 1. DESCRIPTION OF THE INCLUDED SYSTEMATIC REVIEWS

Risk factors	Authors, year, *journal* (country)	Meta-analysis	Research question	Search strategy	Study design of the included studies	Outcomes	Assessment tools
Enamel defects	Kirthiga et al.,[9] 2019* *Pediatric Dentistry* (India)	Yes	"What are the main risk factors for early childhood caries?"	**Databases:** MEDLINE, EMBASE, CINAHL via EBSCO, LILACS, Cochrane Oral Health Group's Specialized Register, IndMED, and the Cochrane Central Database **Search period:** 1981–January 2019 **Language restriction:** No restriction	68 longitudinal studies 21 case–control studies	**Upper-middle-income countries:** enamel defects are the strongest risk factor for ECC with OR: 14.62 (6.10–35.03)	NOS
	Harris et al.,[8] 2004 *Community Dental Health* (Ireland)	No	"To identify risk factors for dental caries in deciduous teeth of children aged six years and under."	**Databases:** PubMed® **Search period:** 1966–April 2002 **Language restriction:** No restriction	43 cross-sectional studies 19 longitudinal studies 8 case–control studies 7 interventional studies	Enamel defects are a potential risk factor for ECC	Key question and quality score
Mutans streptococci	Kirthiga et al.,[9] 2019* *Pediatric Dentistry* (India)	Yes	"What are the main risk factors for early childhood caries?"	**Databases:** MEDLINE, EMBASE, CINAHL via EBSCO, LILACS, Cochrane Oral Health Group's Specialized Register, IndMED, and Cochrane Central Database **Search period:** 1981–January 2019 **Language restriction:** No restriction	68 longitudinal studies 21 case–control studies	**High-income countries:** high levels of mutans streptococci is the risk factor associated with ECC OR: 9.21 (4.97–17.07)	NOS
	Parisotto et al.,[24] 2010 (Brazil)	No	"Are mutans streptococci levels a strong risk indicator/ factor for ECC?"	**Databases:** PubMed®, Scopus, and the Cochrane Library **Search period:** December 1951–November 2007 **Language restriction:** Only English	14 cross-sectional studies 2 longitudinal studies	Higher *Streptococcus mutans* level is a strong risk factor for ECC	Scoring criteria
	Thenisch et al.,[25] 2005 (Switzerland)	Yes	"To assess the association of mutans streptococci and dental caries in preschool children"	**Databases:** MEDLINE and MEDLINE In-Process, EMBASE, and the Cochrane Central Register of Controlled Trials **Search period:** From database inception to December 2003 **Language restriction:** No restriction	9 longitudinal studies	The presence of *Streptococcus mutans* in the plaque or saliva of caries-free children is associated with a considerable increase in the risk of caries Plaque tests with RR = 3.85 (2.48–5.96) Saliva tests with RR = 2.11 (1.47–3.02)	Validity checklist for observational studies
Dietary factors	Kirthiga et al.,[9] 2019* *Pediatric Dentistry* (India)	Yes	"What are the main risk factors for early childhood caries?"	**Databases:** MEDLINE, EMBASE, CINAHL via EBSCO, LILACS, Cochrane Oral Health Group's Specialised Register, IndMED, and the Cochrane Central Database **Search period:** 1981–January 2019 **Language restriction:** No restriction	68 longitudinal studies 21 case–control studies	**Upper-middle-income countries:** • Night breastfeeding with OR: 1.28 (1.11–1.47) **High-income countries:** • Increased consumption of soda with OR: 1.12 (1.03–1.23) • Night bottle-feeding with OR: 1.15 (0.44–3.04) • Liquids in the bottle other than milk with OR: 1.27 (0.83–1.94) • Frequent consumption of sweetened foods with OR: 3.14 (0.89–11.04) • Daily intake of sugary snacks with OR: 1.56 (1.42–1.71) • Intake of sugar beverages with OR: 1.67 (0.25–3.92)	NOS
	Moynihan et al.,[26] 2019 *JDR Clinical & Translation Research* (England)	Yes	"To systematically review published evidence pertaining to the effect of modifiable risk factors on ECC."	**Databases:** MEDLINE, EMBASE, CINAHL, and PubMed® **Search period:** Until August 2017 **Language restriction:** No restriction	2 longitudinal studies 1 case–control study 5 cross-sectional studies	Breastfeeding beyond 24 months is associated with an increased risk of ECC as compared with stopping breastfeeding before two years of age	Cochrane risk of bias tool ROBINS-I GRADE

Table 1 continued on the next page.

Table 1. CONTINUED

Risk factors	Authors, year, *journal* (country)	Meta-analysis	Research question	Search strategy	Study design of the included studies	Outcomes	Assessment tools
	Avila et al.,[11] 2015 *PLOS ONE* (Brazil)	Yes	"To systematically review the scientific evidence relating to the association between feeding practice (breastfeeding vs. bottle-feeding) and dental caries in childhood."	**Databases:** PubMed®, Web of Science, ClinicalTrials.gov, National Institute for Health and Clinical Excellence, and Lilacs **Search period:** No date restrictions to start to March 2015 **Language restriction:** Only English	5 cross-sectional studies 1 case–control study 1 longitudinal study	Bottle-feeding results in a higher risk of dental caries as compared with breastfeeding with OR: 0.43 (0.23–0.8)	NOS
	Hooley et al.,[21] 2012** *Journal of Dentistry* (Australia)	No	"What parental variables have been studied within the context of dental caries development in young children, aged 0–6 years?"	**Databases:** MEDLINE, ISI, Cochrane, Scopus, Global Health, and CINAHL **Search period:** After December 2005 **Language restriction:** English, Portuguese, Spanish, French, and Italian	47 cross-sectional studies 7 longitudinal studies 1 case–control study	Breastfeeding, bottle-feeding, night feeding, and between-meal snacking are indirect risk factors for ECC	Diagnosis, statistical analysis, and characteristics of the sample
Dietary factors	Leong et al.,[22] 2012 *International of Paediatric Dentistry* (Australia)	No	"What factors occurring during an infant's first year of life influence the initiation and progression of ECC?"	**Databases:** MEDLINE Ovid SP and EMBASE Ovid SP **Search period:** 1996–April 2011 **Language restriction:** No restriction	6 RCTs 4 longitudinal studies 3 cross-sectional studies	Feeding habits (bacterial colonization) during the first year of the child's life	Critical Appraisal Skills Program criteria
	Valaitis et al.,[27] 2000 *Candida Journal of Public Health* (Canada)	No	"What is the association between breastfeeding beyond eruption of primary dentition and ECC?"	**Databases:** MEDLINE, CINAHL, Biological Abstracts, and Social Science Index **Search period:** 1980–1996 **Language restriction:** No restriction	24 case–control studies 3 case studies 1 cross-sectional study	The evidence suggested an inconsistent and unclear association between breastfeeding and ECC	Validity tool (appraisals of study design, confounders, data-collection method, definition of ECC, dental health practices, and infant feeding practices)
	Kirthiga et al.,[9] 2019* *Pediatric Dentistry* (India)	Yes	"What are the main risk factors for early childhood caries?"	**Databases:** MEDLINE, EMBASE, CINAHL via EBSCO, LILACS, Cochrane Oral Health Group's Specialized Register, IndMED, and the Cochrane Central Database, **Search period:** 1981–January 2019 **Language restriction:** No restriction	68 longitudinal studies 21 case–control studies	**High-income countries:** • Low maternal education with OR: 1.84 (1.14–2.08) • Maternal age (< 25 years) with OR: 1.26 (0.65–2.45)	NOS
Socio-demographic factors	Rai and Tiwari,[19] 2018 *Frontiers in Public Health* (USA)	No	"To evaluate parental risk factors associated with the development of ECC studies in developing nations."	**Databases:** PubMed®/ MEDLINE, Ovid Med, and Web of Science. **Search period:** 2005–2017 **Language restriction:** Only English	15 cross-sectional studies 2 longitudinal studies 1 case–control study	Low family income and parental education level	Statistical analysis and sample characteristics
	Hooley et al.,[21] 2012** *Journal of Dentistry* (Australia)	No	"What parental variables have been studied within the context of dental caries development in young children, aged 0-6 years?"	**Databases:** MEDLINE, ISI, Cochrane, Scopus, Global Health, and CINAHL **Search period:** After December 2005 **Language restriction:** English, Portuguese, Spanish, French, and Italian	47 cross-sectional studies 7 longitudinal studies 1 case–control study	Lower social class, lower family income, and lower level of patient education are indirect risk factors for ECC	Diagnosis, statistical analysis, and characteristics of the sample

Abbreviations in this table: ECC=Early childhood caries; GRADE=Grading of Recommendations Assessment, Development, and Evaluation; JBI SUMARI=System for the Unified Management of the Assessment and Review of Information; NOS=the Newcastle-Ottawa scale; OR=Odds ratio; ROBINS-I=Risk of Bias in Non-randomized Studies of Interventions; RR=Risk ratio.

*,** Indicate studies duplicated in the table for inclusion in multiple risk factors.

Table 1. CONTINUED

Risk factors	Authors, year, *journal* (country)	Meta-analysis	Research question	Search strategy	Study design of the included studies	Outcomes	Assessment tools
Dentinal caries	Kirthiga et al.,[9] 2019* *Pediatric Dentistry* (India)	Yes	"What are the main risk factors for early childhood caries?"	**Databases:** MEDLINE, EMBASE, CINAHL via EBSCO, LILACS, Cochrane Oral Health Group's Specialized Register, IndMED, and the Cochrane Central Database, **Search period:** 1981–January 2019 **Language restriction:** No restriction	68 longitudinal studies 21 case–control studies	Regarding high-income countries, dentinal caries is the strong risk factor for ECC with OR: 4.21 (2.18–8.16)	NOS
Weight status	Monahar et al.,[23] 2020 *Pediatric Obesity* (Australia)	Yes	"To identify whether children aged younger than 6 years with obesity have a higher dental caries experience compared with children with normal weight, and if so, to identify the common risk factors associated with overweight/obesity and dental caries."	**Databases:** MEDLINE (OVID), Web of Science, EMBASE (OVID), Scopus, CINAHL (EBSCO), PsychInfo, ProQuest Central, CENTRAL, and Google Scholar **Search period:** Until 28 February 2019 **Language restriction:** No restriction	5 longitudinal studies 4 case–control studies	Overweight/obese children have a higher dental caries prevalence There is not enough evidence	JBI SUMARI ROBINS-I
	Angelopoulou et al.,[20] 2019 *Pediatric Dentistry* (USA)	Yes	"To examine the association between body weight status and caries experience status; and determine if overweight, obese, or underweight children are at a greater risk of developing early childhood caries compared to normal-weight children."	**Databases:** PubMed®, Google Scholar, and the Cochrane databases **Search period:** Until April 2018 **Language restriction:** No restriction	32 cross-sectional studies	The results of the included studies were inconsistent The meta-analysis suggested that overweight/obese children are at greater risk of having ECC	Quality Assessment Tool for Observational Cohort and Cross-sectional Studies
Preterm birth	Twetman et al.,[12] 2020 *Acta Pediatrica* (Sweden)	Yes	"Is there a relationship between moderate to late preterm birth and the development of early childhood caries?"	**Databases:** PubMed®, the Cochrane Oral Health Group's Trials Register, and Scopus. **Search period:** January 1, 2000–February 28, 2020 **Language restriction:** Only English	3 longitudinal studies 2 case–control studies 2 population registers 7 cross-sectional studies	Children with moderate to late preterm birth had a significantly higher prevalence of ECC than children with full-term birth OR: 1.48 (1.16–1.89)	NOS
Candida albicans	Xiao et al.,[10] 2018 *Caries Research* (USA)	Yes	"To evaluate whether oral detection (saliva, plaque, and oral mucosal swab) of *Candida albicans* is associated with ECC"	**Databases:** PubMed®, EMBASE, Web of Science, Cochrane Library, LILACS, Scopus, and ClinicalTrials.gov **Search period:** Until March 2017 **Language restriction:** No restriction	15 cross-sectional studies	Children with *Candida albicans* were more than five times more likely to have ECC	Quality Assessment Tool for Observational Cohort and Cross-sectional Studies
Prenatal maternal cigarette smoking	Kellesarian et al.,[13] 2017 *Journal of Clinical Experimental Dentistry* (USA)	No	"Is there an association between prenatal maternal cigarette smoking and ECC?"	**Databases:** Web of Knowledge, PubMed®, Scopus, and EMBASE **Search period:** 2005–2017 **Language restriction:** No restriction	8 cross-sectional studies	There was not enough evidence to determine an association between prenatal maternal cigarette smoking and ECC	NOS

Abbreviations in this table: ECC= Early childhood caries; GRADE= Grading of Recommendations Assessment, Development, and Evaluation; JBI SUMARI= System for the Unified Management of the Assessment and Review of Information; NOS= the Newcastle-Ottawa scale; OR= Odds ratio; ROBINS-I= Risk of Bias in Non-randomized Studies of Interventions; RR= Risk ratio.

*,** Indicate studies duplicated in the table for inclusion in multiple risk factors.

The primary studies were cross-sectional (N equals 12),[8,10-13,19-22,24,26,27] longitudinal (N equals 10),[8,9,11,12,19,21-23,25,26] case-control (N equals nine),[8,9,11,12,19,21,23,26,27] interventional (N equals one),[8] and randomized controlled trial (N equals one),[22] case report (N equals one),[27] and population register (N equals one)[12] in design.

Assessment tools such as the Newcastle-Ottawa scale (N equals four)[9,11-13]; Quality Assessment Tool for Observational Cohort and Cross-sectional Studies (N equals two)[10,20]; System for the Unified Management of the Assessment and Review of Information and Risk of Bias in Non-randomized Studies of Interventions (ROBINS-I; N equals one)[23]; statistical analysis and sample characteristics (N equals one)[19]; critical appraisal skills program criteria (N equals one)[22]; caries diagnosis, statistical analysis, and sample characteristics (N equals one)[21]; key question and quality score (N equals one)[8]; scoring criteria (N equals one)[24]; a validity checklist for observational studies (N equals one)[25]; a validity tool (N equals one)[27]; and Cochrane risk of bias tool, ROBINS-I, and Grading of Recommendations Assessment, Development, and Evaluation (**GRADE**; N equals)[26] were used.

Meta-analyses summary. Figure 3 presents a summary of the meta-analyses of the risk factors for ECC. Six risk factors were reported to have high heterogeneity, including night bottlefeeding, consumption of sweetened foods, intake of sugar beverages, low maternal education, maternal age younger than 25 years, and moderate to late preterm birth,[9,12] while three were of a moderate level such as night breastfeeding, the presence of liquids in the bottle other than milk, and bottlefeeding.[9,11] Furthermore, six factors were reported to show low heterogeneity, such as enamel defects, high levels of mutans streptococci, consumption of soda, daily intake of sugary snacks, the presence of dentinal caries, and obesity.[9,20,23] Finally, two reviews did not report on the heterogeneity level.[10,25]

Degree of overlap. With 15 systematic reviews, including a total of 383 primary studies focusing on risk factors for ECC, the degree of overlap between systematic reviews was low (CCA equals 0.01).[17]

The CCA was 0.01, meaning that one percent of the primary studies appeared multiple times across the included reviews (see **Supplemental Electronic Data–Appendix 2**). Therefore, the risk of stronger weighting in the meta-analyses was insignificant. Importantly, this low overlapping helped to reduce critical concerns in the umbrella review.

Methodological quality. Results of the quality appraisal of the 15 systematic reviews are presented in Table 2. One study (seven percent)[23] was classified as being of high quality per the AMSTAR 2 rating scale, four (27 percent)[9,13,24,26] were classified as being of low quality, and 10 (66 percent)[8,10-12,19-22,25,27] were classified as being of critically low quality.

None of the reviews performed an investigation of publication bias (item 15). Furthermore, the items that were most frequently omitted in the reviews included the source of funding of the primary study (item 10), the study design included in the review (item three), and the risk of bias for single studies included in the review (item nine).

The interexaminer reliability scores based on the Kappa statistics were 0.86 for study selection and 0.9 for rating of the AMSTAR 2 items of the included reviews. These values suggest an "almost perfect" agreement.

Discussion

During a literature search, the authors identified 15 systematic reviews investigating risk factors for ECC; however, no overview synthesized all the inconsistent results and covered the topic comprehensively. To address this issue, the authors herein systematically reviewed and appraised the existing relevant systematic reviews via a transparent methodology. Based on the significant impact of risk factors, low heterogeneity, and quality

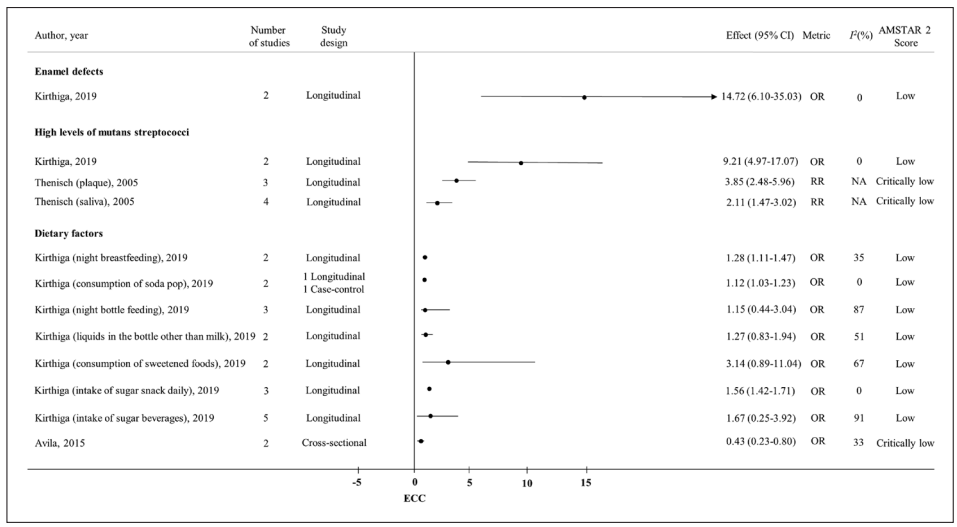

Figure 3a. Summary of meta-analyses; CI: confidence interval, MD: mean difference, NA: not applicable, NR: not reported, OR: odds ratio, RR: risk ratio.

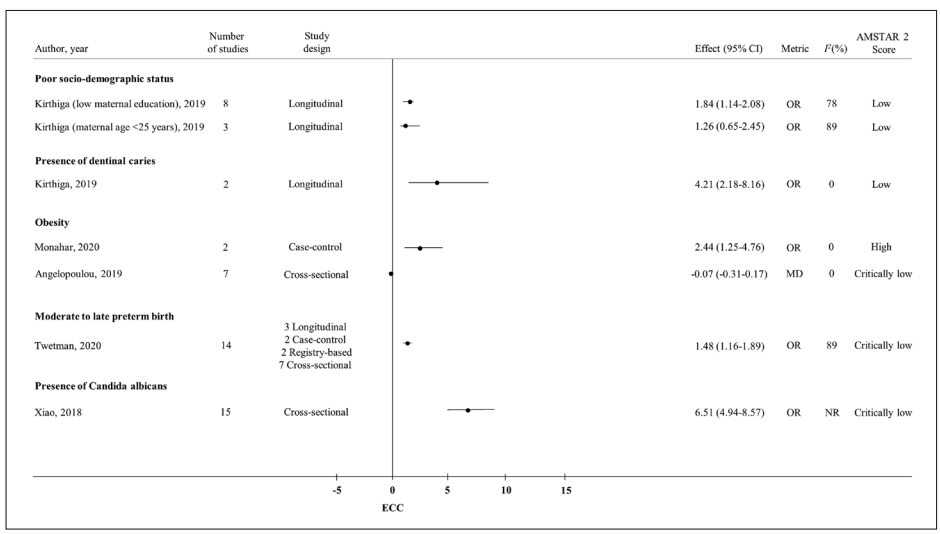

Figure 3b. Summary of meta-analyses; CI: confidence interval, MD: mean difference, NA: not applicable, NR: not reported, OR: odds ratio, RR: risk ratio.

of the included systematic reviews, the authors' review suggests that enamel defects, high levels of mutans streptococci, the presence of dentinal caries, increased consumption of soda, daily intake of sugary snacks, and obesity may be considered as potential risk factors for ECC.

Quality of the included systematic reviews. In the umbrella review, a quality appraisal was performed by the AMSTAR 2 tool, which was designed for the assessment of systematic reviews of both randomized and nonrandomized controlled trials.[18] AMSTAR 2 is a broad assessment tool that assesses flaws that might have occurred in low-quality reviews.[18] Building upon the original version, AMSTAR 2 adds seven more critical domains that may decrease the confidence of the findings.[18] Instead of generating an overall score, AMSTAR 2 provides an overall rating based on the degree of weakness in key domains (e.g., "high," "moderate," "low," and "critically low"). Among the 15 included systematic reviews, one[23] was graded as "high" quality, four[9,13,24,26] were graded as "low" quality, and 10[8,10-12,19-22,25,27] were graded as "critically low" quality. In this context, a "high"-quality review provides an accurate and comprehensive

Table 2. AMSTAR 2 SCORES OF THE SYSTEMATIC REVIEWS

Items		Twetman et al.[12] (2020)	Manohar et al.[23] (2020)	Kirthiga et al.[9] (2019)	Angelopoulou et al.[20] (2019)	Moynihan et al.[26] (2019)	Rai and Tiwari[19] (2018)	Kellesarian et al.[13] (2017)	Xiao et al.[10] (2018)	Avila et al.[11] (2015)	Leong et al.[22] (2012)	Holley et al.[21] (2012)	Parisotto et al.[24] (2010)	Thenisch et al.[25] (2005)	Harris et al.[8] (2004)	Valaitis et al.[27] (2000)
1. Did the research questions and inclusion criteria for the review include the components of PICO?																
2. Did the report of the review contain an explicit statement that the review methods were established prior to the conduct of the review and did the report justify any significant deviations from the protocol?																
3. Did the review authors explain their selection of the study designs for inclusion in the review?																
4. Did the review authors use a comprehensive literature search strategy?																
5. Did the review authors perform study selection in duplicate?																
6. Did the review authors perform data extraction in duplicate?																
7. Did the review authors provide a list of excluded studies and justify the exclusions?																
8. Did the review authors describe the included studies in adequate detail?																
9. Did the review authors use a satisfactory technique for assessing the risk of bias (RoB) individual studies that were included in the review?	RCTs	N/A	N/A	N/A	N/A		N/A	N/A	N/A	N/A		N/A	N/A	N/A	N/A	N/A
	NRSI															
10. Did the review authors report on the sources of funding for the studies included in the review?																
11. If a meta-analysis was performed, did the review authors use appropriate methods for statistical combination of results?	RCTs	N/A	N/A	N/A	N/A		N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
	NRSI						N/A	N/A			N/A	N/A	N/A		N/A	N/A
12. If a meta-analysis was performed, did the review authors assess the potential impact of RoB in individual studies on the results of the meta-analysis or other evidence synthesis?							N/A	N/A			N/A	N/A	N/A		N/A	N/A
13. Did the review authors account for RoB in individual studies when interpreting/discussing the results of the review?																
14. Did the review authors provide a satisfactory explanation for, and discussion of, any heterogeneity observed in the results of the review?																
15. If the review authors performed quantitative synthesis, did they carry out an adequate investigation of publication bias (small study bias) and discuss its likely impact on the results of the review?		N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
16. Did the review authors report any potential sources of conflict of interest, including any funding they received for conducting the review?																
No. of critical domains weaknesses (negatively answered)		2	0	1	3	1	2	1	2	2	4	2	1	3	3	3
Final rating		Critically low	High	Low	Critically low	Low	Critically low	Low	Critically low	Critically low	Critically low	Critically low	Low	Critically low	Critically low	Critically low

Key: = no; = partial yes; = yes; N/A = not applicable.

AMSTAR 2 items assessed:

1, PICO description; 2, protocol registration before the conduct of the review; 3, study design included in the review; 4, comprehensive search strategy; 5, two authors' study selection; 6, two authors' study extraction; 7, justification for excluding individual studies; 8, included studies described in detail; 9, risk of bias for the primary studies being included in the review; 10, source of funding of primary studies; 11, appropriate method of meta-analysis; 12, impact of the risk of bias of primary studies on the results of the meta-analysis; 13, risk of bias consideration when discussing the results of the review; 14, explaining and discussing the heterogeneity; 15, assessing the presence and likely impact of publication bias; 16, conflicts of interest and funding sources declared.

Footnotes:

High: 0–1 noncritical weakness. **Moderate:** > 1 noncritical weakness. The systematic review has more than one weakness, but no critical flaws. **Low:** 1 critical flaw with or without noncritical weaknesses. **Critically low:** > 1 critical flaw with or without noncritical weaknesses.

summary of the results of the primary studies, while "low"-quality reviews may not provide an accurate and comprehensive summary of the primary studies; meanwhile, a grading of "critically low" quality cautions that the review should not be relied on to provide an accurate and comprehensive summary of the primary studies. Consequently, the risk factors for ECC from systematic reviews graded as "critically low" were not considered to establish conclusions.

Across "low"- and "critically low"- quality systematic reviews, publication bias was not assessed. Therefore, publication bias of a variable nature may be possible because of the lack of primary studies in other languages and the inclusion of several publications that could overestimate the effects of the reported risk factors. Moreover, almost all studies in the included systematic reviews were observational. The lack of randomized controlled trials likely influenced the level of synthesized evidence.

Principal findings and possible explanations. In "high"- and "low"- quality systematic reviews, the meta-analyses with low heterogeneity reported enamel defects, high levels of mutans streptococci, the presence of dentinal caries, increased consumption of soda, daily intake of sugary snacks, and obesity significantly influenced ECC.[9,23] Regarding mutans streptococci, a systematic review without a meta-analysis reported a heterogeneous result with high levels of mutans streptococci correlated with the presence of ECC.[24] However, the quality of this review was low. Concerning obesity, although two primary studies included in the meta-analysis were case-control investigations,[28,29] the quality of the systematic review was high. These findings indicate that enamel defects, high levels of mutans streptococci, the presence of dentinal caries, increased consumption of soda, daily intake of sugary snacks, and obesity were potential risk factors for ECC.

Among the other reported risk factors for ECC, there was not enough evidence gathered to confirm an association between prenatal maternal cigarette smoking and ECC[13] because all of the included studies were cross-sectional, with a high risk of bias.[30-37] In addition, the conduct of breastfeeding beyond 24 months[26] was inconsistently associated with an increased risk of ECC in two longitudinal studies.[38,39] Consequently, whether or not prenatal maternal cigarette smoking and breast-feeding beyond 24 months influence ECC prevalence remains unclear.

Strengths. The authors' review has systematically summarized the risk factors for ECC from existing systematic reviews. Furthermore, an evidence-based profile has been revealed regarding the various risk factors for ECC. The following criteria can be considered as a strength: first, a comprehensive search strategy was performed in three electronic databases to avoid missing relevant systematic reviews; second, two independent authors carried out the study selection and data extraction and discrepancies were resolved by a third author; and, finally, AMSTAR 2 was used as a critical assessment tool for systematic reviews in this umbrella review.

Limitations. This study has several limitations that must be considered. First, the authors excluded some systematic reviews that studied children and adolescents. Second, this review did not analyze the heterogeneity of the primary studies, instead only evaluating them preliminarily because of the large number of them. Consequently, recommendations for primary studies were not provided. Finally, this review did not undergo GRADE assessment for the analysis of evidence level.

Future recommendations. During the process of reviewing primary observational studies and systematic reviews on the topic of the risk factors for ECC, several deficiencies in methodology and reporting were identified. To improve the quality of primary observational studies and systematic reviews, the following recommendations are proposed on their conduct and reporting.

1. Study design: Longitudinal cohort studies with risk factor as an "exposure" and ECC as an "outcome" must be performed in different intervals to examine the potential relationship between the risk factor and ECC.
2. Population size: A population size calculation must be based on previous studies or a pilot study. Only an appropriate sample size will have sufficient power to identify statistically significant results.
3. Definition: Future researchers must use consistent definitions of ECC to properly design the criteria for the selection of subjects (inclusion and exclusion criteria) as well as outcome measurement.
4. Outcome measurement: Observational studies must use standardized data collection (self-reported questionnaire for background investigation and standardized measurements for risk factors and dental caries assessment) to reduce the bias from confounding factors such as socioeconomic status, culture, and other aspects. In addition, dental examiners must be trained and calibrated by clinical and radiographic assessment methods to achieve high diagnostic accuracy.
5. Methodology and reporting: The quality of systematic reviews must be improved by adhering to "preferred reporting items for systematic review and meta-analysis" (PRISMA) checklist.

Conclusions

Based on the significant impact of the surveyed risk factors, low heterogeneity, and quality of included systematic reviews, the following conclusions can be made:

1. Enamel defects, high levels of mutans streptococci, the presence of dentinal caries, increased consumption of soda, daily intake of sugary snacks, and obesity may be considered as potential risk factors for early childhood caries.
2. In the future, well-designed longitudinal studies are required to examine the potential relationship between the risk factors and ECC.

Acknowledgments

This study was funded by the Biomedical Research Institute at Jeonbuk National University Hospital, Jeonju, Republic of Korea.

References

1. Phantumvanit P, Makino Y, Ogawa H, et al. WHO global consultation on public health intervention against early childhood caries. Community Dent Oral Epidemiol 2018; 46(3):280-7.
2. Meyer F, Enax J. Early childhood caries: Epidemiology, aetiology, and prevention. Int J Dent 2018;2018:1415873.
3. Abanto J, Carvalho TS, Mendes FM, et al. Impact of oral diseases and disorders on oral health-related quality of life of preschool children. Community Dent Oral Epidemiol 2011;39(2):105-14.
4. Casamassimo PS, Thikkurissy S, Edelstein BL, et al. Beyond the dmft: the human and economic cost of early childhood caries. J Am Dent Assoc 2009;140(6):650-7.

References continued on the next page.

5. Naidu R, Nunn J, Donnelly-Swift E. Oral health-related quality of life and early childhood caries among preschool children in Trinidad. BMC Oral Health 2016;16(1):1-9.
6. Filstrup SL, Briskie D, da Fonseca M, et al. Early childhood caries and quality of life: Child and parent perspectives. Pediatr Dent 2003;25(5):431-40.
7. Benzian H, Monse B, Heinrich-Weltzien R, et al. Untreated severe dental decay: A neglected determinant of low body mass index in 12-year-old Filipino children. BMC Public Health 2011;11(1):1-10.
8. Harris R, Nicoll AD, Adair PM, et al. Risk factors for dental caries in young children: A systematic review of the literature. Community Dent Health 2004;21(1 suppl): 71-85.
9. Kirthiga M, Murugan M, Saikia A, et al. Risk factors for early childhood caries: A systematic review and meta-analysis of case control and cohort studies. Pediatr Dent 2019;41(2):95-112.
10. Xiao J, Huang X, Alkhers N, et al. Candida albicans and early childhood caries: A systematic review and meta-analysis. Caries Res 2018;52(1-2):102-12.
11. Avila WM, Pordeus IA, Paiva SM, et al. Breast and bottle-feeding as risk factors for dental caries: A systematic review and meta-analysis. Plos One 2015;10(11):e0142922.
12. Twetman S, Boustedt K, Roswall J, et al. Systematic review suggests a relationship between moderate to late preterm birth and early childhood caries. Acta Paediatr 2020;109 (12):2472-8.
13. Kellesarian SV, Malignaggi VR, de Freitas P, et al. Association between prenatal maternal cigarette smoking and early childhood caries: A systematic review. J Clin Exp Dent 2017;9(9):e1141-e1146.
14. Aromataris E, Fernandez R, Godfrey C, et al. Umbrella reviews. In: Aromataris E, Munn Z, eds. Joanna Briggs Institute Reviewer's Manual. Adelaide, Australia: The Joanna Briggs Institute; 2017. Available at: "http://reviewersmanual.joannabriggs.org/". Accessed June 24, 2018.
15. Fusar-Poli P, Radua J. Ten simple rules for conducting umbrella reviews. Evid Based Ment Health 2018;21(3): 95-100.
16. Botero JE, Rodriguez C, Agudelo-Suarez AA. Periodontal treatment and glycaemic control in patients with diabetes and periodontitis: An umbrella review. Aust Dent J 2016; 61(2):134-48.
17. Pieper D, Antoine SL, Mathes T, et al. Systematic review finds overlapping reviews were not mentioned in every other overview. J Clin Epidemiol 2014;67(4):368-75.
18. Shea BJ, Reeves BC, Wells G, et al. AMSTAR 2: A critical appraisal tool for systematic reviews that include randomised or non-randomised studies of healthcare interventions, or both. Br Med J 2017;358:j4008.
19. Rai NK, Tiwari T. Parental factors influencing the development of early childhood caries in developing nations: A systematic review. Front Public Health 2018;6:64.
20. Angelopoulou MV, Beinlich M, Crain A. Early childhood caries and weight status: A systematic review and meta-analysis. Pediatr Dent 2019;41(4):261-72.
21. Hooley M, Skouteris H, Boganin C, et al. Parental influence and the development of dental caries in children aged 0-6 years: A systematic review of the literature. J Dent 2012;40(11):873-85.
22. Leong PM, Gussy MG, Barrow SY, et al. A systematic review of risk factors during first year of life for early childhood caries. Int J Paediatr Dent 2013;23(4):235-50.
23. Manohar N, Hayen A, Fahey P, et al. Obesity and dental caries in early childhood: A systematic review and meta-analyses. Obes Rev 2020;21(3):e12960.
24. Parisotto TM, Steiner-Oliveira C, Silva CM, et al. Early childhood caries and mutans streptococci: A systematic review. Oral Health Prev Dent 2010;8(1):59-70.
25. Thenisch NL, Bachmann LM, Imfeld T, et al. Are mutans streptococci detected in preschool children a reliable predictive factor for dental caries risk? A systematic review. Caries Res 2006;40(5):366-74.
26. Moynihan P, Tanner LM, Holmes RD, et al. Systematic review of evidence pertaining to factors that modify risk of early childhood caries. J Clin Transl Res 2019;4(3): 202-16.
27. Valaitis R, Hesch R, Passarelli C, et al. A systematic review of the relationship between breastfeeding and early childhood caries. Can J Public Health 2000;91(6):411-7.
28. Bhoomika W, Ramakrishna Y, Munshi AK. Relationship between severe early childhood caries and body mass index. J Clin Pediatr Dent 2013;37(3):235-42.
29. Davidson K, Schroth RJ, Levi JA, et al. Higher body mass index associated with severe early childhood caries. BMC Pediatr 2016;16(1):1-8.
30. Shulman JD. Is there an association between low birth weight and caries in the primary dentition? Caries Research 2005;39(3):161-7.
31. Iida H, Auinger P, Billings RJ, et al. Association between infant breastfeeding and early childhood caries in the United States. Pediatrics 2007;120(4):e944-e952.
32. Tanaka K, Miyake Y, Sasaki S. The effect of maternal smoking during pregnancy and postnatal household smoking on dental caries in young children. J Pediatr 2009; 155(3):410-5.
33. Majorana A, Cagetti MG, Bardellini E, et al. Feeding and smoking habits as cumulative risk factors for early childhood caries in toddlers, after adjustment for several behavioral determinants: A retrospective study. BMC Pediatr 2014;14(1):1-8.
34. Tanaka K, Miyake Y. Low birth weight, preterm birth or small-for-gestational-age are not associated with dental caries in young Japanese children. BMC Oral Health 2014;14(1):1-6.
35. Tanaka S, Shinzawa M, Tokumasu H, et al. Secondhand smoke and incidence of dental caries in deciduous teeth among children in Japan: Population-based retrospective cohort study. Br Med J 2015;351:h5397.
36. Tanaka K, Miyake Y, Nagata C, et al. Association of prenatal exposure to maternal smoking and postnatal exposure to household smoking with dental caries in 3-year-old Japanese children. Environ Res 2015;143(Pt A):148-53.
37. Bernabe E, MacRitchie H, Longbottom C, et al. Birth weight, breastfeeding, maternal smoking and caries trajectories. J Dent Res 2017;96(2):171-8.
38. Peres KG, Nascimento GG, Peres MA, et al. Impact of prolonged breastfeeding on dental caries: A population-based birth cohort study. Pediatrics 2017;140(1): e20162943.
39. Chaffee BW, Feldens CA, Vitolo MR. Association of long-duration breastfeeding and dental marginal structural models caries estimated with. Ann Epidemiol 2014;24(6): 448-54.

Supplemental Electronic Data

Appendices

Appendix 1. DETAILED SEARCH STRATEGIES FOR EACH DATABASE. MESH TERMS, SEARCH TERMS, AND COMBINATIONS OF THE TWO WERE USED FOR EACH DATABASE SEARCH.

Database	Detailed search strategies	Records founded
MEDLINE/ PUBMED®	("risk factors"[MeSH Terms] OR risk factors[Text Word] OR bmi[All Fields] OR "obesity"[MeSH Terms] OR obesity[Text Word] OR "diet" [MeSH Terms] OR diet[Text Word] OR dietary[Text Word] OR feeding [All Fields] OR "breast feeding"[MeSH Terms] OR breastfeeding[Text Word] OR "parents"[MeSH Terms] OR parental[Text Word] OR "parenting" [MeSH Terms] OR parenting[Text Word] OR "family"[MeSH Terms] OR family[Text Word] OR "mothers"[MeSH Terms] OR maternal[Text Word] OR socioeconomic[All Fields] OR "tooth"[MeSH Terms] OR teeth [Text Word]) AND ("dental caries"[MeSH Terms] OR dental caries[Text Word]) AND ("childhood" OR "child" OR "children") AND ("systematic review" OR "meta-analysis")	264
EMBASE	('risk factors' OR bmi OR 'obesity' OR 'diet' OR dietary OR feeding OR 'breast feeding' OR 'parents' OR parental OR 'parenting' OR parenting OR 'family' OR 'mothers' OR maternal OR socioeconomic OR 'tooth' OR teeth) AND 'dental caries' AND ('childhood' OR 'child' OR 'children') AND ('systematic review' OR 'meta-analysis')	348
Web of Science	(('risk factors' OR bmi OR 'obesity' OR 'diet' OR dietary OR feeding OR 'breast feeding' OR 'parents' OR parental OR 'parenting' OR parenting OR 'family' OR 'mothers' OR maternal OR socioeconomic OR 'tooth' OR teeth) AND 'dental caries' AND ('childhood' OR 'child' OR 'children') AND ('systematic review' OR 'meta-analysis'))	365

Ultimately, 977 records were found, 264 from MEDLINE/PubMed®, 348 from EMBASE, 365 from the Web of Science. Studies were further selected according to the inclusion criteria listed in the Material and Methods (Figure 1).

Appendix 2. CITATION MATRIX FOR REVIEWS ASSESSED THE RISK FACTORS FOR ECC

Primary studies	Systematic reviews														
	Twetman et al.[12] (2020)	Manohar et al.[23] (2020)	Kirthiga et al.[9] (2019)	Angelopoulou et al.[20] (2019)	Moynihan et al.[26] (2019)	Rai and Tiwari.[19] (2018)	Kellesarian et al.[13] (2017)	Xiao et al.[10] (2018)	Avila et al.[11] (2015)	Leong et al.[22] (2012)	Holley et al.[21] (2012)	Parisotto et al[24]. (2010)	Thenisch et al.[25] (2005)	Harris et al.[8] (2004)	Valaitis et al.[27] (2000)
Boustedt, 2020	X														
Soares, 2020	X														
Hisano, 2018	X														
Schuler, 2018	X														
Nishide et al., 2018			X												
Boustedt et al., 2018			X												
Jean et al., 2018			X												
Feldens et al., 2018			X												
Saraiva, 2017	X														
Ribeiro et al., 2017		X													
Cabral et al., 2017			X												
Birungi et al., 2017			X												
Dabawala et al., 2017			X												
Antunes et al., 2017				X											
Krishna et al., 2017				X											
Madsen et al., 2017				X											
Mitrakul et al., 2017				X											
Soares et al., 2017				X											
Peres et al., 2017			X		X										
Sun et al., 2017	X					X									
Bernabe et al., 2017			X				X								
Lozano Moraga et al., 2017								X							
Ozem, 2016	X														
Porhashemi et al., 2016		X													
Ostberg et al., 2016			X												
Warren et al., 2016			X												
Fan et al., 2016			X												
Paglia et al., 2016			X												
Nirunsittirat, 2016	X		X												
Aluckal et al, 2016				X											
da Silva et al., 2016				X											
Davidson et al., 2016		X		X											
Pikramenou et al, 2016				X											
Xiao et al., 2016								X							
Zhang et al., 2016								X							

Thomas et al., 2016								X							
Peltzer and Mongkochali, 2015			X												
Ghazal et al., 2015			X												
Yokomichi H et al., 2015			X												
Winter et al., 2015	X		X												
Kato et al., 2015			X												
Chankanka et al., 2015			X												
Yu et al., 2015			X												
Dantas Cabral de Melo et al., 2015			X												
Rodriguez et al., 2015				X											
Khanh et al, 2015				X											
Jain et al., 2015						X									
Peltzer and Aroonsri, 2015						X									
Sujlana and Pannu, 2015						X									
Folayan et al., 2015						X									
Tanaka, Shinzawa et al., 2015			X				X								
Tanaka, Miyake et al., 2015							X								
Wu et al., 2015								X							
Qiu et al., 2015								X							
Neves et al., 2015								X							
Zaror et al., 2014		X	X												
Gao et al., 2014			X												
Peltzer et al., 2014			X												
Watanabe et al., 2014			X												
Hong et al., 2014			X												
Schroth et al., 2014			X												
Moimaz et al., 2014			X												
Al Mendalwi and Karam, 2014			X												
Chaffee et al., 2014					X										
Wulaerhan et al., 2014						X									
dos Santos Junior et al., 2014	X			X		X									
Tanaka and Miyake, 2014	X						X								
Perera et al., 2014									X						
Majorana et al., 2014			X				X		X						
Mahesh et al., 2013			X												
Tanaka et al., 2013			X												
Menon et al., 2013			X												
Evans et al., 2013			X												
Yen and Hu, 2013				X											
Powell et al., 2013				X											
Bagherian and Sadeghi, 2013				X											
Bhoomika et al., 2013				X											

Appendix 2 continued on the next page.

Costa et al., 2013				X											
Narang et al., 2013						X									
Hamila, 2013						X									
Correa-Faria et al., 2013						X									
Bhoomika et al., 2012		X													
Almeida et al., 2012			X												
Zhou et al., 2012			X												
Nunes et al., 2012			X												
Tanaka et al., 2012			X												
Norberg et al., 2012				X											
Prakash et al., 2012						X									
Menon et al., 2012						X									
Borges et al., 2012						X									
Yang et al., 2012								X							
Qadri et al., 2012									X						
Alm et al., 2011		X													
Wigen and Wang, 2011			X												
Bankel et al., 2011			X												
Parisoto et al., 2011			X												
Targino et al., 2011			X												
Del Rosario Garcia et al., 2011			X												
Melo et al., 2011			X												
Gaur and Nayak, 2011				X											
Campos et al., 2011				X											
Trikaliotis et al., 2011				X											
Vania et al, 2011		X		X											
Ghasempour et al., 2011								X							
Agarwal et al., 2011											X				
Dye et al., 2011											X				
Fontana et al., 2011											X				
Li et al., 2011											X				
Narksawat et al., 2011											X				
Wigen et al., 2011	X		X								X				
Zhou et al., 2011											X				
Sanders and Slade, 2010			X												
Kay et al., 2010		X	X												
Li et al., 2010						X									
Zhou et al., 2010						X									
Nakai et al., 2010										X					
Feldens et al., 2010			X			X				X					
Al-Jewair and Leake, 2010											X				
Begzati et al., 2010											X				
Elfrink et al., 2010											X				
Ferro et al., 2010											X				
Gao et al., 2010											X				

Meurman and Pienihakkinen, 2010			X								X				
Niji et al., 2010											X				
Oliveira et al., 2010											X				
Senesombath et al., 2010											X				
Tanaka et al., 2010											X				
Wigen and Wang, 2010											X				
Campus, 2009	X														
Hong et al., 2009			X												
Warren et al., 2009			X												
Floyd, 2009				X											
Sheller et al., 2009				X											
Ismail et al., 2009			X	X											
Tanaka et al., 2009							X								
Fontana et al., 2009										X					
Adeniyi et al., 2009						X					X				
Bonanato et al., 2009						X					X				
Hashim et al., 2009											X				
Namal et al., 2009											X				
Nunn et al., 2009											X				
Ohsuka et al., 2009											X				
Seow et al., 2009			X								X				
Tiano et al., 2009											X				
Traebert et al., 2009											X				
Wigen et al., 2009											X				
Yonezu and Yakushiji, 2008			X												
Lim et al., 2008			X												
Ismail et al., 2008			X												
Franco et al., 2008										X					
Qin et al., 2008			X							X					
Aida et al., 2008											X				
Cogulu et al., 2008											X				
Declerck et al., 2008											X				
Hanioka et al., 2008											X				
Hong et al., 2008											X				
Lencova et al., 2008											X				
Leroy et al., 2008											X				
Menghini et al., 2008											X				
Oliveira et al., 2008				X							X				
Postma et al., 2008											X				
Tyagi, 2008											X				
Marshall et al., 2007		X													
Campus et al., 2007			X												
Teanpaisan et al., 2007			X							X					
Ilida et al., 2007							X								
Ugun-Can et al., 2007								X							

Du et al., 2007									X		X				
Tiberia et al., 2007											X				
Law and Seow, 2006			X												
Oliveira et al., 2006			X												
Slade et al., 2006			X								X				
Van Palenstein Henderman et al., 2006			X								X				
Yonezu et al., 2006			X								X				
Macek et al., 2006				X											
De Carvalho et al., 2006								X							
Rozkiewicz et al., 2006								X							
Thitasomakul et al., 2006										X					
Astrøm and Kiwanuka, 2006											X				
Brandao et al., 2006											X				
Droz et al., 2006											X				
Ersin et al., 2006											X	X			
Hallett and O'Rourke, 2006											X				
Kalyvas et al., 2006											X				
Mohebbi et al., 2006											X				
Psoter et al., 2006											X				
Skeie et al., 2006											X				
Spitz et al., 2006											X				
Tsai et al., 2006											X				
Bankel et al., 2006												X			
Nelson et al., 2005			X												
Shulman, 2005							X								
Reifsnider et al., 2004				X											
Vachirarojpisan et al., 2004												X			
Levy et al., 2003			X												
Hossain et al., 2003								X							
Wan et al., 2003										X					
Singh et al., 2003										X					
Olmez et al., 2003												X			
Seki et al., 2003													X		
Dasanayake et al., 2002										X					
Nobre-dos-Santos et al., 2002												X			
Ramos-Gomez et al., 2002												X			
Pienihäkkinen and Jokela, 2002													X		
Lulic Dukic et al., 2001			X												
Marchant et al., 2001								X							
Habibian et al., 2001										X					
Mattos-Graner et al., 2001												X			

Creedon & O'Mullane, 2001													X	
Douglass et al., 2001													X	
Karjalainen et al., 2001													X	
Maciel et al., 2001													X	
Al-Malik et al., 2001													X	
Quinonez et al., 2001													X	
Tsai et al., 2001													X	
Ansai et al., 2000			X											
Radford et al., 2000								X						
Du et al., 2000									X					
Milgrom et al., 2000											X		X	
Petti et al., 2000											X			
Isokangas et al., 2000													X	
Kowash et al., 2000													X	
Li et al., 2000													X	
Mattila et al., 2000													X	
Rodrigues & Sheiham, 2000			X										X	
Williams et al., 2000													X	
Tada et al., 1999			X											
Gibson & Williams, 1999													X	
Lin & Tsai, 1999													X	
Lopez et al., 1999													X	
Moss, 1999													X	
Ramos-Gomez et al., 1999													X	
Seow et al., 1999													X	
Thibodeau & O'Sullivan, 1999													X	
Toi et al., 1999													X	
Wendt et al., 1999													X	
Williams et al., 1999													X	
Mattila et al., 1998			X										X	
Ollila et al., 1998			X										X	
Chen et al., 1998				X										
Mohan et al., 1998										X				
Brambilla et al., 1998										X				
Mattos-Graner et al., 1998											X			
al-Ghanim et al., 1998													X	
Angelillo et al., 1998													X	
Hu et al., 1998													X	
Kendrick et al., 1998													X	
Khan & Cleaton-Jones, 1998													X	
Lopez et al., 1998													X	
Petersen & Esheng, 1998													X	
Schwarz et al., 1998													X	

Venugopal et al., 1998														X	
Freeman et al., 1997														X	
Peretz and Kafka, 1997			X												
Lai et al., 1997			X												
Harrison et al., 1997														X	
Holst et al., 1997														X	
Karjalainen et al., 1997														X	
Kawabata et al., 1997														X	
Leverett et al., 1997														X	
Zoitopoulus et al., 1997														X	
Shantinath et al., 1996			X												
Grindefjord et al., 1996			X												
O' Sullivan et al., 1996			X												
Ayhan et al., 1996				X											
Douglass et al., 1996												X			
Thibodeau and O'Sullivan, 1996			X									X	X		
Grindefjord et al., 1996														X	
Holt & Downer, 1996														X	
Li et al., 1996														X	
Muller, 1996														X	
Wendt et al., 1996			X										X	X	X
Wendt et al., 1995			X												
Al-Dashti et al., 1995									X						X
Hallosten et al., 1995												X		X	
Litt et al., 1995													X		
Dasanayake et al., 1995														X	
Grindefjord et al., 1995														X	
Aaltonen et al., 1994			X											X	
Roberts et al., 1994			X						X						X
Twetman et al., 1994													X		
Kalsbeek & Verrips, 1994														X	
Matee et al., 1994														X	X
Reisine et al., 1994														X	
Schroder et al., 1994														X	
Tsubouchi et al., 1994														X	X
Todd et al., 1994															X
O'Sullivan and Tinanoff, 1993												X			
Paunio et al., 1993														X	
Roberts et al., 1993															X
Acs et al., 1992				X											
Matee et al., 1992												X			
Barnes et al., 1992														X	
Marques & Messer, 1992														X	
Petersen, 1992														X	

Verrips et al., 1992														X	
Silver, 1992															X
Vignarajah and Wiliams, 1992															X
Eronat and Eden, 1992															X
Matee et al, 1992a															X
Matee et al, 1992b															X
Fujiwara et al., 1991												X			
Aaltonen, 1991														X	
Kerusho et al., 1991														X	
Tenovuo et al., 1990													X		
Ekman, 1990														X	
Williams & Hargreaves, 1990														X	X
Marino et al., 1989			X												X
Rodriguez Miro et al., 1989													X		
Freeman et al., 1989														X	
Rodriguez-Contreras et al., 1989														X	
Vidal & Schroder, 1989														X	
Wetzel et al., 1989														X	
Babeely et al., 1989															X
Grytten et al., 1988			X											X	
Wetzel, 1988														X	
Holt et al., 1988															X
Albert et al., 1988															X
Milen, 1987														X	
Silver, 1987															X
Tee, 1987															X
Haq et al., 1985															X
Salako, 1985															X
Cleaton-Jones et al., 1984														X	
Alaluusua and Renkonen, 1983													X		
Miller et al., 1982				X											
Derson and Ponti, 1982															X
Adenubi, 1982															X
Holt et al., 1982															X
Johnsen, 1982															X
Richardson et al., 1981															X
Walton and Messer, 1981															X
Dilley et al., 1980															X

Supplemental Table

sTable. EXCLUDED STUDIES, WITH REASONS FOR EXCLUSION

No	Study	Reason for Exclusion
1	Jorgensen MR, Twetman S. A systematic review of risk assessment tools for early childhood caries: Is there evidence? Eur Arch Paediatr Dent 2020;21(2):179-84.	Risk assessment tools for ECC
2	Schmoeckel J, Gorseta K, Splieth CH, et al. How to intervene in the caries process: Early childhood caries - A systematic Review. Caries Res 2020;54(2):102-12.	Treatment of ECC
3	Chen KJ, Gao SS, Duangthip D, et al. Prevalence of early childhood caries among 5-year-old children: A systematic review. J Investig Clin Dent 2019;10(1):e12376.	Prevalence of ECC
4	Xiao J, Alkhers N, Kopycka-Kedzierawski DT, et al. Prenatal oral health care and early childhood caries prevention: A systematic review and meta-analysis. Caries Res 2019;53(4):411-21.	ECC prevention
5	Ganesh A, Muthu MS, Mohan A, et al. Prevalence of early childhood caries in India - A systematic review. Indian J Pediatr 2019;86(3):276-86.	Prevalence of ECC
6	Riggs E, Kilpatrick N, Slack-Smith L, et al. Interventions with pregnant women, new mothers and other primary caregivers for preventing early childhood caries. Cochrane Database Syst Rev 2019;2019(11).	ECC prevention
7	Mishra P, Fareed N, Battur H, et al. Role of fluoride varnish in preventing early childhood caries: A systematic review. Dent Res J (Isfahan) 2017;14(3):169-76.	ECC prevention
8	Henry JA, Muthu MS, Swaminathan K, et al. Do oral health educational programmes for expectant mothers prevent early childhood caries? - Systematic review. Oral Health Prev Dent 2017;15(3):215-21.	ECC prevention
9	Anil S, Anand PS. Early childhood caries: Prevalence, risk factors, and prevention. Front Pediatr 2017;5157.	Narrrative review
10	Javed F, Feng C, Kopycka-Kedzierawski DT. Incidence of early childhood caries: A systematic review and meta-analysis. J Investig Clin Dent 2017;8(4).	Incidence of ECC
11	Contreras V, Toro MJ, Elias-Boneta AR, et al. Effectiveness of silver diamine fluoride in caries prevention and arrest: A systematic literature review. Gen Dent 2017;65(3): 22-9.	Treatment of ECC
12	Gao SS, Zhang S, Mei ML, et al. Caries remineralisation and arresting effect in children by professionally applied fluoride treatment - A systematic review. BMC Oral Health 2016;1612.	Treatment of ECC
13	Yengopal V, Harnekar SY, Patel N, et al. WITHDRAWN: Dental fillings for the treatment of caries in the primary dentition. Cochrane Database Syst Rev 2016; 10CD004483.	Treatment of ECC
14	Li YH, Tanner A. Effect of Antimicrobial interventions on the oral microbiota associated with early childhood caries. Pediatric Dentistry 2015;37(3):226-44.	Treatment of ECC
15	Chaffee BW, Cheng A. Global research trends on early-life feeding practices and early childhood caries: A systematic review. J Oral Dis 2014;2014675658.	Research Trends on Early-Life Feeding Practices and ECC
16	Ammari JB, Baqain ZH, Ashley PF. Effects of programs for prevention of early childhood caries. A systematic review. Med Princ Pract 2007;16(6):437-42.	ECC prevention
17	Ismail AI, Sohn W. A systematic review of clinical diagnostic criteria of early childhood caries. J Public Health Dent 1999;59(3):171-91.	Clinical diagnostic criteria of ECC