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Systematic Literature Review

Systematic Review of Economic Evaluations of Primary Caries Prevention in 2- to 5-Year-Old Preschool Children

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ABSTRACT

Objectives: To describe and summarize evidence on economic evaluations (EEs) of primary caries prevention in preschool children aged 2 to 5 years and to evaluate the reporting quality of full EE studies using a quality assessment tool.

Methods: A systematic literature search was conducted in several databases. Full and partial EEs were included. The reporting quality of full EE studies was assessed using the Consolidated Health Economic Evaluation Reporting Standards (CHEERS) checklist.

Results: A total of 808 studies were identified, and 39 were included in the review. Most papers were published between 2000 and 2017 and originated in the United States and the United Kingdom. The most common type of intervention investigated was a complex multicomponent intervention, followed by water fluoridation. Cost analysis and cost-effectiveness analysis were the most frequently used types of EE. One study employed cost-utility analysis. The proportion of full EEs increased over time. The parameters not reported well included study perspective, baseline year, sensitivity analysis, and discount rate. The CHEERS items that were most often unmet were characterizing uncertainty, study perspective, study parameters, and estimating resources and costs.

Conclusions: Within the past 2 decades, there has been an increase in the number of EEs of caries prevention interventions in preschool children. There was inconsistency in how EEs were conducted and reported. Lack of preference-based health-related quality-of-life measure utilization in the field was identified. The use of appropriate study methodologies and greater attention to recommended EE design are required to further improve quality.

Keywords: cost-effectiveness, dental caries, dentistry, economic evaluation, oral health, pediatric, preschool child, systematic review.

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Introduction

Untreated dental caries is one of the most common diseases affecting humans worldwide.[1,2] Early childhood caries can lead to pain, infections, and difficulties with eating, sleeping, and socializing, thus affecting a child's general health and child and family quality of life.[3,4] It often leads to school absenteeism and parents taking time off work to take their children to a dentist or to hospital.[4,5] Early childhood caries poses an economic burden to individuals, the health sector, and society more broadly.[3] The 2010 global direct financial costs associated with dental caries were estimated to be $298 billion, and indirect costs came to $144 billion.[6] Untreated caries was found to cause 12% of global productivity losses due to dental diseases in 2015: $21.19 billion (11%) owing to untreated caries in permanent teeth and $0.90 billion (0.5%) to caries in deciduous teeth.[7]

A number of child public health caries prevention strategies and intervention types currently exist, and choosing between competing oral public health programs is not always an easy decision for public health planners.[8] In a recent critique, Watt et al[9] recommended that the priority for oral health (OH) research should be the promotion of applied health service and implementation research, with methodologies including economic evaluation (EE), so that planners are able to assess program performance comprehensively.[9] EEs help decision makers to allocate limited resources the best way, to achieve the greatest health benefit. A full EE is "a comparison of two or more alternative courses of action, while considering both inputs (costs) and outputs (consequences) associated with each."[10] The most common types of full EEs are cost-benefit analysis (CBA), cost-effectiveness analysis (CEA), and cost-utility analysis (CUA). A partial EE measures a program/intervention or disease costs but does not involve a comparison with alternative options and does not relate costs to outcomes.[11] Partial EEs include program/intervention cost analysis, cost-outcome description, and cost-of-illness analysis.

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In recent years, the number of published cost-effectiveness studies on the prevention of dental diseases across the life course has increased[12-14]; however, some methodological limitations were found by the previous systematic reviews in the field of EE in dentistry[13] and caries prevention,[12,14] such as absence of sensitivity analysis and discounting and insufficient information on how costs and outcomes were measured.

Experiences and health-related behavior patterns in early life are known to affect OH throughout the life course. Consequently, calls have been made for priority to be given to interventions targeting early ages.[15] Therefore, this age group is the focus of the present systematic review. Recent reviews of EEs of OH improvement programs and interventions[16] and of CUAs of OH interventions[17] (both of which included subjects of all ages) identified only a handful of studies conducted in preschool populations. To our knowledge, there is only 1 nonsystematic review that looked at the evidence on the cost-effectiveness of interventions to improve the OH of younger children, aged 0 to 5 years, in particular.[5] This rapid review with a narrow search time frame (between 2012 and 2016) found only 5 studies that met the inclusion criteria. The authors found scarce cost-effectiveness evidence but warned that this should not be interpreted as evidence that those interventions were not effective or cost-effective.

This is the first systematic review of EEs of primary caries prevention focusing specifically on preschool children aged 2 to 5 years, including both full and partial EEs and using a formal quality assessment tool. The objectives of the present systematic review were to describe and summarize currently available scientific literature on EEs of primary caries prevention in preschool children aged 2 to 5 years and to evaluate the reporting quality of full EE studies using an EE quality assessment tool.

Methods

The review followed the Preferred Reporting System for Systematic Reviews and Meta-Analysis (PRISMA) strategy[18] (Fig. 1). The protocol of this systematic review was registered in the international database of prospectively registered systematic reviews in health and social care (PROSPERO), Centre for Reviews and Dissemination, University of York (No. CRD42017083732).[19]

Eligibility Criteria

A Participants, Interventions, Comparators, Outcomes, and Study design (PICOS) approach[18,20] was used in developing the eligibility criteria. The OH interventions of interest were interventions aimed at primary caries prevention in preschoolers (eg, water fluoridation, fluoride toothpaste, fluoride varnish/gel, fluoride tablets, fissure sealant, OH educational interventions, etc). Studies on interventions aimed at secondary caries prevention were not included (eg, restorative treatment of existing caries). To be included in this review, a study had to report relevant results for children aged between 2 and 5 years (inclusive). At least some age groups from this range had to be reported. Any types of EEs were included: full EEs (eg, employing CEA, CBA, or CUA) and partial EEs (eg, cost analysis, cost-outcome description). A full list of inclusion and exclusion criteria is presented in Appendix Table 1 (in Supplemental Materials found at https://doi.org/10.1016/j.jval.2020.04.1823).

Data Sources and Search Strategy

A systematic literature search was conducted in the following databases: MEDLINE and EMBASE (via the Ovid platform) and EconLit (via the EBSCO platform). Several previous systematic reviews of EEs of OH interventions, their search strategies used, and reference lists were consulted[5,12,13,16,17,21] Reference lists of the studies included in this systematic review were checked for any additional eligible studies.

Search strategies and search terms for this systematic review were developed based on the Canadian Agency for Drugs and Technologies in Health (CADTH) EE filters.[22,23] The guidance for undertaking systematic reviews in healthcare by the University of York's Centre for Reviews and Dissemination (CRD)[24] and a series of papers on how to conduct a systematic review of EEs[25-27] were used in the process of developing and conducting this review.

No publication time or language restrictions were applied. It was planned that should any relevant papers be identified in languages other than English or Russian, these would be translated with a help of professional translation services.

The following blocks of search terms were used: (1) Canadian Agency for Drugs and Technologies in Health–based search filter (including various types of EEs, economics, costs, and economic modeling); (2) OH, caries, and OH intervention terms (OH, caries, early childhood caries, dental decay; toothbrushing, toothpaste, fluoride, fissure sealant, chlorhexidine, mouthwash; educational, preventive, and promotional OH initiatives, etc); and (3) terms related to preschool age (toddler, infant, preschool, early childhood, nursery, kindergarten, early years; Appendix Box 1 in Supplemental Materials found at https://doi.org/10.1016/j.jval.2020.04.1823).

Study Selection Procedure

Titles and abstracts of all retrieved records were screened against the inclusion criteria by the lead author, using a method developed by Bramer et al[28] employing EndNote (Clarivate Analytics, Philadelphia, PA). Citations with a title but no abstract were assessed for relevance based on the title only. Twenty percent of all titles and abstracts were checked by a second reviewer. Any disagreements were resolved by consensus-seeking discussions between all 3 reviewers. The full texts of all potentially relevant articles were retrieved and screened by the author, with any questionable cases discussed with one of the second reviewers or between all 3 reviewers, depending on the nature of an issue.

Data Extraction

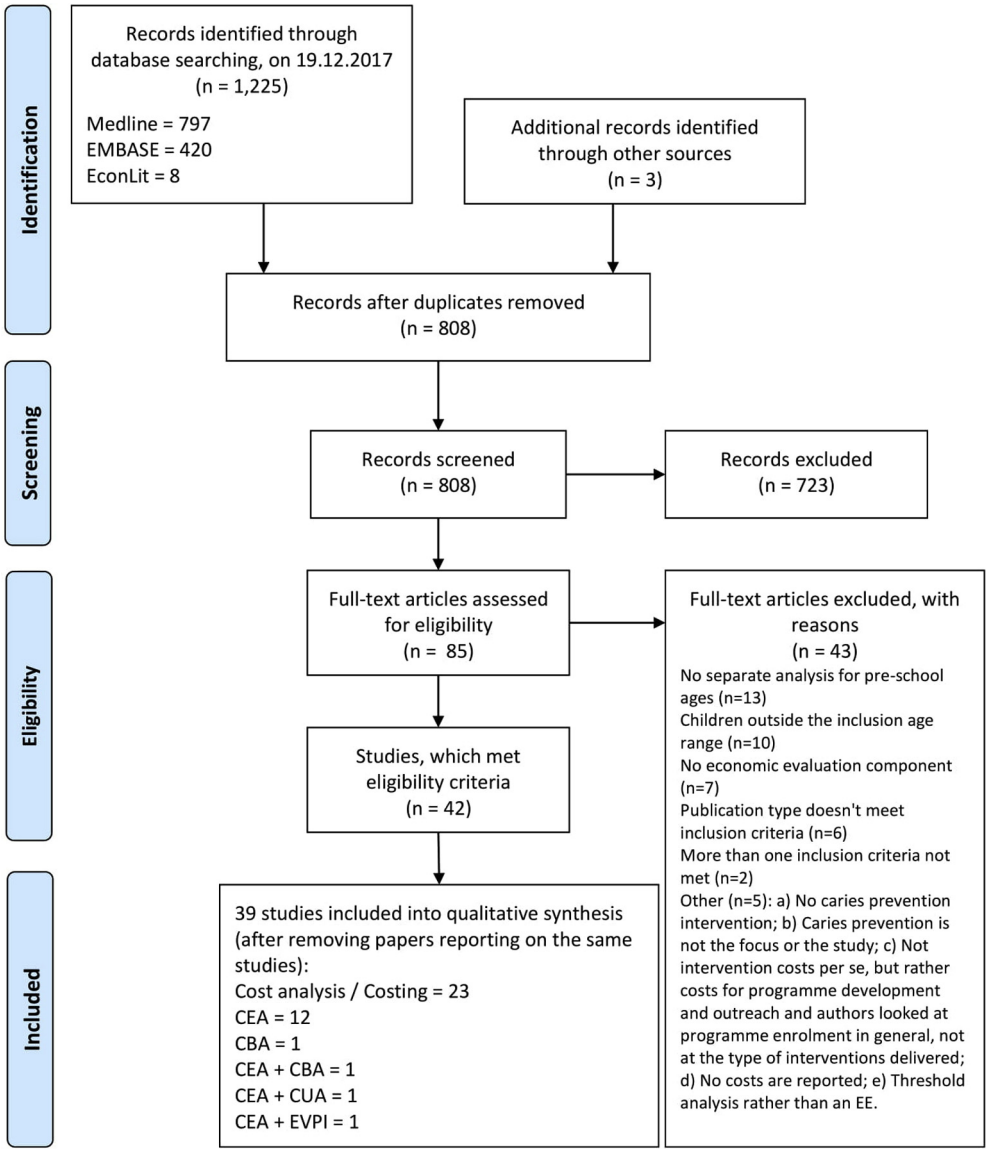
Descriptive study data were extracted using a pretested data extraction template. Several sources were used during the development of an initial draft data extraction template: Centre for Reviews and Dissemination's guidance for undertaking systematic reviews in healthcare,[24] data extraction templates used in 2 previous reviews,[5,17] and the Consolidated Health Economic Evaluation Reporting Standards (CHEERS) checklist.[29] Our own preferences, based on the nature and objectives of this review, were also taken into account. Data were extracted by the lead author, and a randomly selected 20% were checked by a second reviewer. Any disagreements were resolved by a discussion within the reviewers' team.

Reporting Quality Assessment of Full EEs

The quality of full EEs was assessed using the CHEERS checklist,[29,30] which was developed specifically to optimize the reporting of health EEs. The CHEERS checklist contains 24 items subdivided into 6 categories (Appendix Table 2 in Supplemental Materials found at https://doi.org/10.1016/j.jval.2020.04.1823).

Each item of the CHEERS checklist was scored as "1"/"Yes," if the paper met the criteria in full; "0"/"No," if it did not meet the criteria; or "Not applicable." Partial scores were not assigned. Items from the "Other" category ("Source of funding" and "Conflicts of

Figure 1. PRISMA flow diagram.



CBA indicates cost-benefit analysis; CEA, cost-effectiveness analysis; CUA, cost-utility analysis; EVPI, expected value of perfect information analysis; PRISMA, Preferred Reporting System for Systematic Reviews and Meta-Analysis.

interest") were not taken into account when calculating a total score for each paper, as these are not directly relevant to the economics-related reporting quality of a paper. A total of 22 was the maximum possible score. Each study's reporting quality was expressed as a proportion of items fully met for each paper. The lead author assessed all of the selected papers using the CHEERS checklist, with a second reviewer reassessing 20% of these papers, selected at random. Any discrepancies were resolved by discussion between the 2 reviewers.

Results

Literature Databases Search Results

A total of 808 studies were identified, of which 42 met the inclusion criteria. Figure 1, a Preferred Reporting System for Systematic Reviews and Meta-Analysis flow diagram, illustrates the study selection process. A set of 3 papers reported on the same study,[31-33] with 2 reporting on intermediate results. Only the latest of the 3, reporting the study in full, was included in the review.[33] Two papers reported on another study, one of them being a health technology assessment report[34] and another a conventional journal paper.[35] Only the latter[35] was included into the review. The final number of papers included in the review was therefore 39.

Study Characteristics

Of the 39 papers, 25 (64%) were published between 2000 and 2017 (inclusive). The earliest of the identified papers was published in 1968. Twenty-three (59%) were partial EEs, namely cost analyses, and 16 (41%) were full EEs. The type of EE was reported in relation to the age group of interest: 2 to 5 years. There was 1 study that was a CBA for a full age range of participants (2 to 16 years), but only cost data were reported for the 2- to 7-year-old group.[36] This study was classified as partial EE. Table 1 reports various study characteristics.

Partial EEs

Twenty-three partial EE studies were reviewed in total. All partial EEs were cost analyses. Seven studies (30% of the total number of partial EEs) investigated the costs of water fluoridation.[33,36-41] Six (26%) investigated multicomponent interventions,[42-47] 3 investigated topical fluoride (varnish, foam, or gel),[48-50] and 2 compared several different interventions.[51,52] There were single studies investigating each of the following: fluoride drops (for younger children) and fluoride varnish (for older children),[53] microbiological screening,[54] age at the first preventive dental visit,[55] OH education of parents with several additional components,[56] and supervised toothbrushing in nurseries.[57] Reporting of sensitivity analysis, study perspective, discount rate, and base year are shown in Table 2. For further study descriptions, see Appendix Tables 5 and 6 in Supplemental Materials found at https://doi.org/10.1016/j.jval.2020.04.1823.

Full EEs

Sixteen full EE papers were reviewed. Six investigated complex multicomponent interventions,[35,59,62,68-70] 3 looked at OH

Table 1. Study characteristics of all included studies.

Characteristic	No. of studies (%) (total = 39)
Year of publication	
1968-1970	2 (5%); 2 partial EEs
1971-1980	6 (15%); 6 partial EEs
1981-1990	2 (51%); 1 partial and 1 full EE
1991-2000	5 (13%); 3 partial and 2 full EEs
2001-2010	10 (26%); 6 partial and 4 full EEs
2011-2017	14 (36%); 5 partial and 9 full EEs
Type of EE	
Cost analysis*	23 (59%)
CEA	12 (31%)
CBA	1 (3%)
CEA + CBA	1 (3%)
CEA + CUA	1 (3%)
CEA + EVPI	1 (3%)
Type of study	
Observational in nature (non-RCT/nonmodeling study)	24 (61%)
Alongside an RCT	4 (10%)
Markov model	4 (10%)
Calculations using previously published data (but not a formal model)	3 (8%)
System dynamics modeling	2 (5%)
Based on an RCT, but not alongside it (costs of a hypothetical prevention program, based on RCT results)	1 (3%)
EVPI + cost-effectiveness model	1 (3%)
Study country	
United States	16 (41%)
United Kingdom	9 (23%)
Canada	3 (8%)
Sweden	3 (8%)
Australia	2 (5%)
USSR	2 (5%)
Chile	1 (3%)
Finland	1 (3%)
Taiwan	1 (3%)
Uzbekistan	1 (3%)
Type of intervention	
Complex/multicomponent intervention	12 (31%)
Water fluoridation	7 (18%)
Oral health education (with or without additional elements)	4 (10%)
Topical fluoride (varnish, foam, gel)	4 (10%)
Multiple interventions compared	3 (8%)
Primary molar sealants	2 (5%)
Systemic fluoride (with or without additional elements)	2 (5%)
Toothbrushing	2 (5%)
Fluoridated milk and cereal	1 (3%)
Microbiological screening	1 (3%)
Preventive dental visit	1 (3%)

CBA indicates cost-benefit analysis; CEA, cost-effectiveness analysis; CUA, cost-utility analysis; EE, economic evaluation; EVPI expected value of perfect information; RCT, randomized controlled trial.
*One study[36] was a CBA for a full age range of participants, 2 to 16 years, but only cost data were reported for the 2- to 7-year-old group For the purposes of our review, this study was classified as partial economic evaluation, cost analysis.

Table 2. Sensitivity analysis, study perspective, discount rate, and base year (by type of EE: partial, full).

Parameter	Partial EEs: No. of studies (%) (total = 23)	Full EEs: No. of studies (%) (total = 16)
Sensitivity analysis		
Some form of sensitivity analysis	7 (30%)[44,47,51,52,54,56,57]	12 (75%) In addition, 1 (6%) with no formal sensitivity analysis but 2 types of intrachild correlation were modeled, resulting in 2 sets of results[58]
Not employed	12 (52%)	3 (19%)[59-61]
Not applicable	4 (17%)[38,39,43,50]	0 (0%)
EE perspective		
Stated	4 (17%), as follows: Healthcare system perspective: 3 (13%)[40,48,57] Medicaid perspective: 1 (4%)[55]	9 (56%), as follows: Healthcare payer perspective: 3 (19%)[62-64] Public payer perspective: 3 (19%)[35,58,65] Societal perspective: 2 (12%)[66,67] Different perspectives (for the base-case and subgroup analyses): 1 (6%)[68]
Not stated	19 (83%)	7 (44%)[59-61,69-72]
Discount rate	.	
Stated	3 (13%)[37,54,56]	11 (69%)
Not stated	6 (26%)[36,50-53,55]	3 (19%)[59,60,70]
Not applicable (or authors explained why costs/outcomes were not discounted)	14 (61%)[33,38-49,57]	2 (12%)[35,68]
Base year		
Stated	13 (61%)	11 (75%)
Not stated	9 (39%)[36,41,42,46,49,51,53-55]	4 (25%)[59-62]

EE indicates economic evaluation.

education (with or without additional components),[60,66,71] 2 examined primary molar sealants,[58,65] and there was 1 study investigating each of the following: fluoridated milk and milk cereal,[67] fluoride varnish,[63] sodium fluoride tablets (plus other underlying interventions),[72] toothbrushing,[61] and comparing multiple interventions.[64] With regard to study settings, 7 (44%) were modeling studies,[58,59,63-66,71] 3 (19%) were conducted in dental settings (dental practice, dental clinic),[35,68,72] 2 (13%) studies were conducted in multiple settings,[62,70] 2 (13%) at home,[60,61] 1 study (6%) was kindergarten based,[69] and 1 (6%) was community based.[67] The most frequently used type of framework for full EE was CEA (12 papers, 75%).[35,59,61-65,67,68,70-72] Other studies employed CBA[69] or a combination of CEA with 1 of the following: CBA,[60] CUA,[66] and expected value of perfect information.[58] Appendix Table 3 (in Supplemental Materials found at https://doi.org/10.1016/j.jval.2020.04.1823) further illustrates the breakdown of full EE studies by type of intervention and EE framework used, and Appendix Tables 7 and 8 (in Supplemental Materials found at https://doi.org/10.1016/j.jval.2020.04.1823) contain study descriptions.

A wide variety of OH and economic outcomes measures were used in the reviewed full EE studies (Table 3). Four studies[61,66,67,70] used mean dmft, which is the mean number of deciduous teeth decayed (d), missing due to decay (m) or filled (f), with the unit being the tooth (t) and/or dmfs (the same principle as for dmft applies, but the unit of measurement is the tooth surface [s]). Two studies used conversion from caries free to caries active (plus other secondary measures).[35,60] Nine other OH outcome measures were used in 1 study each. Five different cost-effectiveness outcomes were used in individual studies. Only 1 study used the quality-adjusted life-year (QALY) as an outcome.[66] The most widely used options for reporting of costs and outcomes were the incremental cost-effectiveness ratio and the average cost-effectiveness ratio.

Cost-Effectiveness/Cost-Benefit Results

Six of 15 studies that employed CEA concluded that the intervention was cost-effective. The interventions were a complex dental disease management program,[68] OH education programs,[60,66,71] fluoridated milk and milk-cereal,[67] and a study comparing 5 different caries prevention interventions.[64] In 4 cases, the intervention was cost-effective for certain subgroups or for certain scenarios but not the others.[59,62,70,72] In 2 studies on primary molar sealants, the "always seal" intervention was more effective but more costly than standard care.[58,65] Two studies on fluoride varnish indicated that the intervention was not cost-saving.[35,63] The authors of a postal toothbrushing program evaluation[61] did not draw any conclusions on its cost-effectiveness.

Of the 2 studies that employed CBA, 1 study showed that the benefits of a combined hand hygiene and OH promotion program outweighed costs at each discount rate level considered.[69] The other study compared dental health education with several other caries prevention strategies.[60] The results showed that the dental health education program provided better benefit-costs ratios than other preventive programs.

The only study that used QALY as an outcome evaluated the cost-effectiveness of a home visit intervention conducted by OH therapists relative to a telephone-based alternative and no intervention.[66] The home visits and telephone interventions resulted in 7 and 6 QALYs, respectively, gained over the usual care group for the 100 children older than 5.5 years. Both interventions were dominant, as they saved costs and produced health benefits over usual care.

Results of Reporting Quality Assessment of Full EEs

The results of the assessment of full EE studies using the CHEERS checklist showed substantial variation in reporting quality. Figure 2 shows the proportion of studies that did not meet

each criterion. Not every single item was applicable to every study. The items that were most often unmet were #20a, characterizing uncertainty (for single-study–based EEs), with 67% of all studies to which this item was applicable not meeting this criterion; #6, study perspective, with 44% of studies not meeting this criterion; #18, study parameters, 38% not met; and #13a, estimating resources and costs (for single-study–based EEs), 33% not met. Several items were met by all studies to which these items were applicable: items 1 and 2, title and abstract; #10, choice of health outcomes; #11a and #11b, measurement of effectiveness (for single-study–based and model-based EEs, respectively); #13b, estimating resources and costs (model-based EEs); #15, choice of model; #16, assumptions (model); and #21, characterizing heterogeneity (applicable to 2 studies only). Item 12, measurement and valuation of preference-based outcomes, was applicable to 1 study only and was met. Scores by item by study are shown in Appendix Table 4 (Supplementary Material found at https://doi.org/10.1016/j.jval.2020.04.1823).

The overall CHEERS score for each reviewed study is shown in Figure 3. More recent papers were of higher reporting quality than earlier ones. Papers published from 2014 onward met 100% of applicable CHEERS items. For all 16 papers combined, the median proportion of all applicable CHEERS items met was 97.5% and the mean was 81.8%. The range was 50% to 100%. With regard to "other" items (not shown in Fig. 2 and not included in the total score in Fig. 3), only three papers (19%) provided information on their authors' conflict of interest, whereas 9 papers (56%) indicated a source of funding.

Discussion

This is the first systematic review to focus on the EEs of OH improvement interventions targeted at the early life. This period has been shown to be crucial in influencing health in later years.[15,73]

According to a review of publications on EEs of caries prevention programs in all ages,[12] the main methodological problems identified were the limited information provided on adjustments for discounting in addition to inadequate sensitivity analyses. These are similar findings to those of a systematic review of EE publications in dentistry,[13] which also identified insufficient information on how costs and outcomes had been measured and valued. In addition, a more recent systematic review of EEs in child OH research, which included full EE studies involving children aged 18 years old and under,[14] highlighted that a wide range of outcome measures was employed across the reviewed studies, which prevented interstudy comparisons. Lack of meaningful involvement of children and of consideration of their own perspectives and preferences were also emphasized.

The present review has identified that the most widely used type of analysis were cost analysis and CEA, which is similar to the findings of a recent systematic review of EEs in wider child OH research.[14] More than 60% of the reviewed papers were published between 2000 and 2017 (inclusive). The proportion of full EEs increased over time, especially from 2000 onward. Most studies were conducted in the United States and the United Kingdom. Just less than one-third of the studies reviewed investigated complex multicomponent interventions and approximately one-fifth focused on water fluoridation.

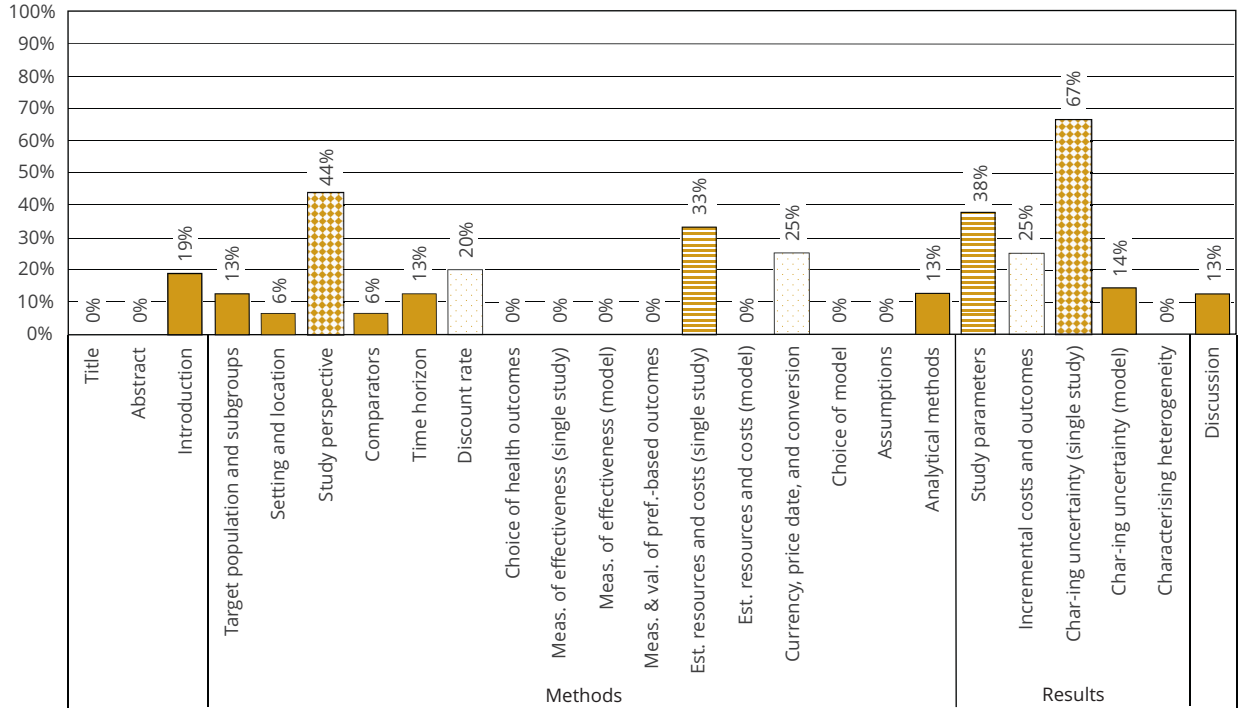
Unlike the previous reviews,[12,13] the current review did not find a mismatch between the study descriptor and actual type of analysis used. All studies that were labeled a CEA or a CBA or a combination of methods were indeed those study types. This may be explained by the fact that the vast majority of full EEs in the field of interest were published relatively recently, by which time guidance on EE methods was established and widely used.

Table 3. Full EE studies: oral health and economic outcomes used and reporting and presentation of costs and outcomes.

Characteristic	No. of studies (%) (total = 16)
Oral health outcomes	
dmft or/and dmfs	4 (25%)[61,66,67,70]
Conversion from caries-free to caries-active (plus other secondary measures)	2 (12%)[35,60]
Cavity-free months	1 (6%)[63]
fs, dfsa	1 (6%)[72]
Mean No. of restorations and extractions averted	1 (6%)[58]
No. of carious surfaces	1 (6%)[59]
No. of carious teeth	1 (6%)[71]
No. of cases/incidence rates of caries and stomatitis	1 (6%)[69]
Rates of dental treatment	1 (6%)[62]
Reduction in dental treatments	1 (6%)[68]
Reduction in No. of carious teeth; reduction in full-mouth dental reconstructions	1 (6%)[64]
N/A (tooth-level model)	1 (6%)[65]
Preference-based outcomes	
QALY (based on Child Health Utility 9 Dimensions [CHU9D]–parental proxy questionnaire)	1 (6%)[66]
Reporting and presentation of costs and outcomes	
ICER	7 (44%)[35,58,62,63,66,67,71]
ACER*	3 (19%)[60,64,72]
B/C ratio*	2 (12%)[60,69]
Cost per carious surface averted, cost-saving threshold	1 (6%)[59]
Cost per event avoided (tooth is not restored or extracted)	1 (6%)[65]
Cost per incremental change in dmfs	1 (6%)[70]
Cost per tooth saved, cost per child saved from caries experience, cost per child saved from extraction experience	1 (6%)[61]
Number of avoided (reduced) restorative or surgical treatment visits in the ambulatory dental clinic or operating room at the hospital	1 (6%)[68]

ACER indicates average cost-effectiveness ratio; ICER, incremental cost-effectiveness ratio; N/A, not applicable; QALY, quality-adjusted life-year.
*One study[60] reported both average C/E and B/C ratios.

Figure 2. Proportion of CHEERS items not met, by item (% of total numbers of studies for which each of the items was applicable). Key: Chequered fill – over 40% of eligible studies did not meet a criterion; Horizontal lines fill – 30% < 40% not met; Dotted fill – 20% < 30% not met; Solid fill – < 20% not met. Notes: 1) The total (100%) was different for various items, as some items were not applicable to all studies. 2) "Other" items, namely "Source of funding" and "Conflicts of interest" were not included when rating the reporting quality of the reviewed papers.



CHEERS indicates Consolidated Health Economic Evaluation Reporting Standards.

Although the reporting quality of partial EEs was not formally assessed in our systematic review, some parameters, which were included in the data extraction template, indicate that, on the whole, partial EEs were inferior to full EEs in relation to reporting these parameters. For example, more than half of the reviewed partial EEs did not employ sensitivity analysis, whereas three-quarters of full EEs studies did. Most full EEs stated the discount rate used, whereas only 3 partial EE studies did so. In addition, a higher proportion of full EE papers indicated the baseline year for their analysis. Previous reviews identified similar methodological limitations, namely, absence of sensitivity analysis, limited information on adjustments for discounting, and not reporting the base year.[12-14,17] A significant proportion of the papers did not state the perspective used in the analysis: 83% of partial EEs and 44% of all full EEs, which is similar to the results of a previous systematic review of CUAs of OH interventions.[17]

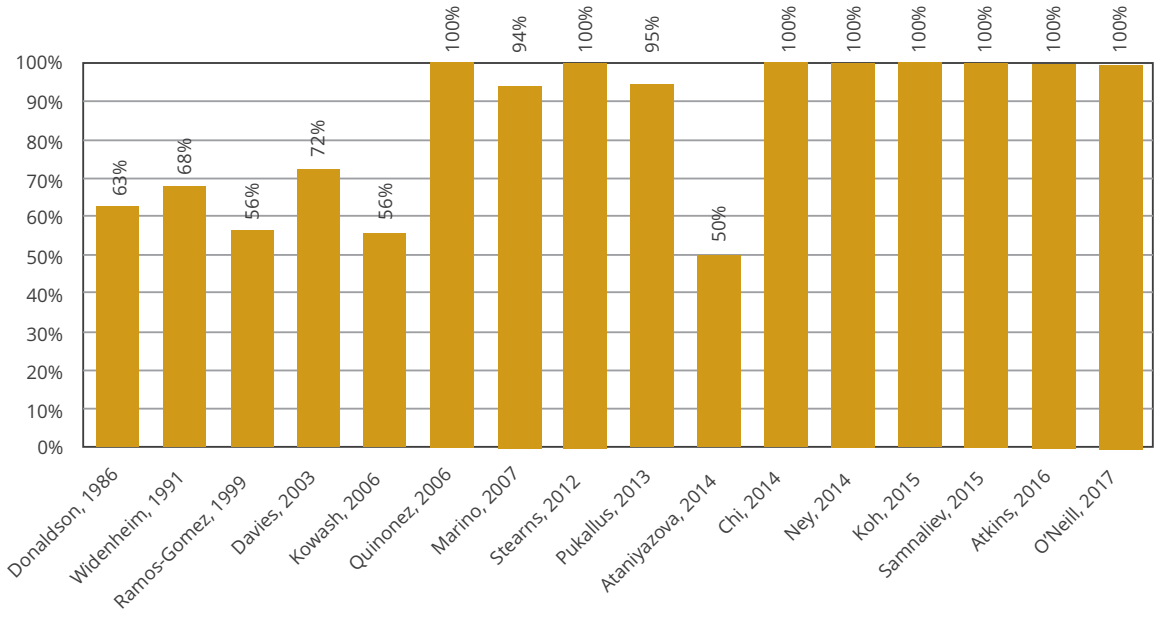
The review identified 16 full EEs, which used a variety of EE methods and techniques and OH outcome and economic outcome measures. This variation makes it challenging to compare the cost-effectiveness of individual caries prevention interventions. This concurs with the conclusions of 2 previous systematic reviews.[14,17] Interpretation of cost-effectiveness ratios for dental health outcomes is similar to the standard challenges of using CEA when comparing different outcomes. Without use of an accepted threshold for a generic outcome such as a QALY, comparability is not possible. It is not clear how much the payer (eg, a healthcare system, public payer, or society) is willing to pay per decayed surface/tooth avoided or per child kept caries free.[74] Only 1 study used a preference-based health-related quality-of-life measure that allows calculation of QALY as one of the outcomes, which, in turn, allows a comparison of cost-utility results of various interventions' evaluations. This lack of evidence reveals a clear gap in relation to preschoolers' OH research.

More than 40% of the reviewed full EE papers concluded in favor of the intervention(s) under investigation. Nevertheless, there were small numbers of studies investigating each intervention type (eg, fluoride varnish, OH education, dental sealants, toothbrushing, fluoridated food and drinks, water fluoridation). The studies were underpowered,[60,66,71] used simple spreadsheet-based calculations,[64,67,69] or were pilot studies,[68] making it challenging to draw reliable conclusions with regard to the value of primary caries prevention.

The only full EE, conducted alongside a well-powered randomized controlled trial and deemed to be of high reporting quality, was O'Neill et al,[35] which concluded that the costs of providing a combined fluoride intervention (fluoride varnish, free toothbrush and fluoride toothpaste, and standardized dental health education) in general dental practice settings outweighed savings in treatment over the 3-year follow-up period. This intervention was unlikely to produce a cost-saving.

The results of our quality assessment of full EEs using the CHEERS checklist showed substantial variation in reporting quality. The items most often unmet were "characterizing uncertainty," "study perspective," "study parameters," and "estimating resources and costs." Of note, more recently published papers were of higher reporting quality. The CHEERS is the most recently developed EE checklist that was created to update previous guidelines.[29,75] It has been widely used as a single tool for

Figure 3. CHEERS score for each reviewed full EE study (% of total applicable items). Note: "Other" items, namely "Source of funding" and "Conflicts of interest" were not included when rating the reporting quality of reviewed papers.



CHEERS indicates Consolidated Health Economic Evaluation Reporting Standards; EE, economic evaluation.

assessing the quality in systematic reviews of EE studies, including some focusing on OH.[17,76]

One of the limitations of this systematic review is that because of the time constraints, only 20% of randomly selected records were assessed or checked independently by a second reviewer. The reporting quality was formally assessed for only full EE studies. The CHEERS checklist cannot be meaningfully used for partial EEs assessment, as many of the items are not applicable. In addition, the overall methodological quality of the reviewed studies was not formally assessed.

Conclusions

Although the number of EE studies relating to OH improvement interventions in preschoolers has been increasing in recent years, a number of items were inadequately reported in a substantial proportion of the reviewed studies. Our review has highlighted wide variation in (1) types of caries prevention interventions investigated, (2) effectiveness measures used, (3) how costs and outcomes are reported, and (4) study perspective (when indicated).

Importantly, only 1 study employed CUA, using a preference-based outcome measure. This notable lack of use of preference-based health-related quality-of-life measures in the field of preschoolers' OH likely reflects the challenges with conducting EE in this young age group, the availability of suitable preference-based measures, and also flags the limitations with the use of these studies for the purposes of decision making in dental healthcare.

Although variation in prevention interventions investigated is entirely expected, the methodological limitations identified preclude meaningful comparisons across studies as well as compromise the evidence base for strategies in relation to the prevention of this disease in this age group. Because of the small numbers of studies investigating each intervention type and the questionable methodological quality of many of the reviewed EEs, it was not possible to arrive at reliable conclusions with regard to the economic value of primary caries prevention.

With dental caries being one of the most common diseases affecting humans worldwide, the identification of cost-effective prevention strategies in children should be a global public health priority. This agrees with the recommendations in the recent articles outlining the challenges and priorities for global OH. For this to be achieved, studies should be designed to include EEs using best practice methods guidance and adhering to standards for reporting and presenting. Such improvements to the evidence base will serve to increase both the availability and quality of economic evidence in this important area.

Supplemental Material

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