

## Cost-effectiveness of caries preventive interventions – a systematic review

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### ABSTRACT

**Objective:** The primary purpose of this study was to assess the cost-effectiveness of caries preventive interventions.

**Material and methods:** A systematic review was conducted, following the PRISMA Statement. Four electronic databases were searched (final search 16 March 2020). Studies fulfilling the inclusion criteria were independently critically appraised, by two reviewers in parallel. Data from each included study were extracted and tabulated: the analysis used a narrative approach to present the results of the estimated cost-effectiveness.

**Results and conclusions:** Twenty-six publications fulfilled the inclusion criteria and were of low or moderate risk of bias. Ten publications were economic evaluations, directly based on empirical studies, and the other 16 were modelling studies. Most of the studies concerned interventions for children and the most common were analyses of fluoride varnish and risk-based programs. Some of the studies showed both reduced cost and improved outcomes, but most studies reported that the improved outcome came with an additional cost. The results disclosed several cost-effectiveness evaluations of caries preventive interventions in the literature, but these target primarily children at high risk. There is a scarcity of studies specifically targeting adults and especially the elderly.

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### KEYWORDS

Caries; cost-effectiveness; economics; prevention; systematic review

### Introduction


Caries, demineralization of dental hard tissue caused by acid-producing bacteria, is globally the most prevalent noncommunicable disease, causing pain and detracting from quality of life [1,2]. Although it is a chronic multifactorial disease, caries is largely preventable through a combination of measures at individual, professional and community levels [3–5]. Once the disease is established there is increased risk of further progression, and this takes its toll, from both health and economic perspectives [6,7]. Dental caries is unevenly distributed in society and there is evidence, in both children and adults, of an association between socioeconomic status and dental caries [8,9]. The same pattern occurs regionally and nationally as well as globally: the oral health of the socially disadvantaged is poorer than that of those with better living conditions [9–11]. For all levels of society to have good dental health, effective oral health preventive interventions need to be implemented.

To ensure effective use of health care resources, health-economic analyses are required [12]. This is an accepted

procedure when new drugs or health technologies are introduced. There are, however, few health economic analyses of dental care, which makes it difficult to assess the cost-effectiveness of interventions. A recent scoping review indicated that the number of economic evaluations in dentistry is increasing [13], but the need is still great and thus more work in this field is necessary.

As the societal cost of caries preventive interventions may not equal the direct cost of the intervention, the cost-effectiveness result will depend on the perspective of the analysis. Furthermore, costs and effects resulting from various interventions usually occur over a longer period than that covered by controlled studies and this applies, for example, to caries preventive interventions. To achieve optimal decision-making, it may therefore be necessary to apply simulation models that take into account long-term consequences. Such models, however, will always be surrounded by uncertainty and the results they provide are dependent on the quality of the data that are used [12].

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A systematic review is used to provide evidence for an intervention, based on the summary of current literature, and to identify knowledge gaps to guide future research within a knowledge field. In systematic reviews which include economic evaluations, information is compiled not only on whether interventions are clinically effective, but also on economic aspects of the interventions. Systematic reviews of health economic analyses, however, do not strive to find a mean cost-effectiveness value based on all studies, but rather to find the most relevant analysis for the specific decision or to find important parameters to use when modelling the cost-effectiveness [14]. Aspects such as the setting where the intervention is implemented, cost level, private or publicly financed, preferences of health, and willingness-to-pay thresholds, can vary between different scenarios and make it impossible to find one true estimation of the cost-effectiveness.

The primary purpose of this study was to assess the cost-effectiveness of caries preventive interventions for individuals of all ages. The specific aim was to help decision-makers to prioritize limited resources for dental care, and furthermore to inform researchers and research funds about the current state of knowledge.

## Methods

A systematic review was conducted. The systematic review is part of a project which will analyse the cost-effectiveness of various caries preventive interventions, applying a decision analytic model. The findings are intended to aid Swedish decision makers to narrow the gap in socio-economically related inequalities in dental health.

To ensure a systematic approach, the systematic review was structured in four subsequent steps: (i) *systematic review questions*, (ii) *sources*, (iii) *study selection*, and (iv) *data extraction, critical appraisal, and analysis*. We followed the *Preferred Reporting Items for Systematic Reviews and Meta-Analyses* (PRISMA) Statement [15], and the systematic review was registered in the International Prospective Register of systematic Reviews (PROSPERO) [16], registration nr CRD42019129173.

### Systematic review questions

The systematic review of the literature on the economic evaluation of caries preventive interventions aimed to address the following questions:

- Which caries preventive interventions have been analysed in terms of cost-effectiveness?
- What are the estimated costs and cost-effectiveness of the interventions analysed?

### Sources

Four electronic databases were searched for publications reporting cost-effectiveness of caries preventive interventions: MEDLINE via PubMed, Scopus via Elsevier, the Web of Science, and the ABI/Inform Global. Mesh-terms as well as

free-text terms were combined, presented in [Supplementary Table 1](#). The final search was conducted on 16 March 2020. In addition, the reference lists of included publications were screened for publications not captured by the electronic searches.

### Study selection

The retrieved publications were assessed according to title and/or abstract by two independent reviewers in parallel and selected according to the systematic review questions, and following eligibility criteria, which were aligned with components of PICO (Population, Intervention, Comparator, Outcomes):

- Population: Humans of all age groups
- Intervention: All caries preventive interventions except water fluoridation
- Comparator: All alternatives with a minimum of fluoride toothpaste
- Outcomes: Measures of cost-effectiveness, any health economic measures relevant for a decision-maker

Interventions undertaken in settings which are not transferable to a European setting were excluded. Also excluded from the systematic review is water fluoridation as this is not permitted in Sweden [17].

All types of economic analyses were accepted if it provides a cost-effectiveness estimate. Publications selected by at least one reviewer were retrieved in full text for further assessment. The publications included were original studies of an economic evaluation of caries preventive interventions. Studies were excluded if they comprised topics other than caries preventive interventions or analyses of water fluoridation. Publications found in the reference lists of the included studies were assessed and included if they were in accordance with the systematic review questions. Disagreements were discussed until consensus was reached.

### Data extraction, critical appraisal, and data analysis

For critical appraisal of the strengths and weaknesses of the methodological risk of bias of the included studies, two checklists were used: one for empirical health economics studies and one for modelling studies [18], both based on the critical appraisal checklist presented by Drummond et al. [12]. Using the checklists, two independent reviewers assessed the studies by selecting a 'Yes', 'No', 'Unclear' or 'Not applicable' option for each signalling question. Thereafter, each reviewer independently undertook a critical appraisal of the risk of bias. Risk of bias is a combined assessment, derived from clinical as well as economic perspectives, and the risk of bias level in this systematic review was defined as the reviewer's final assessment based on all criteria within the checklist. Discrepancies about the appraisal of risk of bias were discussed until consensus was reached. The transferability of the analysis to a European setting was also appraised, with respect to the background caries risk, the treatment pattern and the cost level used in the analysis.

Data from each included study were extracted and tabulated: the analysis used a narrative approach to present the results of the estimated cost-effectiveness.

## Results

### Study selection

As shown in Figure 1, 6254 records were identified after the removal of duplicates, 93 full-text publications were read, and 67 full-text publications were excluded. The excluded studies and the reasons for exclusion are presented in Supplementary Table 2. Twenty-six publications listed in Table 1 fulfilled the inclusion criteria and were of low or moderate risk of bias.

### Study findings

Of the 26 included studies, ten were economic evaluations directly based on empirical studies [19–28] and the other 16 were modelling studies [29–44]. In nine studies, the target population comprised pre-school children up to five years of age [19,22,25,26,31,32,35,36,38]. Twelve studies were analyses of interventions for schoolchildren aged from 6 to 15 years

[20,21,23,24,27–30,33,35,40,41]. Only two studies targeted adults [39,44]. Five studies modelled more or less whole populations [32,34,37,42,43].

A majority ( $n = 18$ ) of the included studies analysed fluoride varnish [19–28,30,35,37–41,44], sometimes as a consequence of a risk-based program [21,23,25,26,28,44], while four studies analysed fissure sealants [29–31,33]. One study analysed the frequency of dental check-ups [32] and two studies [34,42] analysed the adoption of a tax on beverages containing sugar.

Eight studies reported dominant results (lower costs and improved outcomes) of the assessed interventions [25–27,30,34,36,42,43], while the remainder reported increased costs and improved outcomes: thus their cost-effectiveness depends on the willingness to pay per additional added effect. Only four studies used QALY as the outcome measure [30,35–37]. Generally, many studies conclude that the cost-effectiveness of the interventions depends on the caries risk of the population.

## Discussion

In this systematic review we identified 26 studies, with low or moderate risk of bias, which analysed the cost-

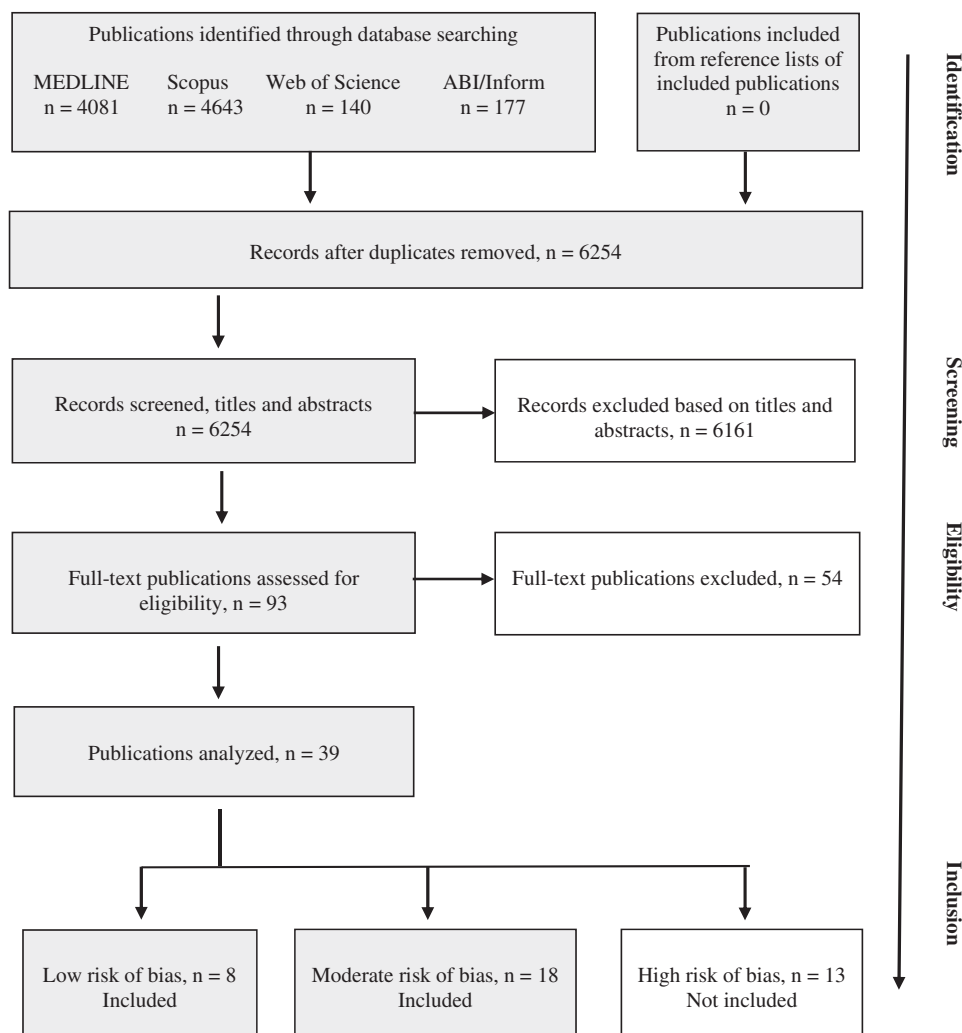


Figure 1. Flow diagram according to PRISMA Statement [15] presenting results of searches and study selection.

effectiveness of caries preventive interventions. In most of the studies the subjects were children and the most common intervention was the application of fluoride varnish.

Most of the findings referred to patients with high caries risk and are not directly applicable at the general population level, where the caries incidence may be lower. However, even in societies with relatively low caries incidence, there may be some pockets of higher incidence, and the economic analyses can therefore be applied to interventions in these areas, hopefully leading to greater equality of dental health in the society. Interventions found to be successful at the population level include risk-based interventions, frequency of dental check-ups, and taxes on sugar. Basically, all these interventions have promising cost-effectiveness results (either a dominant result or very low increased costs).

The findings of the present study may be viewed in the context of those of other recent systematic reviews of economic studies of preventive dentistry. For example, Eow et al. [13] presented a scoping review of economic evaluations in dental care in 2019. Preventive interventions, including fissure sealants and fluoride treatments, were the predominant intervention of interest, comprising 34 studies. In 2019, a systematic review by Fraihat et al. [45], evaluating the clinical effectiveness and cost-effectiveness of oral-health promotion programs for children, identified 19 studies, mostly of high quality, and concluded that such a program achieves a reduction in child DMFT and lowers the costs. A systematic review of economic evaluations applied to children's oral health by Rogers et al. [46] concluded that there is a paucity of high-quality economic evaluations in this field. Furthermore, a systematic review which focussed on decision analytic modelling techniques for the economic evaluation of dental caries interventions found 25 studies, from different settings and using different modelling techniques, concluded that the methodological quality was unsatisfactory [47]. Finally, Hettiarachi et al. [48] presented a systematic review of cost-utility analyses of oral health interventions in 2018, identifying 23 studies of which only four concerned dental caries.

Our current findings are in accordance with those of these recent reviews: differences seem to be attributable primarily to variations in scope. The number of economic evaluations in caries preventive interventions is increasing but is limited mainly to children at high risk of caries. There is, however, a risk for publication bias in economic evaluations, especially because of the difficulty in publishing economic evaluations conducted alongside inconclusive clinical trials. This may have led to that all systematic reviews have missed important information.

A further consideration is the extent to which the evaluations can help decision-makers to direct resources efficiently. Cost-effectiveness analyses in other areas of health care often use QALY as the outcome measure, but the lack of studies using QALY, disclosed by the present review, may hinder decision-makers in prioritizing caries preventive interventions effectively in relation to other interventions. Furthermore, to determine whether an intervention is cost-effective, willingness to pay per improved outcome must be

known, but this is rarely studied. Some interventions, however, led to a dominant result and are thus adequate as a basis for effective decisions (but there may of course still be ethical or political issues to consider). Such dominant results were the case with the sugar tax and some risk-based programs. Many caries preventive interventions measured the outcomes in preventive dmft/DMFT, and there is a need to know the value of such an outcome to know what interventions are cost-effective.

In this systematic review, we found that the perspective of most analyses is clearly stated, i.e. either a dental health care or a societal perspective. The cost-effectiveness estimation of the intervention is directly affected by the perspective, and different willingness-to-pay thresholds may be used depending on perspective. At a societal level, it is the willingness of society to pay for health that sets the threshold for cost-effectiveness, but in the case of a more restricted budget, the threshold may be set at a different level. If dental care is privately financed, the relevant question of cost-effectiveness is then a matter for the individual. If, however, technologies are to be subsidized from public funds, it would be necessary to analyse societal willingness to pay. Furthermore, guidelines may use a broad perspective to strive for a societal optimum, even if individuals pay themselves. In such a situation the individuals can be guided in their decision making, but themselves make the final decision as to whether they find the technology cost-effective in relation to their own willingness to pay. Systematic reviews of health economic analyses differ in some respects from reviews of clinical effects. For example, the latter combines all studies of an intervention and tries to find the mean effect, but the former does not try to find a mean cost-effective value based on all studies. The reason is that this value would be affected by several methodological choices, but even more importantly, by the local context of the intervention, the setting and the attributes and willingness to pay of the person in question. Instead, the main purpose of systematic reviews of economic evaluations is to find the most relevant analysis for the specific decision, or to find important parameters to use when modelling the cost-effectiveness [14]. Therefore it is not meaningful to assess the findings in a summary or try to use any evidence system such as GRADE [49] as a quality indicator of the results. GRADE is useful when grading the evidence of resource use, preferable presented in natural units, but not when combining measures or when results come from simulation models [50].

The present review excluded studies on water fluoridation. However, several such studies were captured in the systematic process and although they were not fully assessed by the reviewers, they seem to show dominant results, i.e. water fluoridation was found to save costs and to reduce caries [51,52]. Also fluoridated salt or milk-products may be cost-effective [53–55] and able to address inequities in dental health, but those studies in the present review were appraised as not transferable.

In conclusion, this review disclosed several cost-effectiveness evaluations of caries preventive interventions in the literature, but these target primarily children at high risk. There

Table 1. Economic evaluations included in the systematic review.

Author Year Reference Country	Study design Population Setting Perspective	Intervention vs control	Costs	Effects	ICER	Risk of bias* and transferability	Further information in the study
Anderson et al. 2019, [19], Sweden	Pre-school children up to five years of age Cluster randomized controlled trial. 1- year-old children in multicultural areas with medium-to-low socioeconomic status. Analysed from both a dental health care and a societal perspective.	I: Standard program supplemented with biannual applications of fluoride varnish C: Standard program (examinations once a year) only	Costs (€) Dental health care perspective I: 96.08 C: 70.12 Incremental I vs C: 25.25 Societal perspective I: 139.58 C: 96.69 Incremental I vs C: 42.18 Costs (\$) I1: 232,141 I2: 186,010 C: 214,510 Incremental I1 vs C: 17,631 I2 vs C: -28,500	defs I: 0.59 C: 0.68 Incremental I vs C: -0.09 (not significant)	Incremental cost (€) per defs avoided Dental health care perspective I vs C: 280.56 Societal perspective I vs C: 468.67	Moderate risk of bias High transferability	Treatment effect used was not statistically significant. A better alternative use of resources is recommended.
Chi et al. 2014, [31], US	Time horizon: 2 years Markov model based on Medicaid claims data. Children younger than 6 years. Dental health care perspective. Time horizon: until the tooth reach the 'adult tooth'-state.	I1: Always seal I2: Never seal C: Standard care	Costs (\$) I1: 232,141 I2: 186,010 C: 214,510 Incremental I1 vs C: 17,631 I2 vs C: -28,500	Number of restorations I1: 340 I2: 2853 C: 2389 Incremental I1 vs C: -2049 I2 vs C: 464	Incremental cost (\$) per restoration avoided I1 vs C: 8.12 C vs I2: 65.62	Moderate risk of bias Moderate transferability	
Davenport et al. 2003, [32], UK	Markov model based on UK epidemiological data. Children 1-6 years. Health care perspective. Time horizon: 6 years	Frequency of dental checks I1: 3-monthly I2: 6-monthly I3: 12-monthly I4: 18-monthly I5: 24-monthly I6: 36-monthly I1: Childsmile (tooth brushing schemes) I2: Fluoride varnish C: No such program	Costs (£) I1: 138.40 I2: 74.40 I3: 43.70 I4: 34.30 I5: 30.20 I6: 27.30 Not presented	Free from dmft/ DMFT I1: 19.03 I2: 18.91 I3: 18.71 I4: 18.53 I5: 18.35 I6: 17.98 Not presented	Incremental cost (£) per dmft or DMFT saved I2 vs I3: 153.5	Moderate risk of bias Moderate transferability	Moving to longer intervals than 6 months would be cost-effective.
Kay et al. 2018, [35], United Kingdom	Decision analytic model. 5-year-old children with high risk. Children living in relatively deprived areas. Expanded health care perspective. Time horizon: Up to 3 years	I1: A home-visit intervention conducted by oral health therapists I2: Telephone-based intervention conducted by oral health therapists C: No	Costs (US\$) I1: 181,870 I2: 204,193 C: 348,903 Incremental I1 vs C: -167,032 I2 vs C: -144,709	Carries lesions I1: 145 I2: 158 C: 258 Incremental I1 vs C: -113 I2 vs C: -100 QALYs I1: 547	Incremental cost (\$) per prevented caries lesions or QALY gained I1 vs C: Costs up to £55 per child I2 vs C: Costs up to £100 per child	Moderate risk of bias High transferability	The interventions have a high probability of being considered cost-effective.
Koh et al. 2015, [36], Australia	Markov model. Cohort of 100 6-month-old children followed until they turn 6 years. Societal perspective (costs to the health systems and parents).	I1: A home-visit intervention conducted by oral health therapists I2: Telephone-based intervention conducted by oral health therapists C: No	Costs (US\$) I1: 181,870 I2: 204,193 C: 348,903 Incremental I1 vs C: -167,032 I2 vs C: -144,709	Carries lesions I1: 145 I2: 158 C: 258 Incremental I1 vs C: -113 I2 vs C: -100 QALYs I1: 547	Incremental cost (\$) per prevented caries lesions or QALY gained I1 vs C: Costs up to £55 per child I2 vs C: Costs up to £100 per child	Moderate risk of bias Moderate transferability	

(continued)

Table 1. Continued.

Author Year Reference Country	Study design Population Setting Perspective	Intervention vs control	Costs	Effects	ICER	Risk of bias* and transferability	Further information in the study
Ó'Neill et al. 2017, [22], Northern Ireland	A randomized controlled trial (RCT). Caries-free children aged 2–3 years. Dental general practices in Northern Ireland. Perspective of the public payer. Time horizon: 3 year	Intervention = usual dental care  I: 22,600 ppm fluoride varnish; free toothbrush and 50 ml tube of 1,450 ppm fluoride toothpaste; and standardized prevention advice. Provided at 6- monthly intervals C: Advice only. Provided at 6- monthly intervals.	Costs (£) I: 1027.31 C: 815.69 Incremental I vs C: 211.62	I2: 546 C: 540 Incremental I1 vs C: 7 I2 vs C: 6 dmfs I: 2.45 C: 3.74 Incremental I vs C: -1.29 dmft: I: 1.15 C: 1.64 Incremental I vs C: -0.49	Incremental cost (£) per dmfs avoided I vs C: 164 Incremental cost (£) per dmft avoided I vs C: 432	Moderate risk of bias High transferability	
Palacio et al. 2019, [38], Chile	Markov model based on Chilean epidemiological studies etc. Pre-school children. Pre- school setting or a primary care setting. Public health system perspective. Time horizon: 2 years	I1: Fluoride varnish application in pre- school without screening I2: Fluoride varnish application in pre- school setting with screening I3: Fluoride varnish application in primary health care setting without screening I4: Fluoride varnish application in primary health care setting with screening C: Counselling only I: A risk-based prevention programme with increasing intensity C: Care as usual	Costs (CLP) C: 2784 I3: 7620 I3 was less costly and more effective than I1, I2 and I4. Incremental I3 vs C: 4836	Caries-free children C: 23.5% I3: 27.2% Incremental effect I3 vs C: 3.7%-units	Incremental cost (CLP) per additional caries- free child I3 vs C: 130,849 I1, I2, and I4 were dominated by I3.	Moderate risk of bias Moderate transferability	High caries rates, only 23% free from caries
Pienihäkkinen et al. 2005, [25], Finland	Long term follow-up of a controlled cohort study, starting with 5-year-old children. Perspective of a public health care centre. Time horizon: 7 years	I: Disease management program including a caries risk assessment tool, and both an in-office and an at-home	Costs (€) I: 505 C: 656 Incremental I vs C: -151	DMFT I: 0.2 C: 0.4 Incremental I vs C: -0.20	Dominant	Moderate risk of bias High transferability	Early prevention of dental caries also has long-term benefits in a 7-year follow-up perspective.
Sammaliev et al. 2014, [26], USA	Children (younger than 5 years) in a cohort compared with individuals in a historical group. Health care, payer, and		Costs (USD) Health care perspective I: 1,271 C: 2,023 Incremental I vs C: -752	Number of hospital- based visits for restorative treatments or extractions I: 1.35	Dominant	Moderate risk of bias Moderate transferability	The intervention appears cost-effective.

(continued)

Table 1. Continued.

Author Year Reference Country	Study design Population Setting Perspective	Intervention vs control	Costs	Effects	ICER	Risk of bias* and transferability	Further information in the study
Bergström et al. 2019, [20], Sweden	a societal perspective. Time horizon: 12 months Cohort study with historical comparator, all 12- to 15-year-olds within a region. A school-based setting. Societal perspective. Time horizon: 4 years	component. C: No such program I: Implementation of the FRAMM guideline, including fluoride varnish applications and information I1: Low risk of caries I2: Moderate risk of caries I3: High risk of caries C: Care as usual C1: Low risk of caries C2: Moderate risk of caries C3: High risk of caries	Societal perspective I: 1,796 C: 2,465 Incremental I vs C: -669  Cost (€) I1: 69.3 I2: 93.5 I3: 170.9 C1: 11.8 C2: 40.6 C3: 140.9 Incremental I1 vs C1: 57.5 I2 vs C2: 52.9 I3 vs C3: 30.0	C: 1.80 Incremental I vs C: -0.45  DFSa I1: 0.08 I2: 0.30 I3: 0.99 C1: 0.10 C2: 0.36 C3: 1.26 Incremental I1 vs C1: -0.02 I2 vs C2: -0.06 I3 vs C3: -0.27 DFSa + DeSa I1: 0.95 I2: 1.27 I3: 1.93 C1: 1.26 C2: 1.82 C3: 2.93 Incremental I1 vs C1: -0.31 I2 vs C2: -0.55 I3 vs C3: -1.00 Children without decay I1: 60,792 I2: 64,672 I3: 65,626 Incremental I3 vs I2: 954 I3 vs I1: 4,834 Proportion of children who developed caries into dentine on at least one permanent molar I1: 19.6% I2: 17.5% Incremental effect not statistically significant. QALY weight and QATY difference not statistically significant	Incremental cost (€) per prevented DFSa I1 vs C1: 2,875 I2 vs C2: 882 I3 vs C3: 111 Incremental cost (€) per prevented DFSa + DeSa I1 vs C1: 186 I2 vs C2: 100 I3 vs C3: 30	Moderate risk of bias High transferability	The FRAMM Guideline significantly reduces the caries increment for all three groups. The most favourable cost-effectiveness in the high caries prevalence group at the age of 12.
Bertrand et al. 2011, [29], Canada	Markov model using a virtual population of 8-year-old children. Various settings modelled. Health care perspective. Time horizon: 10 years.	I1: Sealants delivered in a mixed setting I2: Sealants delivered in a private setting I3: Sealants delivered in a school setting	Costs (\$) I1: 10,890,966 I2: 14,257,324 I3: 11,723,584 Incremental I3 vs I1: 832,618 I3 vs I2: -2,533,740 Costs (£) I1: 529 I2: 457 Incremental I1 vs I2: 72		Incremental cost (\$) per extra child without decay I3 vs I1: 172 I3 vs I2: dominant I2 vs I1: 868 (but dominated by I3)	Moderate risk of bias. Moderate transferability	The school setting is recommended as intervention setting.
Chestnutt et al. 2017, [30], United Kingdom	Model analysis based on a randomized controlled trial (RCT). First permanent molars in 6- and 7- year-olds in the UK (n = 1015). Partial societal perspective. Time horizon: 3 years	I1: Resin-based pit and fissure sealants maintained at 6 monthly intervals I2: Fluoride varnish at 6-month intervals			Incremental cost (£) per child with dentine caries avoided I2 vs I1: dominant Incremental cost (£) per QALY gained I2 vs I1: dominant Incremental cost (£) per QATY gained I2 vs I1: dominant	Low risk of bias High transferability	Fluoride varnish resulted in caries prevention that is not significantly different from that obtained by fissure sealants after 36 months. Fluoride varnish proved less expensive.

(continued)

Table 1. Continued.

Author Year Reference Country	Study design Population Setting Perspective	Intervention vs control	Costs (USD)	Effects	ICER	Risk of bias* and transferability	Further information in the study
Espinoza-Espinoza et al. 2019, [33], Chile	Markov model, 6-year- old children with high prevalence of caries. Public payer perspective. Time horizon: 6 years	I: School-based prevention program for the application of sealants in molars C: No such program	Costs (USD) I: 12.06 C: 10.77 Incremental I vs C: 1.28	QATY I: 3.91 C: 3.71 Incremental I vs C: 0.2	Incremental cost (USD) per QATY gained I vs C: 6.48	Moderate risk of bias Moderate transferability	The authors conclude that the program is cost-effective in populations with a high prevalence of caries.
Hietalalo et al. 2009, [21], Finland	Randomized controlled trial (RCT). 497 11- to 12-year-old children with at least one active initial caries lesion. Health care provider perspective. Time horizon: 3.4 years	I: An individually designed patient- centred regimen for caries control including tooth brushing and diet information. Fluor and CHX varnish + xylitol. Performed by dental hygienists. C: Standard dental care	Costs (€) I: 496 C: 427 Incremental I vs C: 69	DMFS I: 2.56 C: 4.60 Incremental I vs C: -2.04	Incremental cost (€) per DMFS averted I vs C: 34.07	Low risk of bias High transferability	The whole population was also exposed to continuous community-level oral health promotion.
Kay et al. 2018, [35], United Kingdom	Decision analytic model. 12-year old children with high risk. Children living in relatively deprived areas. Expanded health care perspective. Time horizon: Up to 3 years	I1: Supervised tooth brushing I2: Fluoride varnish C: No such program	Not presented	Not presented	Cost-effectiveness using a threshold of £20,000 per QALY gained. I1 vs C: Costs up to £81 per child I2 vs C: Costs up to £143 per child	Moderate risk of bias High transferability	The interventions have a high probability of being considered cost-effective.
Oscarson et al. 2003, [23], Sweden	Prospective cohort study. 116,512-year old children with high risk of developing caries. Societal perspective Time horizon: 4 years	Four preventive programs, representing a stepwise increase in fluoride content, I1: Fluoride tablets I2: Fluoride varnish I3: Individual prevention C: Tooth brushing	Costs (SEK): C: 340 I1: 558 I2: 2775 I3: 2579 I2 vs C: 2435 Savings: I2 vs C: 433 Incremental cost I2 vs C: 2002	DeMFS: C: 6.1 I1: 5.4 I2: 5.0 I3: 5.2 The only significant difference was between strategy I2 and C. I2 vs C: -1.1	Incremental cost (SEK) per DeMFS averted I2 vs C: 2043	Moderate risk of bias High transferability	
Pettersson & Westerberg 1994, [24], Sweden	Long term follow-up based on a randomized controlled trial comprising 16,011- year-old children. Health care perspective. Time horizon: 7 years Model analysis, 12-year- olds.	I: Annual intensified fluoride varnish program with three applications in the time span of 1 week C: Standard fluoride varnish treatment twice a year I1: Dentists applying fluoride varnish in	Incremental cost (SEK) I vs C: 3,880 Saving (due to the prevention of caries increments) I vs C: 5,000 Cost (€) I1: 357	DFS: I: 3.66 C: 6.20 Incremental I vs C: -2.35	Positive cost- benefit ratio	Moderate risk of bias High transferability	The result was mainly driven by the (continued)

Table 1. Continued.

Author Year Reference Country	Study design Population Setting Perspective	Intervention vs control	Costs	Effects	ICER	Risk of bias* and transferability	Further information in the study
Schwendicke & Stolpe 2017, [41], Germany	A mixed public-private-payer perspective in Germany Time horizon: Lifetime	I: Dentists applying fluoride gel in office C: No treatment	I2: 541 C: 230 Incremental I1 vs C: 127 I2 vs C: 311	I2: 9 C: 11 Incremental I1 vs C: -4 I2 vs C: -2	I1 vs C: €39 I2 is dominated by I1	Low risk of bias High transferability	individuals' caries risk. Future studies should focus on caries risk prediction.
Schwendicke et al. 2018, [40], Germany	Markov model analysing starting with 6-year-olds. Three different risk groups. Mixed private-payer perspective in the context of German healthcare. Time horizon: Lifetime	I: Fluoride varnish applied twice yearly between age 6 and 18 years among patients with: I1: Low risk I2: Moderate risk I3: High risk C: No varnish among patients with: C1: Low risk C2: Moderate risk C3: High risk I: Three applications of Duraphat varnish for 1 week, once a year C: One application at the annual check-up	Costs (€) I1: 293 I2: 419 I3: 508 C1: 163 C2: 321 C3: 487 Incremental I1 vs C1: 130 I2 vs C2: 98 I3 vs C3: 21	DMFT I1: 8.1 I2: 15.2 I3: 20.5 C1: 8.5 C2: 16.3 C3: 23.3 Incremental I1 vs C1: -0.4 I2 vs C2: -1.1 I3 vs C3: -2.8	Incremental cost (€) per DMFT avoided I1 vs C1: 343 I2 vs C2: 93 I3 vs C3: 8	Low risk of bias High transferability	Fluoride varnish in the clinic setting is unlikely to be cost-effective in low-risk populations.
Sköld et al. 1994, [27], Sweden	Controlled trial, 13,411-year-old children, Societal perspective. Time horizon: 4 years	I: Three applications of Duraphat varnish for 1 week, once a year C: One application at the annual check-up	Cost (SEK) I: 2345 C: 2389 Incremental I vs C: -44	DMFS: I: 1.5 C: 3.1 Incremental I vs C: -1.6	Cost-effective as effects improved without increasing costs	Moderate risk of bias High transferability	From both a medical and an economic point of view, I2 may be considered the preferred strategy for caries prevention.
Vermaire et al. 2014, [28], the Netherlands	Randomized controlled trial. 6-year old children in general dental practice in the Netherlands. Health care and societal perspective. Time horizon: 3 years	I1: increased professional fluoride application I2: a non-operative caries treatment and prevention programme C: regular dental care	Costs (€) I1: 476 I2: 318 C: 298 Incremental I1 vs C: 178 I2 vs C: 20	DMFS I1: 0.40 I2: 0.34 C: 0.54 Incremental I1 vs C: -0.14 I2 vs C: -0.20	Incremental cost (€) per DMFS avoided I1 vs C: 1,369 I2 vs C: 100	Low risk of bias High transferability	
Adults Schwendicke & Göstemeyer 2017, [39], Germany	Markov model. Adults (elderly). A mixed private-payer-perspective in the context of German healthcare Time horizon: 10 years	I1: Daily 220–800 ppm fluoride rinses I2: Chlorhexidine varnish 2x/year I3: Silver diamine fluoride varnish 2x/year C: No treatment I: Caries Management System (oral examination every sixth month, F- varnish every third month on primary caries), involving a non-invasive strategy to arrest and remineralize noncavitated lesions C: Treatment as usual	Costs (€): I1: 870 I2: 193 I3: 180 C: 130 Incremental I3 vs C: 50	Total years of root caries-free teeth: I1: 150 I2: 149 I3: 151 C: 144 Incremental I3 vs C: 7	Incremental cost (€) per root caries-free tooth-year I1 and I2 were not cost-effective. I3 vs C: 8.30	Low risk of bias High transferability	Root caries preventive treatments are effective and might even be cost saving in high risk populations.
Warren et al. 2016, [44], Australia	Markov model based on a RCT. Private dental practitioner perspective. Time horizon: 7 years and lifetime	I: Caries Management System (oral examination every sixth month, F- varnish every third month on primary caries), involving a non-invasive strategy to arrest and remineralize noncavitated lesions C: Treatment as usual	Costs (AUD) 7 years: I: 5,689 C: 3,613 Incremental I vs C: 2,076 Lifetime: I: 12,421 C: 7,990 Incremental I vs C: 4,431	Number of restorative events 7 years I: 5.46 C: 7.62 Incremental I vs C: -2.15 Lifetime I: 7.96 C: 10.19 Incremental I vs C: -2.24	Incremental cost (AUD) per restorative event avoided 7 year I vs C: 964 Lifetime I vs C: 1,980	Low risk of bias Moderate transferability	RCT was conducted for 3 years, followed by 4-year follow-up. I is associated with increased costs, but if the protocol is adhered, the effect is sustained over time.

(continued)

Table 1. Continued.

Author Year Reference Country	Study design Population Setting	Intervention vs control	Costs	Effects	ICER	Risk of bias* and transferability	Further information in the study
Whole populations Davenport et al. 2003, [32], UK	Markov model based on UK Children/adults 12–80 years. Health care perspective. Time horizon: 68 years	Frequency of dental checks I1: 3-monthly I2: 6-monthly I3: 12-monthly I4: 18-monthly I5: 24-monthly I6: 36-monthly	Costs (£) I1: 515.20 I2: 315.60 I3: 240.30 I4: 225.00 I5: 203.70 I6: 202.00	Free from dmft/ DMFT Adults I1: 17.26 I2: 17.04 I3: 16.90 I4: 16.33 I5: 15.04 I6: 11.94	Incremental cost (£) per dmft or DMFT saved I3 vs I4: 26.8	Moderate risk of bias Moderate transferability	Moving to longer intervals than 6 months would be cost-effective.
Nguyen et al. 2019, [37], Australia	Markov model. Individuals aged 15 years and older. Health care perspective. Time horizon: 70 years	I: Biannual fluoride varnish C: Usual practice (non- routine application)	Costs (AUD\$) I: 3600 C: 2303 Incremental I vs C: 1297	DMFT I: 13.99 C: 15.52 Incremental I vs C: –1.53 QALY I: 15.44 C: 14.74 Incremental I vs C: 0.7	Incremental cost (AUD\$) per prevented DMFT I vs C: 849 Incremental cost (AUD\$) per QALY gained I vs C: 1851	Low risk of bias Moderate transferability	The intervention is likely to be cost- effective for all scenarios tested.
Splith and Fleßa, 2008, [43] Germany	Model study based on epidemiological data. German context. Time horizon: Lifetime	I1: Fluoridated salt I2: Fluoridated salt and fluoride toothpaste I3: Fluoridated salt, fluoride toothpaste and gel I4: Fluoridated salt, fluoride toothpaste and gel plus professional topical fluoride application I5: Professional, topical fluoride application C: No fluoride prevention	Total cost (€) I1: 247 I2: 211 I3: 214 I4: 410 I5: 579 C: 932	Maximum caries preventive effect compared with C I1 vs C: 50% I2 vs C: 60% I3 vs C: 76% I4 vs C: 86% I5 vs C: 40%	All interventions are dominant in comparison to no fluoride prevention	Moderate risk of bias Moderate transferability	Life-long simulations with much uncertainty.
Tax on sugar Jevdjovic et al. 2019, [34], the Netherlands	Markov model. Dutch population aged 6–79 years. Societal perspective. Time horizon: Lifetime	I: a 20% tax on sugar- sweetened beverages C: No such tax	I: Lifetime tax revenues were larger than the administrative costs for taxation. I vs C: savings in terms of dental care expenditures. Treatment costs (billion €) I: 2.64 C: 2.72 Incremental I vs C: –0.08 billion	Caries-free tooth years saved per person I vs C: 2.13	Dominant. Lower costs and improved oral health	Low risk of bias High transferability	Benefits would be the greatest for younger age groups
Schwendicke et al. 2016, [42], Germany	A model-based approach for the German population aged 14 to 79 years. A mixed private-payer perspective. Time horizon: 10 year	I: A 20% taxation of sugar-sweetened beverages C: No such taxation	Million caries increments I: 82.27 C: 83.02 Incremental I vs C: –0.75 million	Dominant	Moderate risk of bias. High transferability	A 20% sales tax on sugar-sweetened beverages is likely to reduce caries increment, especially in young low- income males.	

is a scarcity of studies specifically targeting adults and especially the elderly. The latter often suffer from poor oral health and need effective preventive interventions.

### Prospero registry

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