Supporting Information

Table S1: Table of extracted studies (n=230)

Included in systematic reviews

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Wrong study design

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Table S2: Data extraction and quality appraisal for trials and observational studies (n= 61)

ID NUMBER	AUTHOR, YEAR	COUNTRY	STUDY DESIGN	STUDY POPULATION, SETTING	SAMPLE SIZE	INTERVENTION	OUTCOME MEASURES	KEY FINDINGS & RESULTS	QUALITY APPRAISAL
FLUORIDE VARNISH									
1137	McMahon et al., 2020 (McMahon *et al.*, 2020)	Scotland, UK	RCT double-blind, two-arm	3-year-olds attending nursery schools (P1) within the areas of 4 NHS Health Boards in Scotland (Greater Glasgow and Clyde, Fife, Lothian, and Tayside); Inclusion based on the SIMD of the children: the next most socially disadvantaged areas	n = 1,150 n = 573 (TAU) n = 577 (FV)	**Arm 1:** Childsmile treatment-as-usual (TAU), including supervised toothbrushing using fluoridated toothpaste + "sham" FV **Arm2:** TAU + active FV treatment (every 6 months, max total of 4 applications across the course of the trial) **Follow up:** 24 months	**Primary outcome:** caries worsening measured using d3mft **Secondary outcomes:** worsening in d3mfs, d3t, mt, ft **Tertiary outcomes:** hospital admission for dental extractions under GA **Cost-effectiveness assessment**	**Primary outcome:** worsening of d3mft FV group (arm 2) 26.9% (n = 155) had worsened d3mft TAU group (arm 1) 31.6% (n = 181) OR=0.80 (95%CI 0.62–1.03), p = 0.078. **Secondary outcomes:** worsening of d3mfs OR=0.79 (95%CI 0.61–1.01) p = 0.063, worsening of d3t OR=0.75 (95%CI 0.57–0.99) p = 0.043, worsening of mt OR=1.34 (95%CI 0.75–2.39) p = 0.319, worsening of ft OR=0.77 (95%CI 0.53–1.14) p = 0.191. **Tertiary outcomes:** No differences in hospital admission for dental extractions under GA or the other tertiary endpoints. The **NNT** to prevent one child from having a worsening of d3mft was 21. The **mean cost per child** in the FV group was GBP 32.66 (SD GBP 13.21). Thus, it would cost GBP 685.86 to prevent one child from having a worsening of d3mft.	High
8	Chestnutt, et al., 2017 (Chestnutt *et al.*, 2017)	Wales-UK	RCT- 2 arms	6–7-year-old students using mobile dental clinics in schools located within areas of high social and economic deprivation in South Wales.	n = 835 n = 417 (FS Arm) n = 418 (FV Arm)	**FS Arm:** Fissure Sealant (FS) applied to first permanent molars at 6 months intervals **FV Arm:** Fluoride Varnish (FV) was applied to the first permanent molars at baseline and 6-month intervals **Follow up:** 3 years	**Primary outcome:** the proportion of children developing caries into dentine ($D_{4\text{-}6}$MFT) on any 1 of up to 4 treated First Primary Molars (FPMs) after 36 months.	**Primary outcome:** Children developed $D_{4\text{-}6}$MFT: FS (Arm 1) 19.6% (*n* = 82) FV (Arm 2) 17.5% (*n* = 73) OR= 0.84; 95% CI, 0.59 to 1.21; *P* = 0.35 A non-statistically significant difference between FS and FV treatments Differences in caries prevention between FV and FS were not significant after 36 months	Low
203	Bravo, et al, 2005 (Bravo *et al.*, 2005)	Spain	RCT (Clinical Trial)	6-8-year-olds schoolchildren	n = 120 n = 37 (FS Arm) n = 38 (FV Arm)	**FS Arm:** Fissure Sealant (FS) applied to the first permanent molars at baseline and after 36 months **FV Arm:** Fluoride Varnish (FV) applied to the first permanent molars at baseline and after 42 months **Control group:** n = 45 **Follow up:** 9 years: 4 years: program evaluation 5 years: discontinuation.	**Primary outcome:** Percent caries reduction in first permanent molars with complete occlusal eruption	**Primary outcome:** Caries reductions: FS *vs* control: 65.4% (SE = 8.5%) FV *vs* control: 27.3% (SE = 10.2%) The Fluoride Varnish program was not effective during the discontinuation period	Low

ID NUMBER	AUTHOR, YEAR	COUNTRY	STUDY DESIGN	STUDY POPULATION, SETTING	SAMPLE SIZE	INTERVENTION	OUTCOME MEASURES	KEY FINDINGS & RESULTS	APPRAISAL
FLUORIDE VARNISH									
967	Latifi-Xhemajli et al., 2019 (Latifi-Xhemajli *et al.*, 2019)	Kosovo	RCT	21-month-olds attending eleven Pristina preschool institutions	n = 427 n = 218 (Tg) n = 209 (Cg)	**Test group (Tg):** Fluoride Varnish (FV) was applied in 3 months intervals (4 times/year). **Control group (Cg):** No treatment **Follow up:** 2 years	**Primary outcome:** Dental status based on the International Caries Detection and Assessment System (ICADS)	**Primary outcome:** Dental status: **At baseline:** dmfs was similar: • Tg = 1.2 • Cg = 1 Caries-free prevalence: • Tg = 79.6% • Cg = 80.3% **Post intervention:** dmfs was different ($p < 0.001$):	High

								• Tg = 5.2 • Cg = 10.1 Caries-free prevalence: • Tg = 69.4% • Cg = 40% Fluoride Varnish application four times a year was associated with 49% reduction in dental caries in pre-school children	
480	Effenberger et al., 2021 (Effenberger *et al.*, 2022)	South Africa	Cluster-RCT	4-8-year-olds schoolchildren, high risk population from two schools in township Schoolchildren already practicing supervised toothbrushing with fluoridated toothpaste	n = 513 n = 287 (Tg) n = 226 (Cg)	**Test group (Tg):** Fluoride Varnish (FV) was applied in 3 months intervals by trained local non-professional assistants. **Control group (Cg):** No treatment **Follow up:** 2 years	**Primary outcome:** • The increment of teeth with newly developed cavitated lesions and requiring restoration or extraction over the study period • Treatment and re-treatment costs	**Primary outcome:** **At baseline:** $d_{1\text{-}4}$mft was similar: • Tg = 5.9 • Cg = 6.0 **Post intervention:** Increment of teeth with newly developed cavitated lesions received or required restoration: • Tg = 10.2% • Cg = 10.2% Increment of teeth with requiring extraction: • Tg = 3.9% • Cg = 4.1% Fluoride Varnish Initial treatment cost in South African Rank currency (ZAR) ($p < .05$): • Tg = 727 ZAR • Cg = 2 ZAR Fluoride Varnish re-treatment costs: • Tg = 939 ZAR • Cg = 948 ZAR Fluoride Varnish overall treatment costs after 24 months ($p < .05$): • Tg = 1667 ZAR • Cg = 950 ZAR	High

ID NUMBER	AUTHOR, YEAR	COUNTRY	STUDY DESIGN	STUDY POPULATION, SETTING	SAMPLE SIZE	INTERVENTION	OUTCOME MEASURES	KEY FINDINGS & RESULTS	APPRAISAL
FLUORIDE VARNISH									
1886	Wu et al, 2020 (Wu *et al.*, 2020)	China	RCT	6-8 years old schoolchildren in schools of rural areas of Guangxi province, China.	n = 1748 n = 853 (Tg) n = 895 (Cg)	**Test group (Tg):** Oral health education and Fluoride Varnish (FV) was applied in 6 months intervals (twice/year). **Control group (Cg):** Oral health education only **Follow up:** 3 years	**Primary outcome:** Dental status of newly erupted first permanent molars based the modified International Caries Detection and Assessment System (ICDAS-II)	**Primary outcome:** **At baseline:** prevalence of dental caries ($p < 0.738$): • Tg = 24.0% • Cg = 23.4% DMFT ($p < 0.590$): • Tg = 0.46 • Cg = 0.43 DMFS ($p < 0.285$): • Tg = 0.60 • Cg = 0.53 **Post intervention:** prevalence of dental caries ($p < 0.004$): • Tg = 58.9% • Cg = 65.5% caries increment ($p < 0.002$): • Tg = 34.8% • Cg = 42.1% DMFT ($p < 0.002$): • Tg = 1.38 • Cg = 1.59 DMFS ($p < 0.009$): • Tg = 2.06 • Cg = 2.38 Application of fluoride varnish twice a year in addition to oral health education were significantly effective for preventing caries in first permanent molars than sole application for oral health education	Moderate
1178	Mohammadi et al, 2015 (Mohammadi *et al.*, 2015)	Iran	Cluster-RCT	3-6 years old in Kerman kindergarten	n = 476 n = 190 (Tg) n = 172 (Cg)	**Test group (Tg):** Fluoride Varnish (FV) was applied at baseline, 3 and 6 months **Control group (Cg):** Fluoride Varnish (FV) was applied at 3 and 6 months only **Follow up:** 6 months	**Primary outcome:** Dental status based on the International Caries Detection and Assessment System (ICADS)	**Primary outcome:** Dental status (dmft): **At baseline (Phase 1):** dmft ($p < 0.4$):: • Tg = 5.23 • Cg = 4.91 **After 3 months (Phase 2)::** dmft ($p < 0.043$):: • Tg = 5.15 • Cg = 4.33 **After 6 months (Phase 1):**	Moderate

								dmft ($p < 0.57$): • Tg = 4.87 • Cg = 4.65 **Differences (Paired t-test) in mean dmft in different stages:** **Tg:** Phase 1 & 2 = 0.13 ($p < 0.05$) Phase 2 & 3 = 0.21 ($p < 0.07$) **Cg:** Phase 1 & 2 = 0.08 ($p < 0.00$) Phase 2 & 3 = −1.38 ($p < 0.03$) Fluoride varnish is effective on preventing dental caries in a among 3-6 years old children in	
101	Autio-Gold and Courts, 2001 (Autio-Gold and Courts, 2001)	US	RCT	3-5 years old attending Head Start schools in Alachua County in US The drinking water in the area contained 0.80 ppm Fluoride	n = 142 n = 59 (Tg) n = 83 (Cg)	**Test group (Tg):** Fluoride Varnish (FV) was applied in at baseline and after 4 months **Control group (Cg):** No treatment **Follow up:** 9 months	**Primary outcome:** Caries status based on the differentiation between active and inactive enamel carious lesions on the basis of a combination of visual and tactile criteria	**Primary outcome:** Dental status: **At baseline:** **Dmfs:** • Tg = 2.51 • Cg = 2.58 **dmft:** • Tg = 1.63 • Cg = 2.07 **Post intervention:** **dmfs ($p < 0.05$):** • Tg = 3.05 • Cg = 4.05 **dmft ($p < 0.01$):** • Tg = 1.68 • Cg = 2.57 Inactive caries lesion ($p < 0.001$): • Tg = 81.2% • Cg = 37.8% Fluoride varnish applications was effective in deactivation of active caries in primary teeth and may offer an efficient, nonsurgical approach to the treatment of decay in children caries in pre-school children	Moderate
1949	Kalnina and Care, 2016 (Kalnina and Care, 2016)	Latvia	RCT	10 years old schoolchildren	n = 1748 n = 50 (Cg) n = 21 (FVg) n = 17 (FSg) n = 19 (Og)	**Fluoride Varnish group (FVg):** Fluoride Varnish (FV) was applied and re-applied up to 12 months. **Fissure Sealant group (FSg):** Fissure Sealant (FS) was applied and re-applied up to 12 months. **Ozone group (Og):** Ozone (O) was applied and re-applied up to 12 months. **Control group (Cg):** Oral health education only **Follow up:** 12 months	**Primary outcome:** Percent caries reduction in these initially healthy molars with complete occlusal eruption	**Primary outcome:** **After 12 months follow up:** prevalence of dental caries ($p < 0.106$): • FVg = 0% • FSg = 0% • FVg = 2.9% • Cg = 3.5% Application of fissure sealant, fluoride varnish, or ozone could reduce occlusal pit and fissure caries in permanent premolars in 10 years old schoolchildren. But results were not significant compared to the control group results.	Low

ID NUMBER	AUTHOR, YEAR	COUNTRY	STUDY DESIGN	STUDY POPULATION, SETTING	SAMPLE SIZE	INTERVENTION	OUTCOME MEASURES	KEY FINDINGS & RESULTS	APPRAISAL
FLUORIDE VARNISH									
1912	Zaror et al, 2020 (Zaror *et al.*, 2020)	Chile	Economic Study	2 and 3 years from a low socioeconomic background, living in rural areas in the Chilean Regions of La Araucanía, Los Ríos and Los Lagos who did not present cavitated caries lesions at baseline or previous dental treatments. A cost-effectiveness analysis was carried out based on a clinical decision tree from the payer's perspective. The effectiveness and cost of the varnish were determined from a two-year follow-up triple-blind randomized control trial in public rural preschools in areas without access to fluoridated water.	n = 275 n = 131 (Tg) n = 144 (Cg)	**Test group (Tg):** Fluoride Varnish (FV) was applied 4 times in the total 24 months. **Control group (Cg):** Received placebo **Follow up:** 2 years	**Primary outcome:** The incremental cost-effectiveness ratio (ICER) of the communitywide application of fluoride varnish in the prevention of early childhood caries (ECC). Costs and benefits were discounted at 3% per year. Only direct costs were evaluated,	**Primary outcome:** **Post intervention:** prevalence of dental caries ($p < 0.004$): • Tg = 45% (36%–54%, 95% confidence interval) • Cg = 55.6% (47%–64%, 95% confidence interval) **The weighted cost in Chilean pesos (CLP) to intervene and treat the consequences of ECC:** • Tg = CLP 67,757 (USD98.76) • Cg: CLP 67,739 (USD98.74) **The incremental cost-effectiveness ratio:** ICER = CLP 173 (USD0.25) for each extra healthy child in favour of fluoride varnish. In Chile, it found that fluoride varnish is more effective and less costly in the prevention of ECC in	High

								non-fluoridated areas, compared with a placebo.	
1301	Palacio et al, 2019 (Palacio *et al.*, 2019)	Chile	Economic Study	The use of a decision analytic model (DAM) to evaluate whether fluoride varnish application (FV) increases the proportion of caries-free children in the Chilean preschool population, at an acceptable cost. Different FV interventions in either a preschool setting or during a well-child Programme appointment in a primary care setting were compared with an oral health counselling-only intervention.		**Test group (Tg):** Fluoride Varnish (FV) was applied in 6 months intervals without counselling or screening. **Control group (Cg):** counselling-only **Follow up:** 2 years	**Primary outcome:** incremental cost per child	**Primary outcome:** **Post intervention:** Compared with counselling-only intervention, delivery of FV in a primary care setting without screening increased the prevalence of caries-free children in the population by 3.7%, with an extra cost (in March 2015) of £3 (CLP 4836) per caries-free child. Delivery of FV in a primary care setting without screening was the most effective and the least costly intervention. Compared with counselling-only intervention	High
1255	Norrie and Norrie, 2020 (Norrie and Pharand, 2020)	Canada	Economic Study	1 to 6 years old preschool children in 2 low-income communities in Winnipeg, Canada. Enrolled in the Winnipeg Regional Health Authority Daycare Fluoride Varnish Program in January 2018	n = 873 n = 853 (Tg) n = 895 (Cg)	**Fluoride Varnish group (FVg):** Fluoride Varnish (FV) applied by dental hygienists twice/year, stats at one year-old. **Usual Dental Care group (UDCg):** usual dental care (surgery under general anaesthesia) **Follow up:** 5 years	**Primary outcome:** cost, cavities avoided, and reductions in surgery volume Analyses used Markov model Aggregate retrospective data from published monthly program reports and literature sources	**Primary outcome:** **Post intervention:** Cost per child for 5 years (US Dollar $): • **FVg** = $983 • **UDCg** = $1806 • **Incremental cost (savings)** by using fluoride varnish = of $823 • cavities saved per child by using fluoride varnish = 4.38 • Incremental cost-effectiveness ratio (ICER) per cavity with FV versus usual care = $187.71 Participants' need for dental surgery under GA: • **FVg** = 1.6% • **UDCg** = 19.1% The preventive fluoride varnish (FV) was shown to be cost-effective over usual care involving dental surgery under GA and to provide substantial annual cost savings ($181,060/ year, approximately $41.15 per FV application) for the health care system. Additional benefits are expected to society due to improvements in quality of life and resource savings by parents and other caregivers.	High

ID NUMBER	AUTHOR, YEAR	COUNTRY	STUDY DESIGN	STUDY POPULATION, SETTING	SAMPLE SIZE	INTERVENTION	OUTCOME MEASURES	KEY FINDINGS & RESULTS	APPRAISAL
FLUORIDE VARNISH									
395	Davoodi-Lahijan et al, 2021 (Davoodi-Lahijan *et al.*, 2021)	Iran	Economic Study	7-12 years old school children in all primary schools, who were studying at elementary schools of, in Urmia, northwestern Iran. This study modelled the cost-effectiveness of fluoride varnish therapy plan to prevent dental caries in elementary students with age range between 7-12 years.		**Intervention group:** Fluoride Varnish (FV) was applied to schoolchildren in 2016 **Comparison group (Cg):** Schoolchildren didn't receive Fluoride Varnish in 2012	**Primary outcome:** Incremental cost-effectiveness ratio (ICER) per DALY averted.	**Primary outcome:** **The number of disability-adjusted life year (DALY) for the years 2012 and 2016:** **In 2012 =** 11284 **In 2016 =** 9253 **Number of DALY** Averted = 2031 **ICER** = $200.02 per DALY averted. According to the threshold defined by World Health Organization (WHO) – WHO criteria and report of International Monetary Fund (IMF) (GDP per capita of Iran:27 US$4680 in 2016)-, fluoride varnish therapy intervention in the Iranian study was cost-effective. It found reducing caries, improving quality of life (QOL), and financial saving for families in the long term.	High
147	Bergstrom et al, 2016 (Bergström *et al.*, 2016)	Sweden	Economic Study	all 12-15-years-old, received fluoride varnish applications at school every six months as part of population-based programme implemented by 19 public dental clinics in	n = 27,943 n = 3,132 (group 1) n = 13,490 (group 2) n = 11,321 (Group 3)	A retrospective design with caries data for two birth cohorts extracted from dental records. **Group 1:** born in 1993, had fluoride varnish programme at schools started in 2003	**Primary outcome:** Caries prevalence and increment and to cost analysis of the programme. The total cost of the four-year programme was estimated at 400SEK (≈44€) per adolescent.	**Primary outcome:** Caries prevalence and caries increment in 15 years old were significantly lower after the implementation of the programme. Group 2, without a programme, had the highest caries increment. The cost analysis showed that it was a	High

				Västra Götaland Region in 2003. The programme was extended to include all 112 clinics in the region in 2008.		**<u>Group 2:</u>** born in 1993, had no fluoride varnish programme at school. **<u>Group 3:</u>** born in 1998, when the programme was implemented for all individuals. **<u>Follow up:</u>** 4 years		break-even between costs and gains due to prevented fillings at the age of 15. **Post intervention:** **<u>prevalence of dental caries:</u>** **Group 1 =** 83-86% (Intervention 2003) **Group 2=** 79-81% **Group 3=** 79-84% (Intervention 2008) **<u>Caries increment ($p < 0.001$):</u>** **Group 1 =** 1.41 (Intervention 2003) **Group 2=** 1.60 **Group 3=** 1.09 (Intervention 2008) **<u>Actual costs and savings from 12-15 years (by Swedish Krona (*SEK)*), comparing group 2 with group 3:</u>** **Decrease in cost per adolescence and year** = 391 **Cost of the programme per adolescence and year** = 400 **Accumulated outcome per adolescence and year** = -9 **<u>Estimated costs and savings from 12-19 years (by Swedish Krona (*SEK)*) comparing group 2 with group 3:</u>** **Decrease in cost per adolescence and year** = 1,435 **Cost of the programme per adolescence and year** = 400 **Accumulated outcome per adolescence and year** = 1,035 The school-based fluoride varnish programme, implemented on a broad scale for all 12 to 15 year olds, reduced caries increment at a low cost (estimated at 400SEK (≈44€) per adolescent) for the adolescents	
1940	Anopa et al., 2022 (Anopa *et al.*, 2022)	Scotland - UK	Economic Study	3 years old children attending nursery schools and enrolled in randomized controlled trial (the Protecting Teeth @ 3 Study [PT@3]).	n = 534 n = 265 (FVg) n = 269 (TAUg)	**<u>Fluoride Varnish group (FVg):</u>** Fluoride Varnish (FV) was applied in 6 months intervals (twice/year) plus TAU **<u>Treatment As Usual group (TAUg):</u>** all other components of Childsmile (Children attended their usual sources of dental care during the trial and dental practitioners continued with their normal care; the children also received the other Childsmile interventions, regardless of their treatment allocation) **<u>Follow up:</u>** 2 years	**<u>Primary outcome:</u>** trial cost-utility analysis (CUA) Health outcomes were expressed in quality-adjusted life years (QALYs) accrued over the 2-y follow-up period. incremental cost-utility ratios	**<u>Primary outcome:</u>** **Post intervention:** Cost per child for 2 years (in PGB £): • **FVg** = £ 665.90 • **TAUg** = £ 597.52 • **Mean incremental cost (savings)** by using fluoride varnish = £68.37 (P = 0.382; 95% confidence interval CI], –£18.04 to £143.82) The quality-adjusted life years (QALYs): • **FVg** = £ 1.8590 • **TAUg** = £ 1.8634 • **Mean incremental QALY =** –0.004 (P = 0.636; 95% CI, –0.016 to 0.007). The probability that the FV intervention was cost-effective at the UK threshold of £20,000 per additional QALY was low (11.3%). Thus, applying FV in nurseries in addition to Treatment as usual would not be deemed cost-effective given current UK thresholds	Moderate

ID NUMBER	AUTHOR, YEAR	COUNTRY	STUDY DESIGN	STUDY POPULATION, SETTING	SAMPLE SIZE	INTERVENTION	OUTCOME MEASURES	KEY FINDINGS & RESULTS	APPRAISAL
FLUORIDE VARNISH									
1576	Skinner et al, 2020 (Skinner *et al.*, 2020)	Australia	Economic Study	Disadvantaged primary schools in New South Wales in Australia Most of the cost of the school-based Fluoride Varnish programme can be covered by the Child Dental Benefit Schedule			**<u>Primary outcome:</u>** cost of Fluoride Varnish application	**<u>Primary outcome:</u>** **Post intervention:** Cost of materials for the school-based fluoride Varnish programme (by US Dollar $) • **Costing at 25 students** = $ 75.21 • **Costing at 50 students** = $ 150.36 • **Costing at 100 students** = $ 300.68 Index of Community Socio-Educational Advantages (ICSEA) is a composite scale that represents	Moderate

								levels of educational advantage where lower ICSEA value indicate lower level of educational advantage. ICSEA is also used as an indicator to the socioeconomic aspects of child oral health as the highest prevalence of Dental Caries was found in areas of ICSEA1 (<986) and ICSEA2 (986-1044), Ministry of Health operates Child Dental Mobile Van programme in low ICSEA areas and apply Fluoride Varnish. Four Fluoride varnish applications a year is feasible, and the main costs of the program could be covered by using the Child Dental Benefits Schedule, when targeting schools using a combination of ICSEA and Aboriginal enrolment.	
1371	Pitchika et al, 2013 (Pitchika *et al.*, 2013)	Germany	Observational – Case Control Study	in the Kyffhäuser district (Thuringia, Germany) Non-Randomized sample The basic preventive program in the Kyffhäuser district includes daily supervised tooth brushing with fluoridated toothpaste (500 ppm) in all kindergartens, dietary counselling on healthy meals for the kindergarten staffs and one visit to a dental practice *per* year to reduce dental anxiety.	n = 308 n = 159 (FVg) n = 149 (Cg) Non-Randomised sample	**<u>Fluoride Varnish group (FVg):</u>** Fluoride Varnish (FV) was applied in 6 months intervals (twice/year) **<u>Control group (Cg):</u>** No Fluoride Varnish application **<u>Follow up:</u>** 2 years	**<u>Primary outcome:</u>** *change in caries incidence* **$d_{1\text{-}2}s$** Non-cavitated caries lesions in primary teeth were recorded using WHO and Universal Visual Scoring System (UniViSS) criteria **$d_{3\text{-}4}mfs$** caries index were recorded using World Health Organization (WHO) criteria. Baseline data were used as a reference for the calculation of the 2-year caries incidence.	**<u>Primary outcome:</u>** **At baseline:** **$d_{1\text{-}2}s$** ($p < 0.05$): • **FVg** = **2.5** • **Cg** = **2.3** **$d_{3\text{-}4}mfs$** ($p < 0.05$): • **FVg** = **2.0** • **Cg** = **2.3** **Post intervention:** **$d_{1\text{-}2}s$** ($p < 0.05$): • **FVg** = **3.9** • **Cg** = 4.0 **$d_{3\text{-}4}mfs$** ($p < 0.05$): • **FVg** = **4.2** • **Cg** = **4.6** Fluoride varnish prevention of non-cavitated carious lesions was significant, but when including SES as a confounder into regression model, potential preventive effect was lost.	Moderate

ID NUMBER	AUTHOR, YEAR	COUNTRY	STUDY DESIGN	STUDY POPULATION, SETTING	SAMPLE SIZE	INTERVENTION	OUTCOME MEASURES	KEY FINDINGS & RESULTS	APPRAISAL
TOOTHBRUSHING WITH FLUORIDE TOOTHPASTE									
1366	Pine et al, 2007 (Pine *et al.*, 2007)	Scotland - UK	RCT	5 years old schoolchildren in primary school in Tayside. Low SES	n = 329 n = 175 (Tg) n = 154 (Cg)	**<u>Test group (Tg):</u>** Receiving supervised toothbrushing once a day at school with 1,000 ppm fluoride toothpaste and a home support package encouraging twice-daily toothbrushing **<u>Control group (Cg):</u>** Non-intervention group did not brush at school or receive the home support package **<u>Follow up:</u>** 84 months ***Note:*** The intervention applied for 30 months and the follow up continue 54 months after the intervention cessation.	**<u>Primary outcome:</u>** Difference in net caries increment on first permanent molars between the intervention and non-intervention group,	**<u>Primary outcome:</u>** **Post intervention:** **Caries increments ($p < 0.002$):** • **Tg** = 1.62 • **Cg** = 2.65 **Difference in 0–84-month increments between groups ($p < 0.001$)** = 33% A supervised toothbrushing programme using a 1,000-ppm fluoride toothpaste showed a significant long-term benefit in the dental health of children after the cessation. .	High
1338	Petersen et al, 2015 (Petersen *et al.*, 2015a)	Thailand	RCT - blind	5-7 years old schoolchildren attending schools in in Songkhla Province, Thailand. Fluoridated area	n = 2716 n = 1,373 (Tg) n = 1,343 (Cg)	**<u>Test group (Tg):</u>** Benefit of an enhanced oral health promotion program combined with a closely supervised tooth brushing program in schools, using toothpaste containing 1,450 ppm F- and 1.5% arginine **<u>Control group (Cg):</u>** No intervention **<u>Follow up:</u>** 2 years	**<u>Primary outcome:</u>** Difference in caries increments (DMFT and DMFS) in permanent teeth.	**<u>Primary outcome:</u>** <u>Dental status:</u> **At baseline:** **DMFT:** • Tg = 0.10 • Cg = 0.10 **DMFS:** • Tg = 0.15 • Cg = 0.16 **Post intervention:** **DMFT increment ($p < 0.005$):** • Tg = 1.04 • Cg = 1.19 **DMFS increment ($p < 0.001$):** • Tg = 1.59 • Cg = 1.91 **DMFS reduction in dental caries up to 40.9**% Supervised toothbrushing with fluoridated toothpaste (1,450 ppm Fand 1.5% arginine)	High

								administered by schoolteachers and undertaken via an enhanced school oral health program significantly reduced dental caries	
362	Curnow et al, 2002 (Curnow *et al.*, 2002)	Scotland - UK	RCT	5 years old children in schools in Tayside - Dundee Low SES	n = 461 n = 239 (Tg) n = 222 (Cg)	**<u>Test group (Tg):</u>** Receiving daily supervised toothbrushing once a day at school with 1,000 ppm fluoride toothpaste combined with home toothbrushing supply **<u>Control group (Cg):</u>** No intervention **<u>Follow up:</u>** 2 years	**<u>Primary outcome:</u>** Difference in net caries increment on first permanent molar between the intervention and non-intervention group	**<u>Primary outcome:</u>** <u>Dental status:</u> **At baseline:** **Caries increment:** • Tg = 4.92 • Cg = 4.33 **Post intervention:** **Caries increment ($p < 0.023$):** • Tg = 0.8 • Cg = 1,2 **Reduction in dental caries up = 32%** Children received school supervised toothbrushing plus home supplies had 32% reduction in dental caries on newly erupted first permanent molars.	High
1499	Samuel et al, 2020 (Samuel *et al.*, 2020)	India	RCT - double blind, three parallel arms	3–5 years old preschool children in Tamil Nadu in Chennai district Low SES	n = 342 n = 104 (Tg) n = 111 (ACg) n = 127 (NCg)	**<u>Test group (Tg):</u>** Received intervention includes prohibition of sugary snack consumption in school, teacher supervised daily brushing using fluoridated toothpaste, and oral health education **<u>Active Control group (ACg):</u>** Received oral health education with school supervised toothbrushing **<u>Negative Control group (NCg):</u>** Receiving only oral health education **<u>Follow up:</u>** 2 years	**<u>Primary outcome:</u>** Decayed (early childhood caries (ECC)) was assessed using World Health Organization criteria early childhood caries (ECC)	**<u>Primary outcome:</u>** <u>Dental status:</u> **At baseline:** **Decayed teeth:** • **Tg** = 5.4 • **ACg** = 5.7 • **NCg** = 5.3 **Post intervention:** **Decayed teeth (**Comparison between Tg and ACg p =.002, Comparison between Tg and NCg p =.0.003)**:** • **Tg** = 3.2 • **ACg** = 4.1 • **NCg** = 4.3 **Mean caries increment ($p < 0.05$):** • **Tg** = 0.04 • **ACg** = 0.8 • **NCg** = 0.9 The effect of interventions to prevent ECC in each group was calculated using the Çohen's d, and the scores: • **Tg compared to ACg** = 0.6 • **Tg compared to NCg** = 0.9 Prohibition of sugary snacking in school and daily supervised tooth brushing, with or without oral health education is effective in preventing ECC among preschool children with health neglect in very low-resource settings	Moderate
552	Frazao, 2011 (Frazão, 2011)	Brazil	RCT - double-blinded	5 years old children presenting at least one permanent molar with emerged/sound occlusal surface in pre-schools in the city of Sao Vicente, Brazil. Low SES & Fluoridated area (0.7 mgF/ L).	n = 280 n = 152 (Tg) n = 128 (Cg)	**<u>Test group (Tg):</u>** children underwent professional cross-brushing on surfaces of first permanent molar, rendered by a specially trained dental assistant, five times per year At the remaining school days the children brushed their teeth under indirect supervising of the teachers. **<u>Control group (Cg):</u>** Received oral health education and dental plaque dying followed by toothbrushing. with fluoride dentifrice (1,100 µgF/g) supervised directly by a dental assistant, The dental assistant was not skilled on special toothbrushing methods for erupting molars and was not trained to carry out the cross-brushing technique.	**<u>Primary outcome:</u>** The effectiveness of bucco-lingual technique in increasing the effectiveness of a school-based supervised toothbrushing program on preventing caries	**<u>Primary outcome:</u>** <u>Dental status:</u> **At baseline:** **Dmft:** • **Tg** = 2.27 • **Cg** = 2.02 **Post intervention:** **Incidence density for caries* (per 1,000 exposed surfaces-month):** • **Tg** = 13.0 • **Cg** = 16.1 Among boys whose caries risk was higher compared to girls, incidence density was 50% lower in test group (p = 0.016) Modified program was effective among the boys. It is licit to project a relevant effect in a larger period suggesting in a broader population substantial reduction of dental care needs	Moderate

						At the remaining school days the children brushed their teeth under indirect supervising of the teachers. **Follow up:** 18 months			
328	Clasen et al, 1995 (Clasen *et al.*, 1995)	Germany	RCT	4 years old children in Salzgitter kindergartens	n = 172 n = 83 (LFTg) n = 89 (HFTg)	**Low Fluoride Toothpaste group (LFTg):** Brushed their teeth daily under supervision in their kindergartens Using dentifrices containing sodium fluoride with fluoride concentrations of 250 ppm **High Fluoride Toothpaste group (HFTg):** Brushed their teeth daily under supervision in their kindergartens using dentifrices containing sodium fluoride with fluoride concentrations of 1450 ppm **Follow up:** 22 months	**Primary outcome:** The anticaries effects of two dentifrices containing sodium fluoride with fluoride concentrations of 250 ppm and 1450 ppm on the primary dentition of kindergarten children	**Primary outcome:** Dental status: **At baseline:** **Dmft:** • LFTg = 1.0 • HFTg = 1.2 **dmfs:** • LFTg = 2.0 • HFTg = 2.4 **Caries free prevalence (%)** • LFTg = 71% • HFTg = 72% **Post intervention:** **dmft:** • LFTg = 1.2 • HFTg = 0.8 • **Percent of dental caries reduction in HFTg** = 33% **dmfs:** • LFTg = 2.9 • HFTg = 1.7 • **Percent of dental caries reduction in HFTg** = 39% The mean dmfs increment excluding occlusal surfaces was significantly lower in the toothpaste high-fluoride (1450 ppm) group compared to the low fluoride toothpaste (500 ppm) group. No significant differences in the mean dmft increment were determined	Moderate

ID NUMBER	AUTHOR, YEAR	COUNTRY	STUDY DESIGN	STUDY POPULATION, SETTING	SAMPLE SIZE	INTERVENTION	OUTCOME MEASURES	KEY FINDINGS & RESULTS	APPRAISAL
TOOTHBRUSHING WITH FLUORIDE TOOTHPASTE									
79	Anopa et al, 2015 (Anopa *et al.*, 2015)	Scotland - UK	Economic Study	5 years old children in nurseries	62,419 anonymised child dental records	The nursery toothbrushing programme	**Primary outcome:** Comparing the cost of providing the Scotland-wide nursery toothbrushing programme with associated National Health Service (NHS) cost savings from improvements in the dental health of five-year-old children: through avoided dental extractions, fillings and potential treatments for decay	**Primary outcome:** Unit costs of a filled, extracted and decayed primary tooth were calculated using verifiable sources of information. Total costs associated with dental treatments were estimated for the period from 1999/2000 to 2009/2010. Expected cost savings were calculated for each of the subsequent years in comparison with the 2001/2002 dental treatment costs. The estimated cost of the nursery toothbrushing programme in Scotland was £1,762,621 per year. **The estimated cost of dental treatments in the baseline year 2001/02** = £8,766,297, **In 2002/03 the costs of dental treatments increased by** £213,380 (2.4%). **In the following years the costs decreased dramatically with the estimated annual savings ranging from** £1,217,255 in 2003/04 (13.9% of costs in 2001/02) to £4,731,097 in 2009/10 (54.0%). **The estimated cost of dental treatments in 2009/2010** = £4,035,200. The largest decrease in modelled costs was for the most deprived cohort of children The NHS costs associated with dental treatments for five-year-old children decreased over time. In the eighth year of the toothbrushing programme, the	High

								expected savings (£4,731,097) were more than two and a half times the costs of the programme (£1,762,621 per year) implementation	
1057	Macpherson et al, 2013 (Macpherson *et al.*, 2013)	Scotland - UK	Observational – Cohort Study	5 years-old children in nurseries participating in the national nursery toothbrushing program	n = 99,071	**Intervention:** National supervised toothbrushing in nurseries and distribution of fluoride toothpaste and toothbrushes for home use **Follow up:** 5 years	**Primary outcome:** Uptake in toothbrushing: percentage of nurseries participating in each health service administrative board area. Caries status: $d_3$mft	**Primary outcome:** The uptake of toothbrushing correlated with the decline in $d_3$mft (correlation = -0.64; -0.86, -0.16; p = 0.011). The mean $d_3$mft: • **Years -2 to 0 (relative to that in start-up Year 0)** = 3.06 • **Years 10 to 12** = 2.07 • **Difference** = -0.99 (95% CI -1.08, -0.90; p < 0.001). **The slope of the uptake in toothbrushing was correlated with the slope in the reduction of $d_3$mft.** An improvement in the dental health of five-year-olds was associated with the uptake of nursery toothbrushing.	High
1946	Natapov et al, 2021 (Natapov *et al.*, 2021)	Israel	Observational	5 years old Children in kindergartens from Jewish and Bedouin (Arab) local authorities	n = 283 n = 145 (Tg) n = 138 (Cg)	**Test group (Tg):** Received a supervised tooth brushing program in kindergartens. Children brushed once daily at kindergartens, with fluoridated toothpaste **Control group (Cg):** No intervention **Follow up:** 2 years	**Primary outcome:** The fractions of treated (f/dmf) out of affected teeth The fractions of untreated teeth (d/dmf) out of affected teeth	**Primary outcome:** **The fraction of untreated decayed teeth (d/dmf):** **Among Jewish:** • Tg = 61% • Cg = 65% **Among Bedouin:** • Tg = 69% • Cg = 90% **The fraction of treated decayed teeth (f/dmf):** **Among Jewish:** • Tg = 37% • Cg = 29% **Among Bedouin:** • Tg = 23% • Cg = 8% Dental health of children participating in 2 years supervised toothbrushing programme was better than the control group. This program can be applied to low Socio-economic status communities nationwide.	Moderate
1944	Melo et al, 2018 (Melo *et al.*, 2018)		Observational – longitudinal study	2–12 years old received BDN programme in multiple countries in schools and homes	5,148 children	**Test group (Tg):** Two '21-day Brush Day and Night (BDN) programme' interventions at the beginning and 6–12 months afterward. It included an educational approach for children and school staff, together with the consistent practice of toothbrushing at school for3 calendar weeks, This study included four data collection time-points: • T0: baseline/first intervention • T0D21: 21 days after first intervention • T1: second intervention • T1D21: 21 days after second intervention	**Primary outcome:** Improvement in knowledge and oral hygiene behaviour in schoolchildren involved in BDN Sustainability of improvement after 6–12 months, Age group that more receptive to improvement than others.	**Primary outcome:** Improvement in knowledge and oral hygiene behaviour in schoolchildren involved in BDN after the first intervention = 25% The increased brushing-frequency in children at the first intervention, was sustained after 6–12 months. The BDN programme illustrated a sustainable approach to improve children's oral health knowledge and behaviour. The BDN programme was more effective among the 7–9 years age group.	Moderate
1943	Leal et al, 2002 (Leal *et al.*, 2002)	Brazil	Observational	Children a private nursery of Brasília, DF, Brazil	n = 40 **Divided into 2 age groups:** 3-4 years old n = 20 (G1) 5-6 years old n = 20 (G2)	**Test group (Tg):** The following methods of instruction and reinforcement were applied: I - audio-visual; II - child as a model; III - individual instruction. Professional prophylaxis was then performed, and the children remained 48 hours	**Primary outcome:** Change in Plaque index Ability of preschool children in performing toothbrushing.	**Primary outcome:** The total plaque index decreased in both groups after the application of the three methods of instruction and reinforcement. However, G2 had greater plaque reduction than G1 for all methods ($p<0.05$) Children older than 5 years of age were able to learn and	Moderate

						without any kind of oral hygiene. Plaque disclosing and plaque index were carried out and recorded. The children subsequently brushed their teeth according to each method of instruction and a new plaque index was recorded.		accomplish toothbrushing better than younger children. The individual instruction method for teaching toothbrushing at nurseries showed the greatest reduction in plaque index, followed by the audio-visual and the child as a model	

ID NUMBER	AUTHOR, YEAR	COUNTRY	STUDY DESIGN	STUDY POPULATION, SETTING	SAMPLE SIZE	INTERVENTION	OUTCOME MEASURES	KEY FINDINGS & RESULTS	APPRAISAL
TOOTHBRUSHING WITH FLUORIDE TOOTHPASTE									
1300	Pakhomov et al, 1997 (Pakhomov *et al.*, 1997)	Bulgaria	Observational	**3-** *12 years old attending kindergartens or schools in* area of Pazardjik	n = 1479 (Tg) n = 299 (Cg)	**<u>Test group (Tg):</u>** Provided with an amine fluoride toothpaste (four tubes or 360 grams annually) to be used daily once in kindergartens or schools under teachers' supervision and once a day at home **<u>Control group (Cg):</u>** No intervention **<u>Follow up:</u>** 3 years	**<u>Primary outcome:</u>** Dental caries experience (dmft and DMFT)	**<u>Primary outcome:</u>** **At baseline:** **dmft:** • **Tg** = 1.8 (3y), 4.6 (6y) and 3.9 (9y) • **Cg** = 1.7 (3y), 5.6 (6y) and 4.2 (9y) **DMFT:** • **Tg** = 0.7 (3y), 1.8 (6y) and 3.2 (9y) • **Cg** = 0.6 (3y), 1.4 (6y) and 3.5 (9y) **Post intervention:** **dmft:** • **Tg** = 1.4 (6y), 2.9 (9y) and 2.7 (12y) ($p < 0.001$ compared to baseline dmft for 6y and 9y Tg) • **Cg** = - , 5.2 (9y) and 3.6 (12y) • **Caries reduction within Tg** = 37% (6y) and 31% (9y) ($p < 0.001$) • **Caries reduction between Tg and Cg** = 99% (6y) and 23% (9y) ($p < 0.001$) **DMFT:** • Tg = 0.1 (6y), 1.7 (9y) and 2.4 (12y) ($p < 0.001$ compared to baseline dmft for 3y and 12y Tg) • Cg = 0.7 (6y), 2.0 (9y) and 3.2 (12y) • **Caries reduction within Tg** = 86% (6y) and 25% (12y) ($p < 0.001$) • **Caries reduction between Tg and Cg** = 86% (6y), 15% (9y) and 25% (12y) ($p < 0.001$) Fluoride toothbrushing community-based program was effective in reducing dental caries and it is a feasible and practical method of improving the oral health status of children	Moderate
596	Gasoyan et al, 2019 (Gasoyan *et al.*, 2019)	Armenia	Observational - A repeated cross-sectional study design	6–7 and 10–11-year-old schoolchildren in 2013 and 2017 in Karakert and Lernagog villages in Armenia. Low SES	**In 2013: n = 166** **In 2017: n = 148**	A school-based preventive dental program implemented. The intervention included school-based supervised toothbrushing with fluoride toothpaste and oral hygiene education. **<u>A pre-intervention group:</u>** 6–7 and 10–11-year-old schoolchildren in 2013, before the implementation of prevention programme **<u>An intervention group:</u>** 6–7 and 10–11-year-old schoolchildren in 2017, after the receiving the prevention programme **<u>Follow up:</u>** 4 years	**<u>Primary outcome:</u>** The prevalence of caries and the number of decayed, missing, and filled teeth in permanent dentition (DMFT) and primary dentition (dmft) at two time-points: in 2013 (a pre-intervention group) and in 2017 (an intervention group).	**<u>Primary outcome:</u>** **dmft among 6-7 y:** • **Pre-intervention group (2013) =** 8.24 • **Intervention group (2017) =** 7.29 • **Caries prevalence (2013) =** 98.75% • **Caries prevalence (2017) =** 91.27% • **DMFT among 10-11 y (*p < 0.005)*:** • **Pre-intervention group (2013) =** 2.50 • **Intervention group (2017) =** 1.76 • **Caries prevalence (2013) =** 82.56% • **Caries prevalence (2017) =** 73.33% The study indicates significant lower level of caries among schoolchildren in the studied two villages where the intervention was implemented.	Moderate

475	Duijster et al, 2017 (Duijster *et al.*, 2017)	Lao	Observational a non-randomized clustered controlled trial with a follow-up period of two years	6-7 years old (grade 1) children attending schools implementing the programme in Cambodia, Indonesia and Lao PDR	n = 149 Colombia n = 478 Indosia n = 486 Lao PDR n = 535 Pooled regional sample: n = 768 (Tg) n = 731 (Cg)	**<u>The intervention:</u>** The Fit for School (FIT) programme integrates school health and Water, Sanitation and Hygiene interventions, which are implemented by the Ministries of Education in four Southeast Asian countries. **<u>Intervention group (Tg):</u>** Children attending public elementary schools implementing the FIT programme, including daily group handwashing with soap and toothbrushing with fluoride toothpaste, biannual school-based deworming; as well as construction of group handwashing facilities. **<u>Control group (Cg):</u>** Children attending schools implemented the regular government health education curriculum and biannual deworming **<u>Follow up:</u>** 2 years	**<u>Primary outcome:</u>** Dental caries prevalence and DMFT	**<u>Primary outcome:</u>** **At baseline:** **Dental caries prevalence:** • Tg = 13.1% • Cg = 15.4% **DMFT:** • Tg = 0.20 • Cg = 0.26 **Post intervention:** **Dental caries prevalence:** • Tg = 37.7% • Cg = 44% **DMFT:** • Tg = 0.48 • Cg = 0.63 • Preventive fraction (DMFT) = 23.9% Daily School TB reduced DMFT by 23.9% (preventive fraction for DMFT: 18.3%, 22.4%, 38.0% in Cambodia, Indonesia and Lao PDR, respectively) The FIT programme significantly contributed to the prevention of dental caries in children.	Moderate
241	Cakar et al, 2018 (Cakar *et al.*, 2018)	Australia	Observational	5-12 years old children in a primary school in Queensland, Australia Low SES & Fluoridated area	n = 1742 n = 1191 (Tg) n = 553 (Cg)	**<u>The intervention:</u>** A primary school-based tooth brushing (TB) program conducted in a low socio-economic area of Queensland, Australia **<u>Test group (Tg):</u>** Children in schools received long-term Toothbrushing programs **<u>Control group (Cg):</u>** Children in Non-Toothbrushing schools **<u>Follow up:</u>** 5-9 years	**<u>Primary outcome:</u>** Caries experience (decayed, missing, filled teeth dmft/DMFT]) and caries prevalence in children	**<u>Primary outcome:</u>** <u>Dental status:</u> **At baseline:** dmft/DMFT: • Tg = 2.23/0.74 • Cg = 2.14/0.81 **Post intervention:** **dmfs (*p* < 001):** dmft/DMFT: • Tg = 2.53/0.47 • Cg = 3.06/1.15 • Tg overall caries prevalence = 68% • Cg Caries prevalence = 78% • Overall, the mean annual DMFT increments of Tg children were less compared with Cg children (*P*<.001). A long-term primary school TB program significantly reduced caries experience and caries prevalence in an optimally fluoridated (1-ppm), very low socio-economic district.	Moderate
1941	Al-Jundi et al, 2006 (Al-Jundi *et al.*, 2006)	Jordan	Observational - longitudinal study	Initially 6 and 11 years age two age groups children in schools in Irbid City in Jordan	n = 856 n = 436 (Tg) n = 420 (Cg)	**<u>The Intervention:</u>** A school-based caries preventive program consisted of intensive oral hygiene instructions sessions, and supervised daily tooth brushing using fluoridated toothpaste in schools. **<u>Test group (Tg):</u>** Received caries prevention programme: intensive oral hygiene instructions sessions, and supervised daily tooth brushing using fluoridated toothpaste in schools. **<u>Control group (Cg):</u>** Received only oral hygiene instructions sessions **<u>Follow up:</u>** 4 years	**<u>Primary outcome:</u>** Dental caries status (DMFT and dmft)	**<u>Primary outcome:</u>** <u>Dental status:</u> **At baseline:** **Overall DMFT/dmft(6.3 y, Group 1):** • **Tg** = 4.58 • **Cg** = 4.99 **Caries Free prevalence (6.3 y, Group 1):** • **Tg** = 14.7% • **Cg** = 12.7% **Overall DMFT/dmft (11.7 y, Group 2):** • **Tg** = 1.69 • **Cg** = 1.70 **Caries Free prevalence (11.7 y, Group 2):** • **Tg** = 43.6% • **Cg** = 42.8% **Post intervention:** **Overall DMFT/dmft(Group 1) (p < 0.001):** • **Tg** = 4.6 • **Cg** = 5.25 **Caries Free prevalence (Group 1) (p < 0.001):** • **Tg** = 14.0% • **Cg** = 9.4% **Overall DMFT/dmft (Group 2) (p < 0.001):** • **Tg** = 1.7 • **Cg** = 2.0 **Caries Free prevalence (Group 2) (p < 0.001):** • **Tg** = 43.6% • **Cg** = 33.0%	Low

								The estimates of relative risk values showed that children in the control group are 3.1 and 6.4 times at higher risk of having dental caries than those in the study group for age group 12 and 6 respectively. The supervised daily toothbrushing using fluoridated toothpaste is successful in controlling dental caries in children.	
1183	Monse et al, 2013 (Monse *et al.*, 2013)	Philippines	Observational	First-grade students (6–7 years old) of public elementary schools on the island province of Camiguin, Philippines	N= 412 baseline and 341 follow up	**Intervention group** Daily supervised handwashing; daily supervised brushing with a fluoride toothpaste (0.3 ml; 1,450 ppm; annual deworming with a single dose of albendazole (400 mg) **Control** Biannual deworming carried out by school nurses; distribution of a single (10-ml) commercial toothpaste sachet, a toothbrush; oral health message at the beginning of the school year, and health education **Follow up** 12 months	**Primary outcome:** DMFS	**DMFS** **Baseline** Experimental .82 (.12) Control 1.12 (.16) **Follow up** Experimental 1.54 (.17) Control 1.99 (.24) The increases in caries was reduced but not statistically significant.	Low

ID NUMBER	AUTHOR, YEAR	COUNTRY	STUDY DESIGN	STUDY POPULATION, SETTING	SAMPLE SIZE	INTERVENTION	OUTCOME MEASURES	KEY FINDINGS & RESULTS	APPRAISAL
FLUORIDE SUPPLEMENTS									
1157	Meyer-Lueckel et al, 2010 (Meyer-Lueckel *et al.*, 2010)	Germany	Observational - retrospective cohort study	6–9 years school children using fluoridated salt from four basic schools in the district Steglitz-Zehlendorf in Berlin, Germany	n = 583	**The intervention:** Provision of fluoride tablets among users of fluoridated salt **Follow up:** ≥ 5 years	**Primary outcome:** Dental caries (defs) and fluorosis status.	**Primary outcome:** Dental status: **At baseline:** • **defs** = 3.2 • **Free caries prevalence** = 58% • **Dental fluorosis prevalence** = 12% **Post intervention:** **At baseline:** • **defs** = 4.5 • **Dental fluorosis prevalence** = 35% Fluoride tablets effectively reduced the occurrence of caries in German children (2–4 years: RR = 0.8, 95%CI: 0.7–1.0, ǂ5 years: RR = 0.5, 95%CI 0.3–0.7, reference: 0–1 year use) with low caries levels particular among those using fluoridated salt. However, fluoride tablets increase the occurrence of mild fluorosis in permanent incisors (RR=1.8 (95%CI: 1.1–2.9) and 2.7 (95%CI: 1.6–4.5) for fluoride tablet use of 2–4 years and ǂ5 years, respectively) compared with 0–1 year use.	Low

ID NUMBER	AUTHOR, YEAR	COUNTRY	STUDY DESIGN	STUDY POPULATION, SETTING	SAMPLE SIZE	INTERVENTION	OUTCOME MEASURES	KEY FINDINGS & RESULTS	APPRAISAL
FLUORIDE GEL AND FOAM									
1638	Stokes et al, 2011 (Stokes *et al.*, 2011)	England - UK	RCT - single-centre, single-blind, randomised, parallel-groups trial comprising two test groups and one untreated control group	12–13 years old children at high caries risk (with prior caries experience on first permanent molars).	n = 1,075 n = 106 (Tg) n = 139 (Tg2) n = 228 (Cg)	**Test group 1 (Tg1):** Apply twice weekly supervised brushing with a self-applied gel containing 12,500 ppm fluoride on schooldays **Test group 2 (Tg2):** Apply once weekly supervised brushing with a self-applied gel containing 12,500 ppm fluoride on schooldays **Control group (Cg):** Children who continued with their usual oral hygiene care	**Primary outcome:** Caries status (D_1FS caries increment), **Secondary outcome:** Caries status (D_3FT caries increment), D 1 (all caries lesions, including those confined to enamel, and those into dentine). D 3 (only caries lesions into dentine)	**Primary outcome:** **At baseline:** **D_1MFS (Surface increment):** • **Tg1** = 11.84 • **Tg2** = 11.50 • **Cg** = 11.93 **D_3MFT (Tooth Increment):** • **Tg1** = 2.91 • **Tg2** = 2.86 • **Cg** = 2.98 **Oral clearance (Mean plaque score):** • **Tg1** = 0.26 • **Tg2** = 0.25 • **Cg** = 0.25 **Post intervention:** **D_1FS:**	High

						Follow up: 2 years		• **Tg1** = 10.29 • **Tg2** = 11.03 • **Cg** = 10.50 **D_3FT (**$p < 0.05$**):** • **Tg1** = 1.35 • **Tg2** = 1.57 • **Cg** = 1.82 **Oral clearance (Mean plaque score):** • **Tg1** = 2.51 • **Tg2** = 2.51 • **Cg** = 2.58 Significant differences were found between the three groups overall in the secondary outcome, D 3 FT caries increment. In UK, the study revealed 29% ($p = 0.024$) reduction in dental caries for those with at least 60 times brushes with high-fluoride gel over 2 years compared with the untreated control group who followed their usual oral hygiene routine. Children who brushed with the gel at least 60 times over a 2-year period developed significantly fewer carious lesions into dentine than children who followed their usual oral hygiene routine.	
822	Jiang et al, 2005 (Jiang *et al.*, 2005)	China	RCT - double-blind, cluster-randomized, placebo controlled trial	3-4 years old children from schools in the People's Republic of China	n = 318 n = 167 (Tg) n = 151 (Cg)	**Test group (Tg):** Received a bi-annual professional application of acidulated phosphate fluoride (APF) foam **Control group (Cg):** Received a placebo **Follow up:** 2 years	**Primary outcome:** caries increment in the primary dentition (dmfs)	**Primary outcome:** **At baseline:** **dmfs:** • Tg = 2.4 • Cg = 2.8 **Post intervention:** **dmfs (*p* < 0.05):** • Tg = 3.8 • Cg = 5.0 • Mean Difference between Groups (95% CI) = -1.2 (-2.3, -0.2) The mean increment of dmfs in the experimental group was 24.2% lower than that in the control group ($p < 0.05$). A bi-annual professional application of APF foam was effective in reducing the increment of dental caries in the primary teeth.	High
1608	Splieth, et al, 2011 (Splieth *et al.*, 2011)	Germany	RCT	6 to 8 years old children in first and second grade in schools in Greifswald in Germany,	n = 579 n = 230 (Tg) n = 349 (Cg)	**Test group (Tg):** Received a semi-annual application of elmex fluid **Control group (Cg):** No intervention **Follow up:** 4 years	**Primary outcome:** Caries status (DMFS in first primary molar)	**Primary outcome:** Dental status: **At baseline:** **DMFS:** • Tg = 0.32 • Cg = 0.36 **Post intervention:** **DMFS (*p* < 0.05):** • Tg = 0.81 • Cg = 0.78 The caries increment was almost identical in the intervention and control groups (0.81 ± 1.74 and 0.78 ± 1.81 DMFS) with 72% and 69% of the children, respectively, showing no caries increment. An inclusion of topical fluoride (elmex fluid contains 10,000 ppm amine fluoride) use during the study did not change the outcome Further studies should examine the effect of semi-annual topical fluoride applications after caries decline	Low
1020	Lincir and Rosin-Grget, 1993 (Linčir, 1993)	Croatia	RCT - a double blind clinical trial	3-4 years old kindergarten children in Dubrava, a suburb of Zagreb, Croatia	n = 199 **1stg** n = 55 **2ndg** n = 53 **3rdg** n = 61 **Cg** n = 30	**First group (1st g):** Received topical applications of conventional amine fluoride solution with 10.000 ppmF(l% F. Aminfluorid®. Belupo) every 2 months (5 times a schoolyear) **Second group (2nd g):** Received applications of half-strength topical	**Primary outcome:** Caries status dmfs and dmft	**Primary outcome:** **At baseline:** **dmfs:** • **1stg** = 2.6 • **2ndg** = 3.4 • **3rdg** = 3.4 • **Cg** = 3.0 **dmft:** • **1stg** = 2.1 • **2ndg** = 2.1 • **3rdg** = 2.4 • **Cg** = 2.1	Low

						amine fluoride solution with 5,000 ppm F (0.5% F) in two different frequencies B every 2 months (5 times a schoolyear) **<u>Third group (3rd g):</u>** Received applications of half-strength topical amine fluoride solution with 5,000 ppm F (0.5% F) in two different frequencies once a month (10 times a schoolyear) **<u>Control group (Cg):</u>** Received placeb **<u>Follow up:</u>** 2 years		**Post intervention:** **Differences in mean increments for dmfs:** • **Cg-1st g** = 4.1 ($p < 0.05$) • **Cg-2nd g** = 3.3 • **Cg-3rd g** = 4.5 ($p < 0.05$) • **2nd g-1st g** = 0.8 • **2nd g-3rd g** = 1.2 • **1st g-3rd g** = 0.4 **Differences in mean increments for dmft:** • **Cg-1st g** = 1.2 • **Cg-2nd g** = 0.4 • **Cg-3rd g** = 1.6 ($p < 0.05$) • **2nd g-1st g** = 0.8 • **2nd g-3rd g** = 1.2 • **1st g-3rd g** = 0.4 Increased frequency of application of a low fluoride topical solution (having 0.5% F 10 times a year over 2 years) produced 30.8% reduction ($p<0.05$) in new decay among preschool children with relatively high caries activity	
1860	Winter et al, 2018 (Winter *et al.*, 2018)	Germany	Observational	2-5 years old children in the districts Marburg-Biedenkopf and Waldeck-Frankenberg	n = 805 G1&2 n = 111 G3&4 n = 230 G5&6 n = 464	**<u>Group 1 and 2 (G 1&2):</u>** Received intensive prevention in kindergarten with and without fluoride gel at school **<u>Group 3 and 4 (G 3&4):</u>** Received basic prevention in kindergarten with and without fluoride gel at school **<u>Group 5 and 6 (G 5&6):</u>** Received no organized prevention in kindergarten with and without fluoride gel at school Two dental examinations were performed for assessing caries experience and calculating caries increment from second grade (7-year-olds) to fourth grade (9-year-olds)	**<u>Primary outcome:</u>** caries scores and preventive measures of various subgroups	**<u>Primary outcome:</u>** A significant difference was found in the mean decayed, missing, and filled tooth/teeth (DMFT) depending on socioeconomic status. Children of group 5 who did not participate in a kindergarten program, but were given fluoride gel in school, those with a low SES exhibited a significantly higher caries experience (mean DMFT = 0.47) in permanent teeth than children with a high SES (mean DMFT = 0.18). Class-specific differences were no longer visible among children who had taken part in a basic preventive program. Early toothbrushing and first molar FS are the most important factors for oral health. Low SES increases dental caries risk at the primary teeth. Early prevention, focusing on professionally supported training of toothbrushing in kindergarten and at school, has a positive effect on dental health and can reduce class-specific differences in caries distribution.	Moderate
1859	Winter et al, 2017 (Winter *et al.*, 2017)	Germany	Observational	2-5 years old children in the districts Waldeck-Frankenberg	n = 1079 n = 508 (Tg) n = 571 (Cg)	**<u>Group 1, 2 and 3 Test group (Tg):</u>** Received basic prevention in the participating primary schools: The primary school students received instructions on toothbrushing three to four times a year from specially trained dental assistants and were given free toothpaste to use at home (fluoride content 1400 ppm; elmex® Juniorzahnpasta, elmex research/Colgate-Palmolive Europe sàrl, Therwil, Switzerland) **<u>Group 4, 5 and 6 Control group (Cg):</u>** Received intensive prevention in the participating primary schools: The students receiving intensive prevention (see Table 1, groups 4, 5, and 6) were in addition offered topical fluoride application by the public health service. During the school term, these groups brushed their teeth with fluoride gel (fluoride content 12,500 ppm) under the supervision of the TBFs	**<u>Primary outcome:</u>** caries experience and caries increment	**<u>Primary outcome:</u>** By examining caries experience of second grade it found that the caries experience 19% lower among children who received intensive dental prevention (professionally supported daily toothbrushing) in kindergarten (d3-6mft = 1.74) compared to those who not received that in kindergarten (d3-6mft of 2.17) The caries increment was significantly lower mainly among children who had received the maximum of group prevention (intensive prevention in kindergarten and gel program at school). Intensified preventive programs in kindergartens and schools, based mainly on supervised toothbrushing, have a positive effect on the dental health of primary school children	Moderate

						at intervals of 3 weeks on average. Dental examinations was performed for assessing caries experience and calculating caries increment in second grade (7-year-olds)			
358	Cui, et al, 2020 (Cui *et al.*, 2020)	China	RCT	6 kindergartens in Qingdao	n = 398 n = 187(Tg) n = 211 (Cg)	**<u>The intervention:</u>** Education plus APF Foam 1.23% **<u>Test group (Tg):</u>** Education plus APF Foam 1.23% **<u>Control group (Cg):</u>** Examinations only **<u>Follow up:</u>** 1 year	**<u>Primary outcome:</u>** dmft Dmfs	**<u>Primary outcome:</u>** **<u>Baseline</u>** **Intervention group** Dmft 2.59 (SD 3.27) Dmfs 3.59 (SD 5.59) **Control** Dmft 2.48 (SD 3.33) Dmfs 3.14 (SD 4.66) **<u>Follow up</u>** **Intervention** Dmft 2.94 (SD 3.37) Dmfs 3.94 (SD 5.39) **Control** Dmft 3.81 (SD3.89) Dmfs 5.81 (SD 7.24) Dmft ($p<.05$) and dmfs ($P<.001$) significantly lower in intervention group	Moderate

ID NUMBER	AUTHOR, YEAR	COUNTRY	STUDY DESIGN	STUDY POPULATION, SETTING	SAMPLE SIZE	INTERVENTION	OUTCOME MEASURES	KEY FINDINGS & RESULTS	APPRAISAL
FLUORIDE MOUTHRINSE									
1214	Murthy and Fareed, 2020 (Murthy and FAREED, 2020b)	India	observational Study	6-7 years old children with high caries risk as assessed by the American Academy of Paediatric Dentistry guideline and attending three government primary schools low socio-economic status	n = 110	**<u>The intervention:</u>** The schoolteachers were trained to carry out the Fluoride Mouth Rinse programme by the investigator. In the three years, 58 sessions of mouth rinsing were conducted with dentist being the provider for the first three sessions and the rest were provided by the teachers. **<u>Follow up:</u>** 3 years	**<u>Primary outcome:</u>** Economic cost of utilising teachers for fluoride mouth rinsing in schools **<u>Definitions</u>** **Capital costs** were those that lasted longer than a year (e.g., equipment, instruments, etc.,) and **Recurrent costs** were those that were used 24 up in the course of a year and were usually purchased regularly e.g., personnel, supplies, etc.	**<u>Primary outcome:</u>** The total economic costs of all inputs which amounted to Rs. 2,00,592.1 (US $ 3,283.0). capital costs contributed to only 4.6% Recurrent costs contributed to 95.4% of all costs The capital costs with teachers as program providers were higher than that with the dentist as program provider whereas the recurrent costs with teachers was lower than the dentist as a program provider. Since the recurrent costs that make up 95% of the total costs was lower with teachers as providers than dentists, school-based Fluoride Mouth Rinse program using teachers can be used to provide dental services for underserved children with unmet preventive care needs.	High
1116	Matsuyama et al, 2016 (Matsuyama *et al.*, 2016)	Japan	Observational - An Ecological Study	12-year-olds Japanese children born between 1994 and 2000 in all 47 Japanese prefectures		**<u>The intervention</u>** School-based fluoride mouth-rinse (S-FMR) programs	**<u>Primary outcome:</u>** Caries status: decayed, missing, or filled permanent teeth (DMFT)	**<u>Primary outcome:</u>** An increase of 1% in S-FMR utilization was significantly associated with 0.011 lower DMFT in 12-year-olds, even after considering other variables (average consumption of fluoride toothpaste per capita in each prefecture, dentist density, average sugar consumption per capita in each prefecture38; and mean annual income of each prefecture. High S-FMR utilization was significantly associated with low DMFT at age 12 (coefficient −0.011; 95% confidence interval, −0.018 to −0.005). Higher utilization of fluoride toothpaste, higher income, and higher dentist density were significantly associated with lower DMFT Interaction between S-FMR and dental caries experience at age 3 years showed that S-FMR was significantly more effective in prefectures where the 3-year-olds had high levels of dental caries experience. School-Based Fluoride Mouth Rinse explained 25.2% of the DMFT reduction and decreased	Moderate

								caries-related inequalities between prefectures in Japan Utilization of S-FMR reduced dental caries inequalities via proportionate universalism.	
918	Komiyama et al, 2012 (Komiyama *et al.*, 2012)	Japan	Observational	12 years old school children	n = 881 n = 599 (Tg) n = 282 (Cg)	**<u>The intervention:</u>** School-based fluoride mouth rinsing (S-FMR: weekly using 0.2% NaF solution) in two groups of school children with different periods of exposure to S-FMR in elementary school. **<u>Test group (Tg):</u>** The children participated in S-FMR for six years **<u>Control group (Cg):</u>** The children participated in S-FMR for less than one year in the sixth year of elementary school **<u>Follow up:</u>** six years.	**<u>Primary outcome:</u>** DMFS, DMFT and Caries reduction rate	**<u>Primary outcome:</u>** **Post intervention:** **DMFS:** • Tg = 2.05 • Cg = 3.69 **DMFT:** • Tg = 1.28 • Cg = 2.02 The person rate with DMF was 46.1% in the Tg was significantly lower ($P < 0.05$) from person rate (64.9%) in the Cg. From the results of the present survey, the caries reduction rate of S-FMR in the permanent teeth was 36.6% for DMFT and 42.8% for DMFS No gender differences were observed in the SFMR group. As caries prevalence in the first molars accounted for about 85% regardless of participation to S-FMR, and first molar caries were more common in the mandible than in the maxilla, consideration should be given to preventive measures against pit-and-fissure-caries in addition to S-FMR.	Moderate
429	Divaris et al, 2012 (Divaris *et al.*, 2012)	US	Observational - used clinical and parental-reported data for children in grades 1 through 5 who were examined during the 2003-04 NC Oral Health Survey (OHS)	6-11 years old children in grades 1 through 5 from a probability sample of North Carolina (NC) schoolchildren.	n = 1,363	**<u>The Intervention:</u>** A school-based weekly fluoride mouth rinse (FMR) program To estimate caries risk at program entry, children were matched with NC kindergarten-surveillance data representing school-level mean untreated decay (low-risk school: < 1 and high-risk school: ≥ 1 untreated carious teeth).	**<u>Primary outcome:</u>** caries experience: • decayed and filled primary (d2,3fs) • total (d2,3fs+D2,3MFS) tooth surfaces. To estimate caries risk at program entry, children were matched with NC kindergarten-surveillance data representing school-level mean untreated decay (low-risk school: < 1 and high-risk school: ≥ 1 untreated carious teeth).	**<u>Primary outcome:</u>** **Post intervention:** • **d2,3fs** = 4.1 (95% CL = 3.7, 4.5), and • **D2,3MFS** = 0.7 (95% CL = 0.5, 0.9). FMR was associated with minor reductions in caries prevalence for primary tooth surfaces [PR = 0.98 (95% CL = 0.90, 1.06] or total caries experience [PR = 0.98 (95% CL = 0.91, 1.05]. Caries preventive benefit was larger among children in high-risk schools compared with those in low-risk schools (*i.e.*, 55% *vs*. 10% caries reduction for 5 to 6 yrs. of FMR participation compared to none) The effectiveness of weekly administration of Fluoride Mouth Rinse (FMR) was found week and not significant. Nonetheless, long term application of FMR may provide substantial caries prevention benefits to US children in high-caries risk schools	Moderate
13	Aasenden et al, 1972 (Aasenden *et al.*, 1972)	US	Observational	8-11 years old children from two grammar schools in a middle-class suburban community in Massachusetts. Areas with non-fluoridated water (0.1 ppm)	n= 545 n = 109 (Tg1) n = 114 (Tg2) n = 139 (Cg)	**<u>Test group 1 (Tg1):</u>** Rinsed daily in school with 5 ml of acidulated phosphate fluoride (APF, 0.02 per cent F, 0.1 M phosphate, pH 4.0) **<u>Test group 2 (Tg2):</u>** Rinsed daily in school with neutral NaF (0.02 per cent F) **<u>Control group (Cg):</u>** Rinsed daily in school with neutral placebo **<u>Follow up:</u>** 3 years	**<u>Primary outcome:</u>** Caries increment	**<u>Primary outcome:</u>** **Post intervention:** **Caries increment scores:** • Tg1 = **0.11** • Tg2 = 0.16 • Cg = 0.13 The mean percentage reductions in DFS were 30 and 27 in Tg1 and Tg2, respectively The caries reduction in the teeth initially erupted was 25% in both groups. The mean caries reductions were 40% with using APF mouth rinse and 30% with neutral NaF one, but the result is not significant	Moderate
1451	Ripa and Leske,, 1980 (Ripa and Leske, 1980)	US	Observational	Children in the first through fourth grades in elementary schools housing	n = 125	**<u>The intervention:</u>** A school-based fluoride mouth rinsing programme sing a 0.2 percent neutral sodium fluoride solution, provided weekly rinsing (109 rinses) for children in grades one through four.	**<u>Primary outcome:</u>** Caries scores which	**<u>Primary outcome:</u>** **Post intervention:** *Compared to baseline caries scores of children in the same schools who were examined before the rinsing programme started:* There was a reduction in caries prevalence of 25.5% in primary	Low

						Follow up: 4 years		teeth and 46% in permanent teeth among school children using fluoridated mouth rinse (0.2 percent neutral NaF solution, rinse once a week under supervision of homeroom teachers) for 4 years *The greatest reduction after four years, 28.6% was found for proximal surfaces.* A greater reduction is observed for both teeth and surfaces of the permanent dentition compared to the primary.	

ID NUMBER	AUTHOR, YEAR	COUNTRY	STUDY DESIGN	STUDY POPULATION, SETTING	SAMPLE SIZE	INTERVENTION	OUTCOME MEASURES	KEY FINDINGS & RESULTS	APPRAISAL
FLUORIDATED MILK									
1339	Petersen et al, 2015 (Petersen *et al.*, 2015b)	Bulgaria	Observational - Parallel arm cohort study	3-year-olds in 8 Bulgarian cities/towns	n = 276 n = 180 (Tg) n = 96 (Cg)	**The intervention:** A community milk fluoridation programme **Test group (Tg):** Received 0.5mg F in 100 or 200ml school milk or yogurt provided each school day **Control group (Cg):** Received non-fluoridated milk **Follow up:** 5 years	**Primary outcome:** Dental caries experience of primary, and permanent teeth	**Primary outcome:** **Post intervention:** **Reduction in caries (dmfs) increment:** • Tg = 46% (p<0.001) • Cg = 30% (p<0.01) **Reduction in caries (DMFT) increment:** • Tg = 61% (p<0.001) • Cg = 53% (p<0.001) The nation-wide experiences from milk fluoridation indicate that such a public health scheme can be effective to the global fight against dental caries of children.	Moderate

ID NUMBER	AUTHOR, YEAR	COUNTRY	STUDY DESIGN	STUDY POPULATION, SETTING	SAMPLE SIZE	INTERVENTION	OUTCOME MEASURES	KEY FINDINGS & RESULTS	APPRAISAL
FLUORIDATED SALT									
839	Jordan et al, 2017 (Jordan *et al.*, 2017)	Gambia	Observational	3-5 years old children in two preschools in the Gambian city of Brikama Areas with drinking water had a low fluoride content (0.1 mg F – /L) Young children did not use toothpaste for oral hygiene	n = 441 n = 304 (Tg) n = 137 (Cg)	**The intervention:** Adding fluoridated salt in a communal feeding program for preschool children. **Test group (Tg):** Received meals were prepared with fluoridated salt (250 mg F – /kg salt) **Control group (Cg):** No intervention **Follow up:** 12 months	**Primary outcome:** The difference in the incidence of caries cavities (d3/4mft)	**Primary outcome:** **At baseline:** d3/4mft**:** • Tg = 3.35 • Cg = 2.74 **Post intervention:** d3/4mft**:** • Tg = 4.63 • Cg = 6.57 The difference in the mean caries incidence per person (d3/4mft): • Tg = 1.29 (95% CI: 0.96; 1.62) • Cg = 3.83 (95% CI: 2.94; 4.72) The caries-prevented fraction was 66.3%. No signs of harm due to the intervention were observed. Adding fluoridated salt to a communal feeding programme provided a considerable caries preventive effect in areas of low fluoride in drinking water.	Moderate

ID NUMBER	AUTHOR, YEAR	COUNTRY	STUDY DESIGN	STUDY POPULATION, SETTING	SAMPLE SIZE	INTERVENTION	OUTCOME MEASURES	KEY FINDINGS & RESULTS	APPRAISAL
MULTIPLE FLUORIDE APPLICATIONS									
3002	Kerebel et al, 1985 (Kerebel *et al.*, 1985)	France	RCT	Four Nantes schools No water fluoride 7-8 year old at baseline	n = 198 n = 98 (Tg) n = 100 (Cg)	**The intervention:** Combined prevention programme **Test group (Tg):** Daily supervised toothbrushing at school with 180 mg of fluoridated toothpaste; Professional prophylaxis every 2 months with topical application of fluoride gel; Reinforced motivation **Control group (Cg):** No intervention **Follow up:** 36 months	**Primary outcome:** Plaque index Caries increment Caries attack rate	**Primary outcome:** Primary tooth **CI: caries increment** Controls 4.13 Tests 2.33 **CAR: caries attack rate** Controls 7.38% Tests 3.83% Secondary tooth **CI: caries increment** Controls 4.30 Tests 1.72 **CAR: caries attack rate** Controls 9.77% Tests 3.71%	Moderate

								52% plaque reduction in the test group compared with the control group. Caries reduction was significant at the 0.01% level: 44% for primary teeth and 60% for permanent teeth	
1942	Babaei et al, 2020 (Babaei *et al.*, 2020)	Iran	RCT	19 districts in Tehran Stratified by SES 6 and 7 year old	n = 701 n = 339 (Tg) n = 362 (Cg)	**<u>The intervention:</u>** School brushing plus education plus home packs **<u>Test group (Tg):</u>** School brushing plus education plus home packs **<u>Control group (Cg):</u>** No intervention **<u>Follow up:</u>** 1 month	**<u>Primary outcome:</u>** Improved oral hygiene status OHI-S	**<u>Primary outcome:</u>** **<u>Baseline</u>** **Intervention group** 0.49±0.39 **Control** 0.48±0.37 **<u>Follow up</u>** **Intervention** -0.27±0.02 **Control** 0.02±0.02 Children showed improved oral hygiene status, as measured by the OHI-S, after the program consisting of supervised toothbrushing.	Moderate
454	Driscoll et al, 1992 (Driscoll *et al.*, 1992)	US	RCT	Kindergarten and first grade (P1) Springfield, Ohio, US Non- water fluoride	n = 640 Rinse 229 Tablet 199 Both 212	**<u>The intervention:</u>** Rinse and tablets individually or in combination **<u>Test group (Tg):</u>** Group a Rinsing weekly Group b Tablets Group c Both **<u>Control group (Cg):</u>** No control **<u>Follow up:</u>** 1 year	**<u>Primary outcome:</u>** dmfs	**<u>Primary outcome:</u>** **<u>Baseline</u>** Fluoride rinse 229 dmfs (SD) 0.25 (.77) Fluoride tablet 199 0.21 (.71) Combination 212 0.22 (.72) **<u>Follow up</u>** Fluoride rinse 229 dmfs (SD) 3.57 (4.03) Fluoride tablet 199 2.83 (3.63) Combination 212 2.40 (3.28) Combined rinse and tablet significant for dmfs over rinse alone (not over tablet alone)	Low
1246	Niessen and Douglass, 1984 (Niessen and Douglass, 1984)	US	Economic Study						High

ID NUMBER	AUTHOR, YEAR	COUNTRY	STUDY DESIGN	STUDY POPULATION, SETTING	SAMPLE SIZE	INTERVENTION	OUTCOME MEASURES	KEY FINDINGS & RESULTS	APPRAISAL
MULTIPLE FLUORIDE APPLICATIONS									
412	de Sousa et al, 2002 (da de Sousa *et al.*, 2002)	Brazil	Observational	Optimally fluoridated water in the area (.7ppm) Toothbrushing exposure for 2 years 8 year old children	n = 660 Control 220 Group 1 220 Group 2 220	**<u>The intervention:</u>** Mouth rinse or mouth rinse plus gel over t/b and water F **<u>Test groups (Tg):</u>** 1; Water F and tooth brushing plus mouth rinse 2; Water F and tooth brushing plus mouth rinse and gel **<u>Control group (Cg):</u>** Water F and tooth brushing **<u>Follow up:</u>** 2 years	**<u>Primary outcome:</u>** Caries	**<u>Primary outcome:</u>** **<u>% of caries free children</u>** **Control 55%** **Group 1** mouth rinse 65% **Group 2** mouth rinse plus APF 1.23% gel 65.5% Differences between Programme 1 and 2 in relation to the Control Group were statistically significant (P<0.05). There was no difference between Programme 1 and 2 (P=O.92).	High
1945	Wolff et al, 2016 (Wolff *et al.*, 2016)	Grenada	Observational	'Smile Granada' 6-8 year olds [Also older group 14-15 year olds]	N = 1092 baseline N = 2301 post	**<u>The intervention:</u>** Tooth brushing plus packs Fluoride varnish Also sealants and education **<u>Test groups (Tg):</u>** Tooth brushing plus packs Fluoride varnish Also sealants and education **<u>Control group (Cg):</u>** No control- before and after **<u>Follow up:</u>** 3 years	**<u>Primary outcome:</u>** Decayed and demineralized surfaces	**<u>Decayed</u>** **Baseline** 0.93 ±1.75 **Follow up** 0.23±0.83 **<u>Demineralized</u>** **Baseline** 2.11±2.74 **Follow up** 0.50±0.97	Moderate
896	Kidd et al, 2020 (Kidd *et al.*, 2020)	Scotland - UK	Observational	Local authority school children in Scotland, mean age 5.5	N= 50,379	**<u>The intervention:</u>** Cohort study examining effect of nursery FV and toothbrushing	**<u>Primary outcome:</u>** Caries experience	**FVA** Children targeted for nursery FVAs, in comparison to	Moderate

						Exposure to FVA and supervised nursery tooth brushing No control		children receiving zero applications, had no reduction in the odds of caries experience regardless of the number applied (five applications, aOR=0.97; 95%CI 0.89 to 1.06). **Tooth brushing** Reduction in the odds of caries experience as the number of years of participation in supervised tooth brushing - '>3 years' relative to 'not consented' for brushing having substantial reduced odds of caries experience (aOR=0.60; 95%CI 0.55 to 0.66).	
169	Blair et al, 2004 (Blair *et al.*, 2004)	Scotland - UK	Observational	Socio-economically deprived communities Nursery children from 3- 5	N= 244	**<u>The intervention:</u>** Tooth brushing in nursery and home; various promotion activities **No control –** comparator area **<u>Follow up:</u>** 48 months	**<u>Primary outcome:</u>** dmft	**<u>Primary outcome:</u>** 46% reduction in mean dmft for 36-47 months old Baseline 3.9 (2.8-5.1) Follow up 2.1 (1.6-2.6) 37% reduction in mean dmft for 48-59 months old Baseline 5.9 (5.1-6.8) Follow up 3. (3.1-4.3) Increases in comparator non-intervention area	Moderate
165	Birkeland et al, 2000 (Birkeland *et al.*, 2000)	Norway	Observational	8- to 11- and the 17-year-olds		Use of fluorides and other preventive efforts aimed at pre-school children	**<u>Primary outcome:</u>** Caries and number of fillings in permanent teeth decline between 1966 and 1983.	**<u>Primary outcome:</u>** Fluorides in school-based programmes, lozenges, toothpaste, education and sale of antibiotics were significantly ($p<0.01$) related to the caries decline.	Moderate

ID NUMBER	AUTHOR, YEAR	COUNTRY	STUDY DESIGN	STUDY POPULATION, SETTING	SAMPLE SIZE	INTERVENTION	OUTCOME MEASURES	KEY FINDINGS & RESULTS	APPRAISAL
MULTIPLE FLUORIDE APPLICATIONS									
1163	Milgrom and Tut, 2009 (Milgrom and Tut, 2009)	Marshall Islands	Observational	Majuro atoll in the Republic of the Marshall Islands (RMI) Mean age 64 months (SD 6)	N= 473 360 in group 1 113 in goups 2 and 3.	Pacific Islands Early Childhood Caries Prevention Project. **<u>Three group intervention</u>** **Group 1** Three-times-per school-year topical fluoride varnish; toothbrushes and fluoridated toothpaste sent home once every 3 months **Group 2** Varnish plus twice-per-day supervised toothbrushing with fluoridated toothpaste at school **Group 3** 2 plus three-times-per-day consumption of xylitol containing gummy bear snacks at school and home visits to encourage parental involvement **<u>Follow up</u>** 12 months	**<u>Primary outcome:</u>** The primary clinical evaluation outcomes of the study are the number of decayed, extracted, or filled primary teeth (deft) and the number of decayed first permanent molars (D) defined as a cavitated tooth.	**<u>Baseline</u>** Group 1 8.3 (SD = 4.3) Groups 2 and 3 7.9 (SD = 4.4) **<u>Baseline</u>** Group 1 10.3 (SD = 4.3) Groups 2 and 3 8.2 (SD = 4) A total of 24 percent of the children in group 1 had cavitated lesions in any permanent molar compared with 12.8 percent of the children in groups 2 and 3 combined	Low
500	Escobar-Rojas et al, 2020 (Escobar-Rojas *et al.*, 2020)	Colombia	Observational	Child residents of El Cedro (Colombia) Age at entry (years)a 6.3 (4.3, 8.4) Age at exit (years)a 10.5 (8.5, 12.6)	N = 426	Community-based oral health preventive program. **<u>Intervention</u>** Health promotion; mouthwash (0.2% neutral sodium fluoride); twice daily supervised brushing (1450 ppm F-); dental visits **<u>Follow up</u>** 3.6 years (1.6, 5,7)	**<u>Primary outcome:</u>** The primary outcome variable was primary caries-free survival	**<u>First year of programme (2009)</u>** Average age of presentation of primary dental caries was estimated at 8.3 years (95% CI: 7.6-9.0); Average age of presentation of secondary dental caries was estimated at 9.3 years (95% CI: 8.4-10.3). **<u>2015</u>**	Low

Average age of presentation of primary dental caries was estimated at 12.9 years (95% CI: 12.0-13.8)
Average age of presentation of secondary dental caries was estimated at 14.6 years (95% CI: 12.0-17.2)

Crude and adjusted hazard ratios 2015 (referent 2009)
Primary caries
Crude 0.04 (0.02, 0.10) <.001
Adjusted 0.05 (0.02, 0.11) <.001
Secondary caries
Crude 0.01 (0.00, 0.08) <.001
Adjusted 0.02 (0.00, 0.13) <.001

Average age for presenting a primary dental caries lesion was delayed approximately by 4.6 years and by 5.3 years for secondary caries.

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Table S3: Data extraction and quality appraisal for reviews (n= 13)

ID NUMBER	AUTHOR, YEAR	REVIEW TYPE	OTHER CHARACTERISTICS OF THE REVIEW	QUALITY CRITERIA	TYPES OF INTERVENTIONS	OUTCOMES	KEY FINDINGS & RESULTS	EDUCATIONAL SETTING FINDINGS	QUALITY APPRAISAL
FLUORIDE MILK									
#1902	Yeung 2015 (Yeung *et al.*, 2015)	Systematic review [Cochrane; update to 2005 review]	Number of studies • 1 Participants • All receiving intervention irrespective of age, gender or risk level for caries Duration of studies • Min 2 years/school years follow-up Setting: • Not specified / all settings Study designs included	GRADE the Cochrane Collaboration 'Risk of bias' assessment tool (Higgins 2011)	**Intervention groups** • F milk of any concertation/dosage **Control groups** • Non-F milk **Setting** • nursery schools (kindergartens)	**Primary outcomes** • changes in caries experience/increment in primary (dmft/dmfs) and/or permanent dentition (DMFT/DMFS) • adverse effects: dental fluorosis **Secondary outcomes** • dental pain due to caries • antibiotics due to dental infections • requirement for GA dues to dental procedures for caries	Only 1 study met the inclusion criteria (Maslak et al., 2004). The study was published as an abstract only, however unpublished data was provided by the authors.	Low-quality evidence indicating that F milk might be effective in preventing caries in primary teeth in schoolchildren, however more research is needed. **Caries** **Primary teeth** • a substantial reduction in dmft in F milk group was observed: MD= -1.14 (95%CI -1.86 to -0.42),	High

			• RCTs (including cluster RCTs)				equivalent to PF=31% **Permanent teeth** • after 3 years of intervention a reduction in DMFT in F milk group was noted: MD= -0.13 (95%CI -0.24 to -0.02) note, very low level of caries in the study **Adverse effects** • no adverse effects were reported **Secondary outcomes** • no information on secondary outcomes was reported		
#121	Bánóczy 2013 (Bánóczy *et al.*, 2013)	Historical overview?	Number of studies • 18 studies (22 references) Participants • Not specified Duration of studies • Not specified Setting: • Not specified Study designs included • Not specified		**Intervention groups** • F milk **Control groups** • Non-F milk	**Caries** • Caries in primary dentition • Caries in permanent dentition	Overall, the review concluded that F milk is effective in preventing caries in primary (9 studies) and permanent (12 studies) dentition. There was some indication of increased caries incidence after cessation of F milk programme (1 study). The review concluded that F milk interventions are feasible, safe and carry low cost. The authors highlight that concentration of F in milk is age dependant and such intervention should start in children aged 4 to reach best results. They also recommend that to implement F milk interventions in areas where water has low F levels, where a regular school milk system is in place and where children are able to consume F milk at least 200 days/year. However, this is a historical overview of various F milk programmes which did not explore studies quality or assessed risk of bias in a systematic way. Therefore the findings have to be considered very cautiously.	Some of the studies undertaken in educational settings with majority taking place in an unclear (community settings).	Low

ID NUMBER	AUTHOR, YEAR	REVIEW TYPE	OTHER CHARACTERISTICS OF THE REVIEW	QUALITY CRITERIA	TYPES OF INTERVENTIONS	OUTCOMES	KEY FINDINGS & RESULTS	EDUCATIONAL SETTING FINDINGS	QUALITY APPRAISAL
FLUORIDE SUPPLEMENTS (E.G., TABLETS, DIETARY SUPPLEMENTS)									
#1732	Tubert-Jeannin et al., 2011 (Tubert-Jeannin *et al.*, 2011)	systematic review; [Cochrane]	Number of studies • 11 studies • [7 studies in schools] Participants • All children and adolescents receiving the intervention less than 16 years of age at the start of the study Duration of studies • min 2 years follow-up Setting: • all settings (e.g. school, home) Study designs included • RCTs Quasi RCTs	GRADE	**Intervention groups** F supplements (tablets, drops, lozenges, chewing gum) • with or without use of vitamins • using any F concentration, any F agent, and F amount, any application technique • with or without the use of topical F (e.g. FV, F toothpaste) or non-F preventive measure (e.g. sealants, xylitol, CHLX, OH intervention) • no other systemic source of F such as F water, F milk, was allowed **Control groups**	**Primary outcomes** • changes in caries increment in permanent (DMFS/DMFT) and primary (dmfs/dmft) dentition **Secondary outcomes** • differences in final caries experience in the intervention and control groups (if the groups were comparable at baseline) by the final DMFS/DMFT and dmfs/dmft • any other caries measures (e.g., proportion of children developing new caries) • caries assessed clinically at dentine level (clinically or	Summary of main findings: **Permanent teeth** 3 studies: use of F supplements was linked to a 24% (95%CI 16-33%) reduction in D(M)FS compared to no F supplements **Primary teeth** Unclear effect (1 study: no caries-inhibiting effect vs. 1 study: reduction in caries increment) **Adverse effects** Limited evidence **F supplements vs no F supplements** **D(M)FS PF** • for a follow-up of 24 to 36 months	Participants were recruited from school settings in 7 studies. **supplements vs no F supplements** **D(M)FS PF** • for a follow-up of 24 to 36 months for 3 studies conducted in schools in children aged 6 to 11 years at baseline: no difference between the control and the intervention group which received NaF or APF tablets (1mg F) 1-2x/day (diluted or chewed) • for a longer follow up (1 study, school-	High

No F supplements
- no treatment
- placebo (with or without use of vitamins)
- topical F (e.g. FV, F toothpaste)
- other preventive measures (e.g. sealants, xylitol, CHLX, OH intervention)

clinically and radiographically)

Adverse effects
- any adverse effects, e.g., dental fluorosis

- pooled D(M)FS PF=0.24 (95%CI 0.16 to 0.33) favouring F supplement groups, no heterogeneity
- for 3 studies conducted in schools in children aged 6 to 11 years at baseline: no difference between the control and the intervention group which received NaF or APF tablets (1mg F) 1-2x/day (diluted or chewed)

- for a longer follow up (1 study)
  - school-based study, children aged 6 years at baseline, APF tablets (1mg F) administered 1-2x/day : pooled DMFS PF=0.25 (95%CI 0.12 to 0.35) after 55 months follow-up, and 0.28 (95%CI 0.16 to 0.41) after 72 months of follow-up; both favouring F supplement groups

D(M)FT PF
- for a follow-up of 24 to 36 months
  - 3 school-based studies: pooled D(M)FT PF=0.29 (95%CI 0.19 to 0.39) favouring F supplement groups, no heterogeneity (children aged 5 to 11, APF and NaF tablets with 1mg F administered 1x/day diluted or not compeered with placebo tablets or no treatment)

d(m)fs PF and d(m)fs PF
- for a follow-up of 24 to 36 months
  - pooled dmft PF=0.13 (95%CI -0.09 to 0.35) indicated no difference between groups (1 study, based in school, children aged 5 years at the start of the study, 1mg F tablets vs no intervention)

based) children aged 6 years at baseline, APF tablets (1mg F) administered 1-2x/day : pooled DMFS PF=0.25 (95%CI 0.12 to 0.35) after 55 months follow-up, and 0.28 (95%CI 0.16 to 0.41) after 72 months of follow-up; both favouring F supplement groups

D(M)FT PF
- for a follow-up of 24 to 36 months: 3 school-based studies: pooled D(M)FT PF=0.29 (95%CI 0.19 to 0.39) favouring F supplement groups, no heterogeneity (children aged 5 to 11, APF and NaF tablets with 1mg F administered 1x/day diluted or not compeered with placebo tablets or no treatment)

d(m)fs PF and d(m)fs PF
- for a follow-up of 24 to 36 months pooled dmft PF=0.13 (95%CI -0.09 to 0.35) indicated no difference between groups (1 study, based in school, children aged 5 years at the start of the study, 1mg F tablets vs no intervention)

F supplements vs topical F (rinse, varnish, toothpaste)

D(M)FS PF
- for a follow-up of 24 to 36 months (4 trials, including 3 in schools)
  - pooled D(M)FS PF= -0.10 (95%CI -0.25 to 0.05) suggesting no difference between groups, no heterogeneity
- for a longer follow up (2 studies, including 1 in school setting)
  - no difference between groups were noted after of 48, 60 months follow-ups (considerable heterogeneity at 60 months)
  - school-based study observed a beneficial effect of F supplements at 96 months of follow-up with DMFS PF=0.21 (95%CI 0.04 to 0.38), note: over 60% of drop outs at this point

D(M)FT PF
- for a follow-up of 24 to 36 months
  - 3 school-based studies: pooled D(M)FT PF=0.29 (95%CI 0.19 to 0.39) favouring F supplement groups, no heterogeneity

- a strong beneficial effect of F supplements (tablets and drops, 0.5mg F vs no intervention) in children aged 22 to26 months with cleft lip and/or palate: pooled dmft PF=0.65 (96%CI 0.47 to 0.84), pooled dmfs PF=0.73 (95%CI 0.46 to 0.99)

F supplements vs topical F (rinse, varnish, toothpaste)
D(M)FS PF

- for a follow-up of 24 to 36 months (4 trials, including 3 in schools)
  - pooled D(M)FS PF= -0.10 (95%CI -0.25 to 0.05) suggesting no difference between groups, no heterogeneity
- for a longer follow up (2 studies, including 1 in school setting)
  - no difference between groups were noted after of 48, 60 months follow-ups (considerable heterogeneity at 60 months)
  - school-based study observed a beneficial effect of F supplements at 96 months of follow-up with DMFS PF=0.21 (95%CI 0.04 to 0.38), note: over 60% of drop outs at this point

D(M)FT PF

- for a follow-up of 24 to 36 months
  - 3 school-based studies: pooled D(M)FT PF=0.29 (95%CI 0.19 to 0.39) favouring F supplement groups, no heterogeneity (children aged 5 to 11, APF and NaF tablets with 1mg F administered 1x/day diluted or not compeered with placebo tablets or no treatment)

d(m)fs PF

- for a follow-up of 24 to 36 months (2 studies, including 1 in school setting)
  - pooled dmfs PF=0.13 (95%CI 0.07 to 0.33) indicated no difference between groups

F supplements effect on other outcomes
Caries increment per type of surface

- 2 studies (1 in school setting) found no difference
- 1 study (school setting) indicated that F supplements compared to F rinse were more beneficial on occlusal surfaces

Plaque and gingivitis

- 1 study (school setting) indicated no difference between F supplements and F rinse groups after 2 years

Costs (2 studies)

- 1 study (school setting) 19% reduction in the cost of treatments for permanent and primary dentition was noted for F supplement group; there was a lower number of children undergoing dental treatment under GA in F supplement group

Caries increments pre- and post-eruptive (2 studies, 1 in school setting)

- Children aged 6 to 11 years at baseline followed up for 2 to 6 years, The PF values appeared to be higher for teeth erupting later than for teeth already erupted at the beginning of the study:
  - for teeth erupted at start: PF varied from -0.06 (95%CI -0.16 to 0.28) to 0.27 (95%CI 0.13 to 0.41);
  - for teeth erupting later over the study period: the PF varied from of 0.27 (95%CI 0.13 to 0.41) to 0.50 (95% CI 0.22 to 0.78)

Fluorosis (1 study in school setting)

- fluorosis was recorded on teeth that erupted late during the study period and was present in 18.9% of participants across

d(m)fs PF

- for a follow-up of 24 to 36 months (2 studies, including 1 in school setting)
  - pooled dmfs PF=0.13 (95%CI 0.07 to 0.33) indicated no difference between groups

all study groups (questionable to severe fluorosis), placebo group: 15%
1 APF tablet a day: 20%
2 APF tablets a day: 22%

F supplements vs other preventive measures
D(M)FS PF

- for a follow-up of 24 to 36 months (1 study)
  - no difference between groups was noted with DMFS PF=0.00 (95%CI -0.59 to 0.59) when comparing F lozenges with xylitol vs xylitol only in children aged 10 to 12 years at the start of the study

F supplements effect on other outcomes
Caries increment per type of surface

- 2 studies (1 in school setting) found no difference
- 1 study (school setting) indicated that F supplements compared to F rinse were more beneficial on occlusal surfaces

Plaque and gingivitis

- 1 study (school setting) indicated no difference between F supplements and F rinse groups after 2 years

Costs (2 studies)

- 1 study did not conduct cost-effectiveness analysis (F supplements vs toothbrushing information) because there was no significant effect between groups
- 1 study (school setting) 19% reduction in the cost of treatments for permanent and primary dentition was noted for F supplement group; there was a lower number of children undergoing dental treatment under GA in F supplement group

Caries increments pre- and post-eruptive (2 studies, 1 in school setting)

- Children aged 6 to 11 years at baseline followed up for 2 to 6 years,

The PF values appeared to be higher for teeth erupting later than for teeth already erupted at the beginning of the study:
- for teeth erupted at start: PF varied from -0.06 (95%CI -0.16 to 0.28) to 0.27 (95%CI 0.13 to 0.41);
- for teeth erupting later over the study period: the PF varied from of 0.27 (95%CI 0.13 to 0.41) to 0.50 (95% CI 0.22 to 0.78)

Fluorosis (1 study in school setting)
- fluorosis was recorded on teeth that erupted late during the study period and was present in 18.9% of participants across all study groups (questionable to severe fluorosis), placebo group: 15%
1 APF tablet a day: 20%
2 APF tablets a day: 22%

alt

ID NUMBER	AUTHOR, YEAR	REVIEW TYPE	OTHER CHARACTERISTICS OF THE REVIEW	QUALITY CRITERIA	TYPES OF INTERVENTIONS	OUTCOMES	KEY FINDINGS & RESULTS	EDUCATIONAL SETTING FINDINGS	QUALITY APPRAISAL
OTHER F-BASED INTERVENTIONS									
#1082	Marinho et al., 2016 (Marinho *et al.*, 2016)	Systematic review [Cochrane] FMR	Number of studies • 37 studies (62 reports) • 35 trials (60 reports) for quantitative synthesis/meta-analysis Participants • Children and adolescents aged 16 and under at the time of the start of the study irrespective of initial caries levels, background F exposure, dental treatment level, nationality Duration of studies • Min 1 year/school year Setting: • All settings • Included studies: All studies – school setting with 2 studies also including home use of the FMR Study designs included • RCTs • Quasi RCTs	GRADE the Cochrane Collaboration 'Risk of bias' assessment tool (Higgins 2011)	**Intervention groups** • Topical F in the form of mouth rinse (FMR) ○ Swished and expectorated, not swallowed ○ Any formulations and F concentrations (ppm F) ○ Any volume, duration and frequency of application ○ Any application technique • Characteristics of the studies included: ○ All trials were set in schools with 2 studies also including use in home ○ Almost all trials included NaF mouth rinse, mostly on a weekly (230 ppm F) or biweekly basis (900 ppm F), **Control groups** • no intervention • placebo	**Primary outcomes** • Caries increment in permanent dentition: D(M)FS/D(M)FT • Caries increment in primary dentition: d(e/m)fs/d(e/m)ft **Secondary outcomes** • Proportion of children developing new caries • Proportion of children not remaining caries-free • Tooth staining (proportion) • Sings of acute toxicity during application e.g., nausea, gagging, vomiting • Mucosal irritation or oral soft tissue allergic reactions • Overall dropouts or withdrawals during the trial (indirect measure of treatment acceptability)		Regular supervised use of FMR was found to be associated with a large reduction in caries increment in permanent dentition in children and adolescents (moderate certainty of the size of the effect). The authors suggest that although the majority of the evidence originated from studies carried out in school settings, the findings might be applicable to children in other settings with supervised or unsupervised FMR. However, the size of the preventive effect of such interventions is uncertain **D(M)FS PF** (35 trials) • Pooled estimate PF=0.27 (95%CI 0.23 to 0.30) indicating a large preventive benefit of FMR, note: some heterogeneity was observed • There was no association between estimates and the prespecified trial characteristics or the type of control group **D(M)FT PF** (13 trials) • Pooled estimate D(M)FT PF=0.23 (95%CI 0.18to	High

								0.29) indicating moderate to large preventive effect FMR, note: some heterogeneity was found **d(e/m)fs/t PF** • No data available **Secondary outcomes** • New caries development (2 trials) Pooled RR=0.77 (95%CI 0.46 to 1.29), note: substantial heterogeneity • Not remaining caries-free – no data available • Tooth staining ○ 1 study: amine fluoride FMR resulted in significantly more staining compared to control, no significant staining in comparison to control group was noted for NaF FMR ○ 2 studies: incomplete reporting with 1 study indicating that children with poor oral hygiene presented with some yellow discolouration "somewhat more noticeable "in the test group • Signs of acute toxicity during application – no data available • Mucosal irritation/oral soft tissue allergic reaction (1 study) incomplete report, "no cases of mucosal hypersensitivity after periodical examinations of every subject" • Dropouts/exclusions (unacceptability of treatment; 4 studies) Pooled risk ratio of dropping out from the test group vs control group (no treatment) RR=1.33 (95%CI 0.62 to 2.83), note: high heterogeneity		
#1083	Marinho et al., 2015 (Marinho *et al.*, 2015)	Systematic review [Cochrane]	Number of studies • 28 studies (44 reports) • 27 studies (42 reports) for quantitative synthesis/meta-analysis Participants • Children and adolescents up to age 16 years, irrespective of initial caries levels, background F exposure, dental treatment level, nationality Duration of studies • Min 1 year/school year	GRADE the Cochrane Collaboration 'Risk of bias' assessment tool (Higgins 2011)	**Intervention groups** • Topical F only in the form of gel ○ Operator-applied or self-applied ○ Using any F agent ○ Any concentration of F (ppm F) ○ Any amount and duration of application ○ Any application technique ○ Applied min 1x/year	**Primary outcomes** • Caries increments in permanent dentition (DMFS/DMFT) • Caries increment in primary dentition (dmfs/dmft) **Secondary outcomes** • Proportion of children developing new caries • Proportion of children not remaining caries-free • Tooth staining (proportion) • Sings of acute toxicity during application of	Based on a moderate quality evidence, F gel showed a large caries-inhibiting effect in permanent dentition. Limited and low-quality evidence indicated that F gel has a large caries-preventive effect. Very limited evidence was found on adverse effects and acceptability of the treatment.	The included trials were predominantly undertaken in schools/educational settings **D(M)FS PF** (25 trials) • Pooled estimate PF=0.28 (95%CI 0.19 to 0.36) indicating a large preventive benefit of F gel, note: considerable heterogeneity • There was no association between estimates and the	High

Setting:

- Any setting
- Included studies:
  25 studies – school
  1 study – nursery
  1 study – paediatric clinics
  1 study – unclear setting

Study designs included

- RCTs
- Quasi RCTs

- No other caries preventive agents/approaches additional to F gel were allowed: F based or non-F based, e.g., GI, sealants, CHLX, xylitol)

<u>Control groups</u>

- no intervention (for tray or cotton-tips gel application, but not for brushing or flossing methods)
- placebo (for any method of gel application)

gel/treatment, e.g., nausea, gagging, vomiting
- Mucosal irritation or oral soft tissue allergic reactions
- Overall dropouts or withdrawals during the trial

prespecified trial characteristics
- The effect of F gel varied depending on the type of control group used:
  No treatment group (10 studies) D(M)FS PF=0.38 (95%CI 0.24 to 0.52)
  Placebo groups (15 studies) D(M)FS PF=0.21 (95%CI 0.15 to 0.28)

<u>D(M)FT PF</u> (10 trials)

- Pooled estimate D(M)FT PF=0.32 (95%CI 0.19 to 0.46), note: considerable heterogeneity
- The effect of F gel varied depending on the type of control group used:
  No treatment group (6 studies) D(M)FT PF=0.43 (95%CI 0.29 to 0.57)
  Placebo groups (4 studies) D(M)FT PF=0.18 (95%CI 0.09 to 0.27)

<u>d(e/m)fs PF</u> (3 studies)

- Pooled estimate d(e/m)fs PF=0.20 (95%CI 0.01 to 0.38), note: no heterogeneity but needs to be viewed with caution due to methodological limitations

<u>d(e/m)ft PF</u>

- No data available

<u>Secondary outcomes</u>

- New caries development (1 study, new DFS) RR=0.82 (95%CI 0.68 to 0.99)
- Not remaining caries-free (2 studies, risk ratio)
  - No difference between groups in permanent dentition: RR=0.72 (95%CI 0.46 to 1.14)
  - No difference between groups in primary dentition: RR=0.53 (95%CI 0.26 to 1.07)
- Tooth staining – no data available
- Signs of acute toxicity during application of gel (e.g., nausea, gagging, vomiting) caries-free (2 studies, risk difference)
  - 1 study had no events in either arm
  - Pooled estimate of the risk difference between the gel and placebo arms RD=0.01 (95%CI -0.01

						to 0.02) indicated no difference between groups (slightly favoured placebo/no treatment group), note: no heterogeneity ○ No difference between groups in primary dentition: RR=0.53 (95%CI 0.26 to 1.07) • Mucosal irritation/oral soft tissue allergic reaction – no data available • Dropouts/exclusions during the trial period (unacceptability of treatment; 19 trials, risk ratio) Pooled estimate of dropping out of the F gel arm bs the control group arm RR=1.03 (95%CI 0.89 to 1.19), note: substantial heterogeneity	
#689	Haugejorden et al., 1981 (Haugejorden and Helöe, 1981)	Number of studies • 5 studies on school water fluoridation • 11 studies on F tablets at school • 2 studies on salt F (unclear setting) • 1 study on milk/beverage F (unclear setting) • 10 studies on STB at school • 3 studies on supervised rinsing with F solution (unclear setting) • 6 studies on interventions using several F agents (unclear setting) Participants • Children receiving the intervention Duration of studies • Not specified Setting: • Schools • Other community setting Study designs included • Not specified	Not specified	**<u>Intervention groups</u>** • School water F • F tablets at school • Salt F (unclear setting) • Milk F or F in other drinks (e.g., juice) (unclear setting) • STB at school • Supervised rinsing with F solution (unclear setting) • Interventions combining multiple F based approaches (unclear setting) **<u>Control groups</u>** Not specified	Not specified Based on included studies: • Caries reduction ○ DMFS/DMFT • Cost-effectiveness analysis • Cost-benefit analysis	The review indicated that the following F-based interventions were effective in preventing caries **<u>Intervention groups</u>** • School water F Caries reduction between 33% in early erupting teeth to 57% in late erupting teeth. Overall reduction across studies between 22% and 40% in children aged 6-17 years after 8-12 years at school • F tablets at school Caries reduction varied across the studies from 16% to 84% (in permanent dentition in children aged 3 to 11 years at the start of the intervention, the interventions took between 2 and 8 years) • Salt F (unclear setting) Caries reduction across the studies ranged from 48% to 67% • Milk F or F in other drinks (e.g., juice) (unclear setting) Caries reduction varied considerably across studies, no conclusions were drawn due to limited data (based on studies exploring milk F at 1mg F/l and juice F at 10mg F/l over the period of 3-6 years) • STB at school Across studies using solutions/gels with 0.5-1.23% F for STB 4-5x/year for 2-3 years caries reduction ranged from 3% to 44%	Low

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FLUORIDE VARNISH (FV)									
#409	de Sousa et al., 2019 (de Sousa *et al.*, 2019a)	Systematic review	Number of studies • 19 trials • 17 trials included in at least one meta-analysis Participants • children up to age 71 months (5 years and 11 months: preschoolers).	the Cochrane risk of bias tool	**Intervention groups** • FV intervention alone or associated with an OH programme (e.g., STB and/or OH education and/or dietary counselling) • Characteristics of the studies included: • Supervised rinsing with F solution (unclear setting) Daily, weekly and fortnightly supervised rinsing showed about a 40% caries reduction in permanent dentition of 5- to 16-year-olds. Weekly rinsing with neutral 0.2% NaF for 2 years showed a 20% caries reduction in 7- to 9-year-olds • Interventions combining multiple F based approaches (unclear setting)] Additional reduction in caries levels was noted for interventions combining systemic and topical F application and interventions combining different topical F • Cessation of F based interventions Conclusions were not drawn due to limited longitudinal evidence of long-term impacts of cessation of community F programmes • Economic outcomes Community water F appears to be the most cost-effective preventive intervention. Other methods that appear to be cost-effective were: ○ Daily 1mg F tablets at school ○ Weekly STB at school ○ Fortnightly rinsing with F solution at school ○ School water F The authors indicated that a successful community or a school-based caries prevention interventions should: • require no effort or very little effort to participate • be acceptable to participants and those commissioning the interventions • cover large population groups • have high efficacy and effectiveness • be easy to implement, cheap and cost-effective under changing circumstance • have no adverse effects	**Outcome measures** Caries at dentine level in primary teeth • Caries index, e.g., dmfs, dmft • Measurement of disease occurrence, e.g., proportion of children who developed new caries (dentine level)	Overall, FV had modest and unclear effect in terms of caries prevention in preschoolers. The authors point to the need to review the cost-effectiveness of FV intervention to determine further inclusion/exclusion of	No focus on the setting, clinical or otherwise; not possible to determine where the studies took place without identifying full text of the studies included in the review.	Moderate

Duration of studies
- Min 1 year follow up

Setting:
- Not specified (see "educational setting findings" column)

Study designs included
- RCTs
- Quasi RCTs

- Age: 6 months to 5 years Setting

Control groups
- no intervention
- placebo
- usual care

- Hospitalisation due to caries

Other outcomes
- Short-term adverse effects (e.g., allergy, itch, discomfort)
- Long-term adverse effects (e.g., dental fluorosis)

FV from dental practice.

FV intervention
- Little evidence of protective effect of FV: pooled RR=0.88 (95%CI 0.81 to 0.95)
  - FV vs usual care RR=0.84 (95%CI 0.72 to 0.98)
  - FV vs no intervention RR=0.85 (95%CI 0.73 to 0.98)
  - FV vs placebo RR=0.86 (95%CI 0.72 to 1.03)
- Some evidence of protective effect of FV: dmft/dmfs preventive fractions (PF)
  - pooled dmfs PF=24.2% (95%CI 12.9% to 35.4%)
  - pooled dmft PF=31.1% (95%CI 21.1% to 41.2%)
- Some evidence of protective effect of FV: dmft/dmfs weighted mean difference (WMD)
  - dmfs WMD=-0.77 (95%CI -1.23 to -0.31)
  - dmft WMD=-0.30 (95%CI -0.69 to -0.09)
- limited evidence: 1 unit increase in mean baseline dmfs appeared to result in 1% increase in (95%CI 0.99 to 1.02)
- adjusted R^2 indicated that 25.9% between-study variance was explained by baseline caries levels

Hospitalisation due to caries
- No evidence (no study reported this outcome)

The number needed to treat (NNT) for an additional beneficial outcome
- NNT=17 (95%CI 11 to 40), in populations where 50% of children developed new dentine caries.

Adverse effects
- Limited evidence due to infrequent reporting across all the studies
- Some of the reported short-term effects: vomiting, unpleasant smell, burning sensation, dissatisfaction with tooth appearance after FV application

Long-term effects (dental fluorosis): no

								difference between groups (1 study only)	

#1084	Marinho et al., 2013 (Marinho *et al.*, 2013)	Systematic review [Cochrane]	Number of studies
			• 22 studies
			• 21 trials (36 references) for quantitative synthesis / / meta-analysis
			
			Participants
			• children or adolescents up to age 16 years at the start of the study irrespective of initial level of caries, background exposure to F, level of dental treatment and nationality
			
			Duration of studies
			• min 1 year
			
			Setting:
			• 11 trials were conducted in schools or nurseries,
			• 8 studies conducted in clinics
			• remaining 3 trials: unclear setting
			
			Study designs included
			• RCTs
			• Quasi RCTs
				GRADE
				
				the Cochrane Collaboration's tool for assessing risk of bias
					<u>Intervention groups</u>
					• Topical fluorides in the form of fluoride varnish (FV) only at any F concentration (ppm F), any amount and any duration of application, any technique of application, prior or post application.
					• No other preventive agents or procedures were allowed (e.g., other F based measures, CHLX, sealants, OH interventions, xylitol)
					• Characteristics of the studies included:
					  • Setting: schools or dental clinics
					  • Age: from 1 to 15 years at the start of the trial
					  • NaF-based varnish in all trials (7000ppm F – 56,300ppm F, majority of studies 22,600ppm F)
					  • Frequency: 2x/year (17 trials), 4x/year (3 trials)
					
					<u>Control groups</u>
					• no intervention
					• placebo
						<u>Outcome measures</u>
						Caries increment in permanent and primary teeth (caries at dentine or both dentine and enamel level)
						• D(M)FS
						• d(e/m)fs
						<u>Other outcomes</u>
						• Coronal caries and dental fillings in primary and permanent teeth
						• Tooth loss
						• Dental pain
						• Specific adverse effects, e.g., oral allergic reactions, mucosal irritation, adverse symptoms such as nausea, gagging, vomiting
						• Use of health service resources (e.g., visits to dental care units, length of dental treatment time
							Overall, the evidence was indicative of effectiveness of FV in caries prevention, however the evidence was judged to be of moderate quality with considerable heterogeneity across studies.
							
							<u>Permanent dentition D(M)FS prevented fraction (PF)</u>
							• Evidence of considerable benefit of using FV: pooled D(M)FS PF=0.43 (95%CI 0.30 to 0.57), note: substantial heterogeneity (13 trials)
							• There was no significant association between D(M)FS PF and
							  ○ the pre-specified factors (baseline caries severity, background exposure to F., prior prophylaxis, concentration of F, frequency of application)
							  ○ the post hoc factors: type of control group whether (placebo or no treatment), length of follow-up, type of randomisation (individual or cluster)
							
							<u>D(M)FT prevented fraction (PF)</u>
							• Evidence of considerable benefit of using FV: pooled D(M)FT PF=0.44 (95%CI 0.11 to 0.76), note: substantial heterogeneity (5 trials)
							
							<u>proportion of children developing new caries (whole tooth)</u>
							• No evidence of effectiveness of FV in permanent dentition: RR = 0.75 (95%CI 0.53 to 1.05), note: substantial heterogeneity (5 trials)
							
							<u>Primary dentition d(e/m)fs prevented fraction (PF)</u>
							• Evidence of considerable benefit of using FV: pooled d(e/m)fs PF=0.37 (95%CI 0.24 to 0.51), note: substantial heterogeneity (10 trials)
							• There was no significant association between d(e/m)fs PF and
							  ○ the pre-specified factors
								11 trials were conducted in schools or nurseries, 8 in clinics and the setting was unclear in the remaining 3 trials
								
								No occlusions regarding the setting were drawn.
								
								The authors recommended undertaking a FV effectiveness review with a focus on the setting delivery, e.g., schools.
									High

(baseline caries severity, background exposure to F, application features e.g., prior prophylaxis, concentration of F, frequency of application)
    - the post hoc factors: type of control group whether (placebo or no treatment), length of follow-up, type of randomisation (individual or cluster)

d(e/m)f prevented fraction (PF)

- Evidence of considerable benefit of using FV: pooled d(e/m)ft PF=0.65 (95%CI 0.48 to 0.82), note: no statistical evidence of heterogeneity (2 trials)

proportion of children developing new caries (whole tooth)

- No evidence of effectiveness of FV in primary dentition: RR = 0.81 (95%CI 0.62 to 1.06), note: substantial heterogeneity (5 trials)

Other outcomes

Very limited evidence (only few studies reported on any of the other relevant outcomes).

ID NUMBER	AUTHOR, YEAR	REVIEW TYPE	OTHER CHARACTERISTICS OF THE REVIEW	QUALITY CRITERIA	TYPES OF INTERVENTIONS	OUTCOMES	KEY FINDINGS & RESULTS	EDUCATIONAL SETTING FINDINGS	QUALITY APPRAISAL
SUPERVISED TOOTHBRUSHING (STB)									

#443	dos Santos et al., 2018 (dos Santos *et al.*, 2018)	Systematic review	**Supervised toothbrushing (STB)** in children and adolescents up to age 18 years
			
			Number of studies
			• 4 studies
			
			Participants
			• Children and adolescent up to age 18 years
			
			Duration of studies
			• Min 1 year follow-up
			• range of follow-up: 21 months – 4 years
			
			Setting:
			• not specified but all trials included in the review were undertaken in schools
			
			Study designs included
			• RCTs
			• Quasi RCTs
				the Cochrane Collaboration's tool for assessing risk of bias	**Intervention groups**
					• Supervised toothbrushing (STB)
					• Characteristics of the studies included:
					  • Setting: schools
					  • Participant age: 2-14 years
					  • Toothbrushing with no F toothpaste, 500ppm F toothpaste, and 1000ppm F toothpaste
					
					Control groups
					• no STB, however, the control group was exposed to F toothpaste with the same F concentration as the intervention group
					
					Characteristics of the studies included
					• Setting: schools
					• Participant age: 2-14 years
					• Toothbrushing with no F toothpaste, 500ppm F toothpaste, and 1000ppm F toothpaste
						Outcome measures
						• Incidence of caries at dentine level in primary or permanent dentition using any caries index (e.g., deft, DMFT)
							There is no conclusive evidence on the effectiveness of school STB on caries incidence.
							
							The studies included in the review presented with considerable variation in terms of children's age, F content of the toothpaste, baseline caries level and measurement of caries incidence.
							
							2 out of 4 studies included in the review indicated some beneficial effect of school-based STB (however there were methodological concerns e.g., insufficient information on magnitude and/or the precision of the effect estimate)
							
							The search undertaken in the course of the review returned several studies indicating effectiveness of STB, however these studies were excluded from the review because of not meeting inclusion criteria regarding
								All included studies took place in schools, however no specific conclusions were drawn based on the setting.
								
								2 out of 4 studies included in the review indicated some beneficial effect of school-based STB (however there were methodological concerns e.g., insufficient information on magnitude and/or the precision of the effect estimate)
									Moderate

								control group treatment (no intervention at all or brushing with toothpaste of a different F concentration than the intervention group).		
#441	dos Santos et al., 2013 (dos Santos *et al.*, 2013)	Systematic review	Number of studies • 8 studies Participants • Children in primary dentition phase at the beginning of the study who were not over the age of 7 years when the outcome was assessed Duration of studies • Min 1 year follow-up Setting: • Not specified Study designs included • RCTs (Individual or cluster randomised) • Quasi-RCTs (Individual or cluster randomised)	the Cochrane Collaboration's tool for assessing risk of bias	**<u>Intervention groups</u>** • F toothpaste (irrespective of F concertation, F agent, abrasive system, pH). • No other F product (e.g., FV, F gel, F mouth rinse) or other non-F product (CHLX, xylitol, sealants) were allowed • Interventions aimed at children in primary dentition phase at the beginning of the study • The intervention may have included an oral health education **<u>Control groups</u>** • no intervention • placebo	Caries • dmft/dmfs increment • proportion of children developing new caries in primary dentition	**<u>dmfs increment</u>** • 2 studies comparing low F toothpastes to no intervention: pooled dmfs PF=40% (95%ci 5%-75%) • 5 studies comparing standard F toothpastes (1450ppm) to placebo/no intervention: pooled dmfs PF=31% (95%CI 18%-43%) **<u>dmft increment</u>** • 2 studies comparing low F toothpastes to no intervention: pooled dmfs PF=24% (95%CI -17% to 66%). • 1 study comparing standard F toothpaste (1450ppm) to no intervention: pooled dmfs PF=16% (95%CI 8%-25%) **<u>proportion of children developing new caries</u>** • 2 studies comparing low F toothpastes to no intervention and 2 studies: pooled RR=0.87 (95%CI 0.65 to 1.17). • 2 studies comparing standard F toothpaste (1450ppm) to no intervention: dmfs RR=0.86 (95%CI 0.81-0.93) **<u>number needed to treat for an additional beneficial outcome (NNTB)</u>** • For scenario of high (70%) caries incidence NNTB==11 (95%CI 7-20) • For scenario of medium (50%) caries incidence NNTB=15 (95%CI 10-28) • For scenario of low (20%) caries incidence NNTB=37 (95%CI 26-59)	The setting was not the focus although the majority of included studies were carried out in schools. The authors indicated that school-based programmes improved OH short term however there was no clear evidence indicating positive impact on caries incidence.	Moderate

REVIEWS ON ECONOMIC OUTCOMES

ID NUMBER	AUTHOR, YEAR	REVIEW TYPE	OTHER CHARACTERISTICS OF THE REVIEW	QUALITY CRITERIA	TYPES OF INTERVENTIONS	OUTCOMES	KEY FINDINGS & RESULTS	EDUCATIONAL SETTING FINDINGS	QUALITY APPRAISAL
ECONOMIC OUTCOMES									
#57	Amilani et al., 2020 (Amilani *et al.*, 2020)	Scoping review	Number of studies • 15 studies Participants • Schoolchildren aged 5 to 18 years Duration of studies • Not specified • The time horizon presented in the supplementary materials (not able to access these) Setting: • schools Study designs included • RCTs • Interventional studies	The Consolidated Health Economic Evaluation Reporting Standards (CHEERS) checklist	**Intervention groups** • Any school-based intervention aiming to prevent dental caries • Intervention could be focused on primary or secondary prevention • Interventions could included clinical approaches or health education or promotional schemes • Interventions had to be carried out within school premises • Any community-based versions of water, milk of salt F were not allowed **Control groups** • Any allowed	Cost-effectiveness of the intervention in relation to the tooth-related outcomes or child's QoL outcomes Economic evaluations • Incremental cost-effectiveness ratio reported (ICER, 14 studies) • Average cost-effectiveness ratio reported (ACER, 1 study)		• Almost all interventions aimed at preventing caries were cost-saving and potentially cost-effective against usual care, although the outcomes reported across the studies differed. • The majority of the studies (80%) assessed the cost-effectiveness of school-based interventions which focused on topical F and fissure sealants • Majority of the evidence originated in HIC, more data from LMIC countries is needed • Fissure sealants o Cost-saving when targeted at those with higher caries risk: higher risk surfaces (1 study) or higher risk individuals (1 study) or children in lower SEP (1 study) o Most effective materials for sealants were high-viscosity glass-ionomer cement (HGVIC) and light-emitting diode (LED) thermo-cursed HVGIC and glass-carbomer • Combined STB and F mouth rinse (FMR): cost-saving in general cohort (1 study) • Combined fissure sealant and FMR (1 study): cost-saving in high-risk population • Milk F and FMR: Cost-saving (2 studies) • Interventions based on oral health promotion o Outreach school-based check-up programme was reported to be cost-saving when the outcome was quality-adjusted tooth years (QUATY) but less effective when the outcome was prevented DMFT o A comprehensive preventive programme in schools was more effective but costlier compared to standard care (1 study) • 1 study reported caries preventive programme was reported to be cost-effective in high-risk groups when adapting a lower threshold and cost-effective in all groups when adapting a higher threshold	Low
#1213	Murthy et al., 2020 (Murthy and Fareed, 2020a)	Systematic review	Number of studies • 32 studies Participants • School children aged 6 to 15 years Duration of studies • Not specified • Included studies: the time horizon ranged from 2 to 10 years, most frequently being 4 years Setting: • Schools • Some studies included in the review Study designs included • Not specified	The Consolidated Health Economic Evaluation Reporting Standards (CHEERS) checklist	**Intervention groups** • Any intervention aiming to prevent caries based in school • Following interventions were included: o Pit and fissure sealants (17 studies) o F mouth rinsing (FMR) (10 studies) o FV (6 studies) o F toothpaste (6 studies) o school water F (3 studies) o milk F (2 studies) o F gels (2 studies) o F tablets (2 studies) o OH education and dental check-up (2 studies)	Outcomes in studies included in the review • Caries increment, averted DMFS/DMFT, restorations prevented (CEA studies) • Disability-adjusted Life Years (DALY) and Quality-adjusted Life Years (QALY) lost due to caries (CUA studies) • Cost of dental care/restorations prevented (CBA studies) Economic evaluations • Cost-effectiveness analysis (CEA, 18 studies) • Cost analysis (8 studies)	.	**Main findings:** • Interventions found to be cost-effective were school-based interventions carried out under general supervision, longer in duration and targeting high caries risk groups • FMR was more cost effective compared to sealants or F gel (4 studies) • The use of sealants was shown to be more cost-effective than no sealants (2 studies) • When compared to single intervention or routine dental care, comprehensive programmes or combined interventions were shown to provide favourable incremental cost effectiveness rations (ICERs, 3 studies)	Moderate

				○ Routine dental care (1 study) ○ Screening and referral (1 study) ○ A comprehensive school health program (1 study) ○ Xylitol chewing gum (1 study) **Control groups** • Not specified	• Cost-benefit analysis (CBA, 5 studies) • Cost-utility analysis (CUA, 1 study)			
#954	Ladewig et al., 2018 (Ladewig *et al.*, 2018)	Expert review ??	Number of studies • 24 studies (prevention) • 3 (treatment) Participants • Duration of studies • Setting: • Study designs included • RCTs • Cohort • Observational • Retrospective • Cross-sectional • Simulation (Markov model)	**Intervention** • Any intervention aiming to prevent caries in children, in any setting **Control groups** • Not specified (expert opinion)	**Outcomes** •	• Water F and STB were the only well-established cost-effective preventive interventions identified in the review • The majority of available evidence focuses on the cost description rather than cost-effectiveness	• A Chilean cohort study by Mariño et al. (2012) evaluated 3 community programs (water-F, salt-F and sealants) and 4 school-based programs (milk F, F mouth rinses, topical F gel and STB with F toothpaste). The majority of the school-based programmes showed cost-effectiveness with salt-F being most cost--effective (USD 16.21 to prevent one carious tooth) and APF-F gel least cost-effective (USD 21.30 to prevent one carious tooth). Note: conservative models likely underestimate the benefit. • A Swedish RTC by Skold et al. (2008) indicated that 2x/year application of FV at school was cost-effective (ratio of benefits to cost 1.8:1) whilst F mouth rinsing was not (application on the first 3 and the last 3 days of the semester, ratio 0.9:1). • Klein et al. (1985) in their cohort study of school-based weekly F mouth rinsing, daily F tablets, 2x/year F paste prophylaxis and gel application, 2x/week brushing and flossing indicated that the reduction of DMFS increment	Low

STUDIES INCLUDED IN THE REVIEWS

REVIEW		INDIVIDUAL STUDIES		
ID NUMBER	AUTHOR, YEAR	ID NUMBER	AUTHOR, YEAR	NOTES
FLUORIDE SUPPLEMENTS (E.G., TABLETS, DIETARY SUPPLEMENTS)				
#1902	Yeung 2015	n/a	Maslak et al., 2004	
#121	Banoczy 2013	n/a	Imamura, 1959	
		n/a	Rusoff et al., 1962	
		n/a	Wirz, 1964	
		n/a	Ziegler, 1964	
		n/a	Lopes et al., 1984	
		n/a	Stephen et al, 1981	
		#1629	Stephen et al., 1984	
		n/a	Bánóczy et al., 1983	
		n/a	Bánóczy et al., 1985	
		n/a	Gyurkovics et al.,1992	
		n/a	Legett et al., 1987	
		n/a	Zahlaka et al., 1987	
		#1297	Pakhomov et al., 1995	
		n/a	Atanassov et al., 1999	
		n/a	Mariño et al., 2001	
		n/a	Pakhomov et al., 2005	
		n/a	Riley et al., 2005	
		#156	Bian et al., 2003	
		#888	Ketley et al., 2003	
		n/a	Maslak et al., 2004	
		n/a	Weitz and Villa, 2004	
		n/a	Steckén-Blicks et al., 2009	
		n/a	Petersson et al., 2011	
#1732	Tubert-Jeannin et al., 2011	n/a	Aasenden 1972	
		n/a	DePaola 1968	
		n/a	Driscoll 1974	
		n/a	Heifetz 1987	
		n/a	Holm 1975	
		n/a	O'Rourke 1988	
		n/a	Poulsen 1981	
TOOTHBRUSHING (TB)				
#443	dos Santos et al., 2018	n/a	Al-Jundi et al., 2006	
		#727	Hilgert et al., 2015	
		#1361	Pieper et al., 2016	
		n/a	Spears et al., 1978	
#441	dos Santos et al., 2013	#72	Andruškeviciene et al., 2008	
		#1841 excl.	Whittle et al., 2008	
		#389 excl.	Davies et al., 2002	
		#1534	Schwarz et al., 1998	
		#1906	You et al., 2002	
		#1476	Rong et al.,2003	
		#799	Jackson et al., 2005	
		#509 excl.	Fan et al., 2008	
FLUORIDE VARNISH (FV)				
#409	de Sousa et al., 2019	#23	Agouropoulos et al., 2014	
		#67 excl.	Anderson et al., 2016	
		#186	Borutta et al., 2006	
		#196 excl.	Braun et al., 2016	
		#320 excl.	Chu et al., 2002	
		#560 excl.	Frostell et al., 1991	
		n/a	Grodzka et al., 1982	
		#734 excl.	Holm et al., 1979	
		n/a	Jiang et al., 2014	
		#971 excl.	Lawrence et al., 2008	
		#1151 excl.	Memarpour et al., 2015	
		#1150 excl.	Memarpour et al., 2016	
		#1206	Muñoz-Millán et al., 2018	
		#1282 excl.	Oliveira et al. 2014	

		#1349 excl.	Petersson et al., 1998	
		#1580 excl.	Slade et al., 2011	
		#1699 excl.	Tickle et al., 2017	
		#1826 excl.	Weintraub et al., 2006	
		#1897	Yang et al., 2008	
#1084	Marinho et al., 2013	#93	Arruda et al., 2012	
		n/a	Borutta et al., 1991	
		#186	Borutta et al., 2006	Also referenced in de Sousa 2019
		#200	Bravo et al., 1997	
		#201 excl.	Bravo et al., 1997	
		#202 excl.	Bravo et al., 1996	
		#203 excl.	Bravo et al., 2005	
		#320 excl.	Chu et al., 2002	
		#1033 excl.	Lo et al., 2001	
		#1868 excl.	Wong et al., 2011	
		#1866 excl.	Wong et al., 2005	
		n/a	Clark et al., 1985	
		#560 excl.	Frostell et al., 1991	
		n/a	Gugwad et al., 2011	
		#674	Hardman et al., 2007	
		#734 excl.	Holm et al., 1979	
		#737 excl.	Holm et al., 1984	
		n/a	Koch et al., 1975	
		#971 excl.	Lawrence et al., 2008	
		#1023 excl.	Liu et al., 2012	
		#1169	Milsom et al., 2011	
		n/a	Modeer et al., 1984	
		n/a	Salazar et al., 2008	
		n/a	Sköld et al., 2005	
		#1659 excl.	Tagliaferro et al., 2011	
		n/a	Tewari et al., 1990	
		#1827 excl.	Weintraub et al., 2006	
		#1897	Yang et al., 2008	Also referenced in de Sousa 2019
OTHER FLUORIDE-BASED INTERVENTIONS				
#1082	Marinho et al., 2016	n/a	Ashley et al., 1977	
		n/a	Bastos et al., 1989	
		n/a	Blinkhorn et al., 1983	
		n/a	Brandt et al., 1972	
		n/a	Craig et al., 1981	
		#404 excl.	deLiefde et al., 1989	
		n/a	DePaola et al., 1977	
		#419 excl.	DePaola et al., 1980	
		n/a	Driscoll et al., 1982	
		n/a	Duany et al., 1981	
		n/a	Finn et al., 1975	
		n/a	Gallagher et al., 1974	
		#700	Heidmann et al., 1992	
		#701 excl.	Heidmann et al., 1993	
		n/a	Heifetz et al., 1973	
		n/a	Heifetz et al., 1982	
		#758	Horowitz et al., 1971	
		n/a	Koch et al., 1967	
		n/a	Koch et al., 1967 a	
		n/a	Koch et al., 1967 b	
		n/a	Laswell et al., 1975	
		n/a	McConchie et al., 1977	
		#1578 excl.	Moberg Sköld et al., 2005	
		#1180 excl.	Molina et al., 1989	
		n/a	Moreira et al., 1972	
		n/a	Moreira et al., 1981	
		n/a	Packer et al., 1975	
		n/a	Petersson et al., 1998	
		n/a	Poulsen et al., 1984	
		n/a	Radike et al., 1973	
		n/a	Ringelberg et al., 1979	
		n/a	Ringelberg et al., 1982	
		n/a	Rugg-Gunn et al., 1973	
		n/a	Ruiken et al., 1987	
		n/a	Spets-Happonen et al., 1991	

		n/a	Torell et al., 1965	
		n/a	van Wyk et al., 1986	
#1083	Marinho et al., 2015	n/a	Abadia et al., 1978	
		n/a	Bijella et al., 1981	
		n/a	Bryan et al., 1970	
		n/a	Cobb et al., 1980	
		n/a	Cons et al., 1970	
		#419 excl.	DePaola et al., 1980	
		n/a	Englander et al., 1967	
		n/a	Englander et al., 1971	
		#495 excl.	Englander et al., 1978	
		#608 excl.	Gisselsson et al., 1999	
		n/a	Hagan et al., 1985	
		n/a	Heifetz et al., 1970	
		n/a	Horowitz et al., 1971	
		#755	Horowitz et al., 1969	
		n/a	Horowitz et al., 1974	
		n/a	Ingraham et al., 1970	
		#825	Jiang et al., 2005	
		n/a	Mainwaring et al., 1978	
		n/a	Marthaler et al., 1970	
		n/a	Marthaler et al., 1970a	
		n/a	Mestrinho et al., 1983	
		#1285	Olivier et al., 1992	
		#1415 excl.	Ran et al., 1991	
		n/a	Shern et al., 1976	
		n/a	Szwejda et al., 1972	
		#1721 excl.	Treide et al., 1988	
		n/a	Trubman et al., 1973	
		n/a	Truin et al., 2005	
		#1728 excl.	Truin et al., 2005a	
		#1765 excl.	van Rijkom et al., 2004	
#689	Haugejorden et al., 1981	n/a	Horowitz el al., 1965 (43)	5 studies on school water fluoridation
		n/a	Barron and Lewis, 1968 (7)	~~27, 66, 75~~
		n/a	Horowitz et al., 1968 (46)	
		n/a	Horowitz et al., 1972 (45)	
		#704	Heifetz et al., 1978 (40)	
		n/a	Binder et al., 1978	11 studies on F tablets at school
		n/a	Niedenthal et al., (11)	
		n/a	Wrzodek et al., (11)	11
		n/a	Ziemnowic-Glowaka et al., (11)	51
		n/a	Kamocka et al., (11)	57
		n/a	Schutzmansky et al., (11)	21
		n/a	Berner et al., (11)	24
		n/a	Grissom et al., 1964 (36)	36
		n/a	DePaola and Lax, 1968 (21)	61
		n/a	Marthaler, 1969 (61)	78
		#1631 excl.	Stephen and Campbell, 1978 (78)	Also in Murthy et al., 2020
		n/a	Driscoll et al., 1978 (24)	
		n/a	Marthaler et al., 1978 (63)	f2 studies on salt F (unclear setting)
		n/a	Toth, 1979 (81)	
		n/a	Borrow and Davis, 1976 (15)	1 study on milk/beverage F (unclear setting)
		n/a	Berggren and Welander, 1960 (8)	10 studies on STB at school
		n/a	Berggren and Welander, 1964 (9)	
		n/a	Brochmann, 1965 (16)	
		n/a	Bullen et al., 1966 (17)	
		n/a	Conchie et al., 1969 (19)	
		n/a	Gallagher et al., 1975 (33)	
		n/a	Heifetz et al., 1970 (39)	
		n/a	Horowitz et la., 1974 (47)	

n/a	Hundstadbraten, 1966 (50)	
n/a	Robak, 1964 (74)	
n/a	Ripa and Leske, 1979 (72)	3 studies on supervised rinsing with F sol
n/a	Birkeland and Torell, 1978 (12)	
n/a	Malmberg, 1978 (59)	
n/a	Bagramian et al., 1978 (5)	6 studies on interventions using several F agents
n/a	Heifetz et al., 1979 (38)	58, ~~71, 22, 14~~, 64, 62, 56, 35
n/a	Muhler, 1960 (65)	
n/a	Radike et al., 1973 (70)	
n/a	Horowitz et al., 1979 (48)	
n/a	Englander et al., 1971 (26)	
n/a	Davies, 1974 (20)	Cost-effectiveness
n/a	Forrester and Schultz, 1974 (32)	
n/a	Burt, 1978 (18)	
#759 excl.	Horowitz and Heifetz, 1979 (44)	
n/a	Jonsson, 1980 (51)	
		25

REVIEW		INDIVIDUAL STUDIES		
ID NUMBER	AUTHOR, YEAR	ID NUMBER	AUTHOR, YEAR	NOTES
ECONOMIC OUTCOMES				
#57	Amilani et al., 2020	#1232	Neidell et al., 2016	Also in Murthy et al., 2020 Also in Ladewig et al., 2018
		#146 excl.	Bergström et al., 2019	Also, in Murthy et al., 2020
		n/a	Griffin et al., 2002	
		n/a	Nguyen et al., 2017	
		#723 excl.	Hietasalo et a;., 2009	
		#1496	Sakuma et al., 2010	
		#1085	Marino et al., 2012	Also in Ladewig et al., 2018 Also in Murthy et al., 2020
		n/a	Zabos et al., 2002	Also, in Murthy et al., 2020
		#1045	Louw et al., 1995	
		#616 excl.	Goldman et al., 2017	Also,, in Murthy et al., 2020
		#1088	Mariño et al., 2018	Also,, in Murthy et al., 2020.
		#1189 excl.	Morgan et al., 1998	
		n/a	Huang et al., 2019	Also,, in Murthy et al., 2020
		n/a	Bertrand et al., 2011	
		n/a	Goldman et al., 2011	
#1213	Murthy et al., 2020	n/a	Ast et al., 1970	
		#1631 excl.	Stephen and Campbell, 1978	Also, in Haugejorden et al., 1981
		n/a	Doherty et al., 1984	
		n/a	Klein et al., 1985	Also, in Ladewig et al., 2018?
		n/a	Doherty et al., 1987	
		#1069	Manau et al., 1987	
		#1269	O'Rourke et al., 1988	
		n/a	Garcia, 1989	
		#348 excl.	Crowley et al., ~~1996~~ 2000	
		n/a	Morgan et al., 1997	
		n/a	Alanen et al., 2000	
		n/a	Werner et al., 2000	
		n/a	Holland et al., 2001	
		n/a	Zabos et al., 2002	Also, in Amilani et al., 2020
		n/a	Scherrer et al., 2007	
		#1579	Skold et al., 2008	Also in Ladewig et al., 2018
		n/a	Tuominen, 2008	
		#1496	Sakuma et al., 2010	
		n/a	Bertrand et al., 2011	Also, in Amilani et al., 2020
		#1085	Marino et al., 2012	Also in Amilani et al., 2020 Also in Ladewig et al., 2018
		n/a	Goldman et al., 2014	
		#1232	Neidell et al., 2016	Also in Amilani et al., 2020 and Also in Ladewig et al., 2018
		#146 excl.	Bergström et al., 2019	Also, in Amilani et al., 2020

		#617 excl.	Goldman et al., 2016	
		n/a	Griffin et al., 2016	
		n/a	Johnson et al., 2017	
		n/a	Dudovitz et al., 2017	
		#616 excl.	Goldman et al., 2017	Also, in Amilani et al., 2020
		#883	Kay et al., 2018	
		#1088	Marino et al., 2018	Also, in Amilani et al., 2020
		#146 excl.	Bergström et al., 2019	Also, in Amilani et al., 2020
		n/a	Huang et al., 2019	Also, in Amilani et al., 2020
#954	Ladewig et al., 2018	#1268 excl.	O'Neil et al., (2017)	
		n/a	Griffin et., (2016)	
		#617 excl.	Goldman et al., (2016)	Also,, in Murthy et al., 2020
		#1232	Neidell et al., (2016)	Also in Amilani et al., 2020 and Also in Murthy et al., 2020
		#96 excl.	Atkins et al., (2016)	
		n/a	Fyfe et al., (2015)	
		n/a	Vermaire et al., (2015)	
		n/a	Chi et al., (2014)	
		n/a	Pukallus et al., (2013)	
		#1615 excl	Stearns et al., (2012)	
		#1085	Mariño et al., (2012)	Also in Amilani et al., 2020 and Also in Murthy et al., 2020
		#553 excl.	Frazão (2012)	
		n/a	Beil et al., (2012)	
		n/a	Leskinen et al., (2008)	
		#1579	Skold et al., (2008)	Also in Murthy et al., 2020
		n/a	Bhuridej et al., (2007)	
		#927 excl.	Kowash et al., (2006)	
		n/a	Quiñonez et al., (2005)	
		n/a	Dasanayake et al., (2003)	
		#390 excl.	Davies et al., (2003)	
		#1414 excl.	Ramos-Gomez et al., (1999)	
		n/a	Weintraub et al., (1993)	
		n/a	Donaldson et al., (1986)	
		n/a	Klein et al., (1985)	Also,, in Murthy et al., 2020
		n/a	Tonmukayaku et al., (2016)	
		n/a	Schwendicke et al., (2015)	
		n/a	Schwendicke et al., (2013)	

References

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Table S4: PRISMA checklist

Section and Topic	Item #	Checklist item	Location where item is reported
TITLE			
Title	1	Identify the report as a systematic review.	Page1: lines 2-3
ABSTRACT			
Abstract	2	See the PRISMA 2020 for Abstracts checklist.	Page2--3: lines 29-60
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of existing knowledge.	Page3-4: lines 62-101
Objectives	4	Provide an explicit statement of the objective(s) or question(s) the review addresses.	Page4-5: lines 103-111
METHODS			
Eligibility criteria	5	Specify the inclusion and exclusion criteria for the review and how studies were grouped for the syntheses.	Page5-6: lines 122-134
Information sources	6	Specify all databases, registers, websites, organisations, reference lists and other sources searched or consulted to identify studies. Specify the date when each source was last searched or consulted.	Page5: lines 116-121
Search strategy	7	Present the full search strategies for all databases, registers and websites, including any filters and limits used.	Page5: lines 116-121
Selection process	8	Specify the methods used to decide whether a study met the inclusion criteria of the review, including how many reviewers screened each record and each report retrieved, whether they worked independently, and if applicable, details of automation tools used in the process.	Page6: lines 136-139
Data collection process	9	Specify the methods used to collect data from reports, including how many reviewers collected data from each report, whether they worked independently, any processes for obtaining or confirming data from study investigators, and if applicable, details of automation tools used in the process.	Page6: lines 136-139

Section and Topic	Item #	Checklist item	Location where item is reported
Data items	10a	List and define all outcomes for which data were sought. Specify whether all results that were compatible with each outcome domain in each study were sought (e.g. for all measures, time points, analyses), and if not, the methods used to decide which results to collect.	Page6: lines 136-139
	10b	List and define all other variables for which data were sought (e.g. participant and intervention characteristics, funding sources). Describe any assumptions made about any missing or unclear information.	Page6: lines 136-139
Study risk of bias assessment	11	Specify the methods used to assess risk of bias in the included studies, including details of the tool(s) used, how many reviewers assessed each study and whether they worked independently, and if applicable, details of automation tools used in the process.	Page6: lines 140-142
Effect measures	12	Specify for each outcome the effect measure(s) (e.g. risk ratio, mean difference) used in the synthesis or presentation of results.	Page6: lines 143-145
Synthesis methods	13a	Describe the processes used to decide which studies were eligible for each synthesis (e.g. tabulating the study intervention characteristics and comparing against the planned groups for each synthesis (item #5)).	Page6: lines 146-150
	13b	Describe any methods required to prepare the data for presentation or synthesis, such as handling of missing summary statistics, or data conversions.	Page6: lines 146-150
	13c	Describe any methods used to tabulate or visually display results of individual studies and syntheses.	Page6: lines 146-150
	13d	Describe any methods used to synthesize results and provide a rationale for the choice(s). If meta-analysis was performed, describe the model(s), method(s) to identify the presence and extent of statistical heterogeneity, and software package(s) used.	Page6: lines 146-150
	13e	Describe any methods used to explore possible causes of heterogeneity among study results (e.g. subgroup analysis, meta-regression).	Page6: lines 146-150
	13f	Describe any sensitivity analyses conducted to assess robustness of the synthesized results.	Page6: lines 146-150
Reporting bias assessment	14	Describe any methods used to assess risk of bias due to missing results in a synthesis (arising from reporting biases).	Page6: lines 140-142
Certainty assessment	15	Describe any methods used to assess certainty (or confidence) in the body of evidence for an outcome.	Page6: lines 140-142 and Page6: lines 146-150
RESULTS			
Study selection	16a	Describe the results of the search and selection process, from the number of records identified in the search to the number of studies included in the review, ideally using a flow diagram.	Page8: lines 185-188
	16b	Cite studies that might appear to meet the inclusion criteria, but which were excluded, and explain why they were excluded.	Page8: lines 185-188 and S1 Table
Study characteristics	17	Cite each included study and present its characteristics.	Page 8: lines 189-199 and S2 and S3 Tables
Risk of bias in studies	18	Present assessments of risk of bias for each included study.	Page 8: lines 189-199 and S2 and S3 Tables

Section and Topic	Item #	Checklist item	Location where item is reported
Results of individual studies	19	For all outcomes, present, for each study: (a) summary statistics for each group (where appropriate) and (b) an effect estimate and its precision (e.g. confidence/credible interval), ideally using structured tables or plots.	S2 and S3 Tables
Results of syntheses	20a	For each synthesis, briefly summarise the characteristics and risk of bias among contributing studies.	S2 and S3 Tables
	20b	Present results of all statistical syntheses conducted. If meta-analysis was done, present for each the summary estimate and its precision (e.g. confidence/credible interval) and measures of statistical heterogeneity. If comparing groups, describe the direction of the effect.	Pages 16-17: lines 350-368
	20c	Present results of all investigations of possible causes of heterogeneity among study results.	Pages 16-17: lines 350-368
	20d	Present results of all sensitivity analyses conducted to assess the robustness of the synthesized results.	Pages 16-17: lines 350-368
Reporting biases	21	Present assessments of risk of bias due to missing results (arising from reporting biases) for each synthesis assessed.	Pages 16-17: lines 350-368
Certainty of evidence	22	Present assessments of certainty (or confidence) in the body of evidence for each outcome assessed.	Pages 16-17: lines 350-368
DISCUSSION			
Discussion	23a	Provide a general interpretation of the results in the context of other evidence.	Pages 16-17: lines 350-368
	23b	Discuss any limitations of the evidence included in the review.	Pages 16-17: lines 350-368
	23c	Discuss any limitations of the review processes used.	Pages 16-17: lines 350-368
	23d	Discuss implications of the results for practice, policy, and future research.	Pages 16-17: lines 350-368
OTHER INFORMATION			
Registration and protocol	24a	Provide registration information for the review, including register name and registration number, or state that the review was not registered.	PROSPERO 2021 CRD42021284641 Available from: https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42021284641
	24b	Indicate where the review protocol can be accessed, or state that a protocol was not prepared.	The protocol was assessed
	24c	Describe and explain any amendments to information provided at registration or in the protocol.	Not applicable
Support	25	Describe sources of financial or non-financial support for the review, and the role of the funders or sponsors in the review.	The Borrow Foundation Fund
Competing interests	26	Declare any competing interests of review authors.	There are no conflicts of interest
Availability of data, code and other materials	27	Report which of the following are publicly available and where they can be found: template data collection forms; data extracted from included studies; data used for all analyses; analytic code; any other materials used in the review.	Yes

From: Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ 2021;372:n71. doi: 10.1136/bmj.n71

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