

Appendix 1. Search strategy for MEDLINE via PubMed

#1 DENTAL CARIES [mh]
#2 TOOTH DEMINERALIZATION [mh]
#3 DMF INDEX [mh]
#4 (dmft or dmfs or dft or dfs)
#5 ((tooth or teeth or dent*) and (caries or carious or decay or deminerali* or cavit*))
#6 #1 or #2 or #3 or #4 or #5
#7 FLUORIDES [mh]
#8 FLUORIDES, TOPICAL [mh]
#9 CARIOSTATIC AGENTS [mh]
#10 (fluor* or cario*)
#11 #7 or #8 or #9 or #10
#12 DENTIFRICES [mh]
#13 TOOTHPASTES [mh]
#14 (dentifric* or toothpaste* or tooth paste*)
#15 #12 or #13 or #14
#16 #6 and #11 and #15

Appendix 2. Characteristics of included studies.

Davies et al. [2002]		
Participants	Children born in nine health districts in the north west of England, where the prevalence of caries in 5-year-olds was high. They were 12 months-old at baseline and 5½ years-old at outcome assessment	
Interventions	Test group (2472 children allocated): 440 ppm F toothpaste (Colgate 0-6 Gel) Control group (2488 children allocated): 1450 ppm F toothpaste (Colgate Great Regular Flavour) Another control group not considered Leaflets encouraged parents to use a pea-sized amount of the toothpaste and to brush their child's teeth twice daily	
Outcomes	mean dmft (primary outcome), mean mt and prevalence of caries experience (dmft>0)	
Risk of bias		
Item	Authors' judgement	Description
Adequate sequence generation?	Yes	Quote: "within each of the nine districts children were given an identity number and centrally allocated to either one of the two test groups or a control group using random number tables"
Allocation concealment?	Yes	Quote: "centrally allocated"
Blinding?	Yes	Comment: single-blind Quote: "dental examinations were conducted under blind conditions but as <i>off the shelf</i> toothpaste (without over wrapping or repackaging) was delivered to the participants, subjects and their families were aware of which toothpaste they were using"
Incomplete outcome data addressed?	Yes	Quote: "a further two analyses were performed for the primary outcome dmft to try to estimate the population effect. The first included data from all children who were clinically examined and were originally part of the study population but included those who did not complete the study. The second also included subjects initially randomised but not examined clinically by imputing the means and standard deviations from the control group"
Free of selective reporting?	No	Comment: dmfs not reported
Losses to follow-up less than 20%?	No	Comment: withdrawals in both intervention groups of 32%; children were excluded after randomization. Quote: "children were withdrawn from test and control groups if toothpaste or questionnaires were returned by the post office as undeliverable"; "reply paid cards were returned by the parents of 641 test children, indicating that they did not wish their children to participate and during the five years of the study 1,432 children moved away from the area. Five children withdrew from the 1450 ppm F toothpaste group, one because the dentist advised this, three because of concerns about fluorosis and one because of an allergy to the toothpaste"
Diagnosis reliability?	Unclear	Comment: the study does not mention the number of examiners or the intra and inter-examiner reliability

		Quote: “in each district the clinical examinations were undertaken by trained, standardized and calibrated examiners according to the standards set by BASCD”
Baseline characteristics balanced?	Unclear	Comment: the study does not provide information about baseline socio-demographic characteristics. Also, children were not examined at baseline; it was assumed that all children were caries-free at the beginning of the trial
Free of contamination?	Unclear	Comment: no strategies to avoid contamination between groups were reported; it is not possible to rule out contamination at home or school as the randomization was performed within each district

Gerdin [1974]		
Participants	Children aged 3.25-3.74 years old at the beginning of the trial, who were participants in a dental care program for preschool children in Gothenburg, Sweden, and lived in the same part of the city	
Interventions	Test group (115 children allocated): 250ppm toothpaste, non-abrasive polymethyl metacrylate, potassium fluoride and manganese, pH 5.5 Control group (115 children allocated): 1000ppm toothpaste, non-abrasive polymethyl metacrylate, sodium fluoride, pH 6.5 Toothbrushing at home, supervised and aided by parents, twice daily, vertical technique and rubbing with small movements, pea size amount of toothpaste, no rinsing with water after toothbrushing	
Outcomes	caries increment: dft and dfs	
Risk of bias		
Item	Authors' judgement	Description
Adequate sequence generation?	No	Comment: non-random allocation Quote: “the groups were randomized according to the children's birth-month so that the children born in even months formed one group, and children born in odd months formed the other group”
Allocation concealment?	No	Comment: non-random allocation prevents allocation concealment
Blinding?	Yes	Comment: double-blind Quote: “the toothpastes were coded by means of symbols. Toothpaste (1) was labeled with blue flowers, and toothpaste (2) was labeled with red butterflies. Adhesive labels with the same symbols were handed out for use on the children's special recording cards, on their visiting cards, on their toothbrushes etc. so each should know if he or she was a <i>flower</i> or a <i>butterfly</i> ”; “the recorders were the same during the whole trial, and they had no knowledge of the contents of the trial toothpastes”
Incomplete outcome data addressed?	No	Comment: the study does not provide information about incomplete outcome data
Free of selective reporting?	No	Comment: proportion of children developing caries not reported
Losses to follow-up less than 20%?	Yes	Comment: 6% test group and 9% control group Quote: “each group comprised 115 children at the beginning of the

		trial”; “in the groups remained at the recordings after two years, 105 (boys 54, girls 51) and 108 (boys 56, girls 52) respectively”; “the non-responses from the groups were small and were only caused by the moving of a child from the city”
Diagnosis reliability?	Unclear	Comment: the study does not mention the inter and intra-examiner reliability Quote: “the caries recordings were performed in independent examinations by two dentists”; “the recorders were calibrated with respect to both their clinical and their roentgenological recordings at the beginning of the trial and after two years”
Baseline characteristics balanced?	Unclear	Comment: although it is mentioned that the groups were similar regarding socio-economic status, consumption habits, oral hygiene, individual fluoride prophylaxis etc., only data about caries baseline levels and sex distribution are provided
Free of contamination?	Unclear	Comment: no strategies to avoid contamination between groups were reported; it is not possible to rule out contamination at home or school as children were allocated to the groups according to their birth-month

Sonju-Clasen et al. [1995]		
Participants	Children aged 5-6 years old at final examination, from 10 (out of a total of 30) Salzgitter (Germany) kindergartens	
Interventions	Test group (5 kindergartens and 155 children allocated): 250 ppm F, xanthan, carbopol 956, sorbitol, silica as abrasive, sodium fluoride as the active substance, cocamidopropyl-betain-1,5 as detergent, pH 6,5 Control group (5 kindergartens and 164 children allocated): 1450 ppm F, xanthan, carbopol 956, sorbitol, silica as abrasive, sodium fluoride as the active substance, sodium laurylsulphate as detergent, pH 6,8 Daily toothbrushing in the kindergartens with a pea-sized amount of the toothpaste (supervised by the kindergarten staff). All children used a 250 ppm F toothpaste at home	
Outcomes	dmfs, dmft, proportion of caries-free children	
Risk of bias		
Item	Authors' judgement	Description
Adequate sequence generation?	Unclear	Comment: the method of randomization was not mentioned Quote: "to assure an even distribution of kindergartens from different areas and social groups in each study group, Salzgitter was divided into five geographical areas from which two kindergartens were randomly assigned to one of the two study groups"
Allocation concealment?	Unclear	Comment: as it is not possible to know which method of randomization was used, allocation concealment cannot be assessed
Blinding?	Yes	Comment: double-blind Quote: "at the time of the examinations the examiner was not aware if the child belonged to a study group or not"; "neither the kindergarten children nor the kindergarten staff were aware of the purpose of the study, nor were they told that a toothpaste containing a different amount of fluoride was given to other kindergartens"

Incomplete outcome data addressed?	No	Comment: the study does not provide information about incomplete outcome data
Free of selective reporting?	Yes	Comment: dmft, dmfs and proportion of children developing caries reported
Losses to follow-up less than 20%?	No	Quote: “of the 319 children examined at baseline, 172 were available for examination after 22 months (83 in the low-fluoride group and 89 in the high-fluoride group), giving a drop-out rate of 46% (46,5% in the low-fluoride group and 45, 7% in the high-fluoride group)”; “the majority of the subjects who failed to complete the study either went to new kindergartens in the area or, to a lesser extent, changed residence”
Diagnosis reliability?	Yes	Comment: one examiner Quote: “the intra-examiner reliability, calculated as Scott's <i>pi</i> (for dmfs), was 0.89; this reflects very good intra-examiner reliability”
Baseline characteristics balanced?	Unclear	Comment: although it is mentioned that the groups were similar regarding age, sex and baseline caries levels, the number of boys was greater in the control group. It is assumed that there was an even distribution according to socioeconomic status, although the method of randomization is not clearly stated Quote: “the groups were not significantly different with respect to sex, age or proportion of caries-free children”; “to assure an even distribution of kindergartens from different areas and social groups in each study group, Salzgitter was divided into five geographical areas from which two kindergartens were randomly assigned to one of the two study groups”
Free of contamination?	Yes	Comment: contamination avoided at kindergartens due to the allocation scheme; contamination at home not probable Quote: “the children's toothbrushing routines at home were not interfered with: they all used a 250 ppm fluoride toothpaste at home”

Vilhena et al. [2010]		
Participants	4-year-old children that attended all primary schools of São José dos Campos, São Paulo, Brazil (0.6-0.8 ppm F in the drinking water)	
Interventions	Test group (59 classrooms and 354 children allocated): liquid toothpaste, 550 ppm F, NaF, pH 4.5 Control group (56 classrooms and 360 children allocated): 1100 ppm F toothpaste, NaF, pH 7.0 (Sorriso Fresh, Colgate Palmolive, São Paulo, Brazil) Two more test groups not considered Supervised toothbrushing performed on school days, for one minute Parents were asked to brush their children’s teeth for 1 min at least twice a day. The liquid toothpastes were applied to the toothbrushes using the ‘drop’ technique	
Outcomes	dmfs	
Risk of bias		
Item	Authors’ judgement	Description
Adequate sequence	Yes	Quote: “for the random allocation to the groups, the classrooms were considered as units of draw, in order that only 1 type of

generation?		toothpaste was distributed in each classroom”; “assignment of the included children to the study groups was done by 1 of the researchers..., using a previously established algorithm.... the software... generated random numbers ranging from 0 to 1”
Allocation concealment?	No	Quote: “open random allocation schedule”
Blinding?	Yes	Comment: single-blind Quote: “the study was blinded only for the examiner, since the commercial toothpaste was maintained in its original package”
Incomplete outcome data addressed?	Yes	Comment: missing data not associated to the outcome
Free of selective reporting?	No	Comment: only dmfs reported
Losses to follow-up less than 20%?	No	Comment: withdrawals of 29% (test group) and 25% (control group) Quote: “the drop-out rate was around 25% which is a little bit higher than expected”
Diagnosis reliability?	Yes	Comment: two examiners; intra-examiner reliability examiner 1 (k= 0.91) and examiner 2 (k= 0.95); inter-examiner reliability first examination (k= 0.85) and second examination (k= 0.87)
Baseline characteristics balanced?	Unclear	Comment: the study shows that the groups were similar regarding baseline dmfs, age and sex. Individual information about socioeconomic status was not assessed, so it is not possible to know whether the method used to balance the groups according to this variable was successful
Free of contamination?	Yes	Quote: “only 1 type of toothpaste was distributed in each classroom”; “family kits containing 5 toothbrushes, 6 toothpaste tubes (120 g each) and 1 leaflet about oral hygiene care and compliance need were distributed for all participants every 4 months. The kits were supplied to be used by the whole family in order to guarantee the use of the respective toothpaste by the children, thus facilitating compliance with the study protocol”

Winter et al. [1989]		
Participants	Preschool children with a starting age of 2 years resident in the Norwich Health District, England	
Interventions	Test group: 550 ppm toothpaste containing a mixture of 0.209 % sodium monofluorophosphate and 0.060% sodium fluoride, calcium glycerophosphate as abrasive Control group: 1055ppm toothpaste containing 0.80% sodium monofluorophosphate, calcium glycerophosphate as abrasive There is no information regarding the number of children allocated to each group Parents were instructed to clean the child’s teeth at least twice a day and to use a pea size amount of toothpaste	
Outcomes	dmft, dmfs, ms, fs, proportion of caries-free children	
Risk of bias		

Item	Authors' judgement	Description
Adequate sequence generation?	Unclear	Comment: the method of randomization is not mentioned Quote: "children included in the study were randomly allocated into test (J) and control (R) groups. However, twins were allocated as pairs"
Allocation concealment?	Unclear	Comment: as it is not possible to know which method of randomization was used, allocation concealment cannot be assessed
Blinding?	Yes	Comment: double-blind Quote: "double-blind clinical trial"; "toothpaste was supplied in 50g tubes bearing the name of the Eastman Dental Hospital, the date of manufacture and the group code"
Incomplete outcome data addressed?	No	Comment: the study does provide mention information about incomplete outcome data
Free of selective reporting?	Yes	Comment: dmft, dmfs and proportion of children developing caries reported
Losses to follow-up less than 20%?	No	Comment: the study does not provide the drop-rates separately Quote: "at the end of the trial, 2177 (72%) children were examined clinically"
Diagnosis reliability?	No	Comment: clinical diagnosis (three examiners): kappa inter 0.65-0.71 and kappa intra 0.90-0.97; radiographic diagnosis (one examiner): kappa intra 0.92
Baseline characteristics balanced?	Unclear	Comment: the groups were similar regarding sex and social class; children were not examined at the baseline; it was assumed most children were caries-free Quote: "group J was made up of 550 boys and 554 girls and group R of 554 boys and 519 girls, the compositions of which were not significantly different; "the social class distributions of children in groups J and R were little different"; "the reason for conducting a trial at its inception on 2-year-old-children was based on the expectation that most would be free from caries"
Free of contamination?	Yes	Quote: "sufficient toothpaste was provided for the whole family in 50g tubes bearing the name of the Eastman Dental Hospital, the date of manufacture and the group code"; "collection of used and partially used tubes was made at each of the monthly visits, ensuring that fresh paste was employed throughout the trial and gauging indirectly its utilization"